As filed with the Securities and Exchange Commission on November 27, 2017.

Registration No. 333-221522

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

AMENDMENT NO. 1
TO
FORM S-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

DENALI THERAPEUTICS INC.
(Exact name of Registrant as specified in its charter)

Delaware	2836	46-3872213
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification Number)

151 Oyster Point Blvd., 2nd Floor
South San Francisco, California 94080
(650) 866-8548
(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

Ryan J. Watts, Ph.D.
President and Chief Executive Officer
Denali Therapeutics Inc.
151 Oyster Point Blvd., 2nd Floor
South San Francisco, California 94080
(650) 866-8548
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Tony Jeffries Jennifer Knapp Wilson Sonsini Goodrich & Rosati, P.C. 650 Page Mill Road Palo Alto, California 94304 (650) 493-9300	Steve E. Krognes Chief Financial Officer and Treasurer Denali Therapeutics Inc. 151 Oyster Point Blvd., 2nd Floor South San Francisco, California 94080 (650) 866-8548	Alan F. Denenberg Stephen Salmon Davis Polk & Wardwell LLP 1600 El Camino Real Menlo Park, California 94025 (650) 752-2000

Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this registration statement.

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. ☐

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒ (Do not check if a smaller reporting company)	Smaller reporting company	☐
		Emerging growth company	☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act. ☒

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered (1)	Proposed Maximum Offering Price Per Share (2)	Proposed Maximum Aggregate Offering Price (1)(2)	Amount of Registration Fee (3)
Common stock, $0.01 par value per share	9,583,333	$19.00	$182,083,327	$22,670

(1) Includes the additional shares that the underwriters have the right to purchase from the Registrant.
(2) Estimated solely for the purpose of computing the amount of the registration fee pursuant to Rule 457(a) under the Securities Act of 1933, as amended.
(3) The Registrant previously paid $12,450 in connection with the initial filing of the Registration Statement.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

The information in this preliminary prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell nor does it seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION. DATED NOVEMBER 27, 2017

8,333,333 Shares

Common Stock

This is an initial public offering of shares of common stock by Denali Therapeutics Inc.

Prior to this offering, there has been no public market for our common stock. It is currently estimated that the initial public offering price will be between $17.00 and $19.00 per share.

We have applied to list our common stock on the NASDAQ Global Select Market under the symbol “DNLI.”

We are an “emerging growth company” as defined under the federal securities laws and, as such, have elected to comply with certain reduced reporting requirements for this prospectus and may elect to do so in future filings.

Investing in our common stock involves risks. See the section titled “Risk Factors” beginning on page 13 to read about factors you should consider before buying shares of our common stock.

Neither the Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities, or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

	Per Share	Total
Initial public offering price	$	$
Underwriting discounts(1)	$	$
Proceeds, before expenses, to us	$	$

(1) See the section titled “Underwriting” for additional information regarding compensation payable to the underwriters.

Certain of our existing stockholders, including one that beneficially owns more than 5% of our outstanding common stock, have indicated an interest in purchasing an aggregate of $50.0 million or more in shares of our common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no shares in this offering to any of these stockholders, or any of these stockholders may determine to purchase more, less or no shares in this offering. The underwriters will receive the same underwriting discounts and commissions on any shares purchased by these stockholders as they will on any other shares sold to the public in this offering.

To the extent that the underwriters sell more than 8,333,333 shares of common stock, the underwriters have the option to purchase up to an additional 1,250,000 shares from us at the initial public offering price less the underwriting discount.

The underwriters expect to deliver the shares against payment in New York, New York on , 2017.

Goldman Sachs & Co. LLC **Morgan Stanley** **J.P. Morgan**

Evercore ISI

Prospectus dated , 2017.

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Prospectus

Through and including , 2018 (the 25th day after the date of this prospectus), all dealers effecting transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to a dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to an unsold allotment or subscription.

We and the underwriters have not authorized anyone to provide you any information other than that contained in this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We and the underwriters are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus is accurate only as of the date on the front cover of this prospectus. Our business, financial condition, results of operations and prospects may have changed since that date.

For investors outside of the United States: we have not and the underwriters have not done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than the United States. Persons outside of the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside of the United States.

PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in this prospectus and is qualified in its entirety by the more detailed information and financial statements included elsewhere in this prospectus. It does not contain all of the information that may be important to you and your investment decision. You should carefully read this entire prospectus, including the matters set forth under the sections titled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and related notes. In this prospectus, unless context requires otherwise, references to "we," "us," "our," "Denali," or "the company" refer to Denali Therapeutics Inc. See the section titled "Glossary" for definitions of key scientific and technical terms used in this prospectus.

Overview

Our goal is to discover and develop therapeutics to defeat degeneration.

Neurodegeneration represents one of the most significant unmet medical needs of our time, with few effective therapeutic options available for patients with Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, or ALS, and other neurodegenerative diseases. We believe the time is right to make a strong and ambitious effort to defeat neurodegeneration. Recent genetic insights are revealing the underlying biology of neurodegeneration and potential drug targets while enabling better patient selection, similar to how genetic insights have transformed the field of oncology. Identifying and selecting targets based on validated genetic drivers of neurodegeneration is a core principle of our strategy. The second core principle of our strategy is to develop medicines that effectively cross the blood-brain barrier, or BBB, and target the brain. We have engineered a proprietary BBB platform technology that we believe will enable therapeutically relevant concentrations of our product candidates in the brain. The third core principle of our strategy is to develop and use biomarkers for better patient selection and demonstration of target and pathway engagement of our product candidates. By executing this strategy with a team of experienced and passionately dedicated scientists and drug developers, we believe we can succeed in a field that has seen limited progress over the past several decades. We commenced operations in May 2015 and recently began our first clinical trials.

Our Team

We have assembled a team with deep scientific, clinical, business and leadership experience and expertise in biotechnology, and specifically in neurodegenerative diseases, who worked together at Genentech for many years prior to the founding of Denali. Our Co-Founder and Chief Executive Officer, Ryan J. Watts, Ph.D., is a world-leading drug developer and neuroscientist, with particular expertise in BBB therapeutic delivery. Dr. Watts most recently led the neuroscience research team at Genentech and has led multiple discovery teams, including programs in Alzheimer's disease, Parkinson's disease and ALS. Our Co-Founder and Chief Operating Officer, Alexander O. Schuth, M.D., held various operational and leadership roles at Genentech for nearly ten years, including leading the partnering groups for neuroscience as well as technology innovation and diagnostics. Dr. Schuth has led more than 35 partnering transactions and a clinical stage development program. Our Co-Founder and director, Marc Tessier-Lavigne, Ph.D., is a world-leading neuroscientist, was formerly Chief Scientific Officer at Genentech and serves as President of Stanford University. Carole Ho, M.D., our Chief Medical Officer, brings over a decade of clinical development experience, most recently as Vice President, Non-Oncology Early Clinical Development at Genentech. Dr. Ho has overseen or contributed to more than ten IND filings and three drug approvals. Our Chief Financial

Officer, Steve E. Krognes, brings over two decades of operational and corporate finance experience, most recently serving six years as Chief Financial Officer and member of the Executive Committee at Genentech. Mr. Krognes has led more than 40 strategic deals and led or contributed to several capital raising transactions.

Our leadership team is joined by approximately 125 employees, approximately two-thirds of whom hold Ph.D. or M.D. degrees. Together, they bring expertise across relevant disciplines, including neuroscience, BBB biology, genetics, oncology, immunology, translational science, antibody engineering, chemistry and biomarker development.

To complement our internal capabilities, we have entered into arrangements with biopharmaceutical companies such as Genentech and F-star, numerous leading academic institutions such as Harvard University, Massachusetts General Hospital, Washington University in St. Louis, the University of California, San Diego and Vlaams Instituut voor Biotechnologie, foundations such as the Michael J. Fox Foundation and patient-focused data companies such as 23andMe and Patients Like Me to gain access to new product candidates, deepen our scientific understanding of certain areas of biology and enable and accelerate the development of our programs. We believe that accessing external innovation is important to our success, and we plan to remain active in accessing external innovation through business development activities.

Our Strategy

Our strategy is guided by three overarching principles:

- **Genetic Pathway Potential**: We select our therapeutic targets and disease pathways based on genes that, when mutated, cause, or are major risk factors for, neurodegenerative diseases, which we refer to as degenogenes.
- **Engineering Brain Delivery**: We engineer our product candidates to cross the blood-brain barrier and act directly in the brain.
- **Biomarker-Driven Development**: We discover, develop and utilize biomarkers to select the right patient population and demonstrate target engagement, pathway engagement and impact on disease progression of our product candidates.

We believe that the application of these principles will significantly increase the probability of success and will accelerate the timing to bring effective therapeutics to patients with neurodegenerative diseases.

Degenogenes

Since 2007, the number of genetic associations discovered in neurodegenerative diseases has grown rapidly, with more than 100 genes associated with Alzheimer's disease, Parkinson's disease and ALS collectively. As the cost of genome sequencing has decreased, there has been an increase in the discovery of genetic mutations that have been linked to neurodegeneration (Figure A).

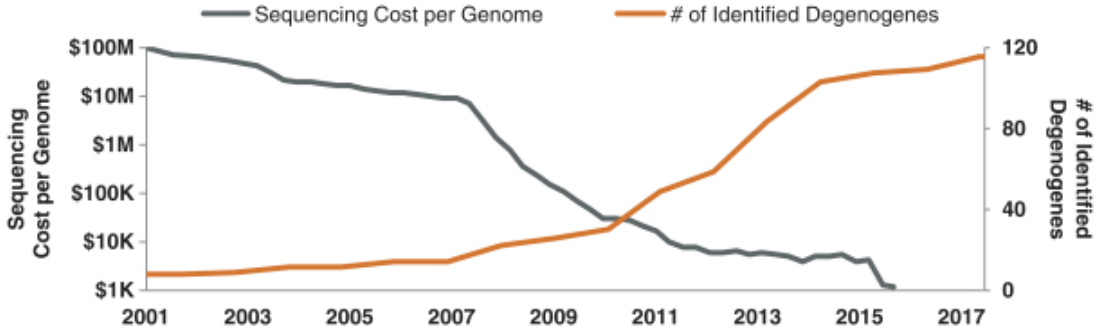


Figure A: This figure shows the increasing number of identified degenogenes linked to Alzheimer's disease, Parkinson's disease and ALS from 2001 to 2017 and the declining cost of genome sequencing from 2001 to October 2015 (the latest date for which we have data). There has been a dramatic reduction in the cost of DNA sequencing which has recently contributed to the discovery of numerous genetic mutations that have been linked to Alzheimer's disease, Parkinson's disease and ALS.

The degenogenes directly point to important disease pathways that are disrupted in neurodegeneration and are our scientific foundation for identifying and pursuing promising targets for drug development. We have chosen to initially focus on three such pathways:

- **Lysosomal Function**: Dysfunction of the lysosomal system is associated with several neurodegenerative diseases, including Parkinson's disease and neurodegeneration in the context of lysosomal storage diseases, or LSDs. Degenogenes linked to lysosomal function include LRRK2, aSyn and lysosomal enzymes, including IDS and GBA.
- **Glial Biology**: Degenogenes implicate immune dysfunction in the brains of patients with Alzheimer's disease and other neurodegenerative diseases. These genes include TREM2 and numerous other genes that are highly expressed in inflamed microglia, the resident immune cells of the brain. We believe the impact of immune modulation in neurodegeneration is a promising approach to treating disease. Specifically, RIPK1, a kinase downstream of the TNF receptor pathway, is overactive in inflamed microglia and several other cells in the brain.
- **Cellular Homeostasis**: Defects in protein or RNA homeostasis lead to the death of neurons and dysfunction of the nervous system. This includes spreading of protein aggregates resulting in proteinopathy in Alzheimer's and Parkinson's diseases. The clearance of macromolecules in the brain is particularly susceptible to imbalances that result in aggregation and degeneration in nerve cells. Degenogenes linked to cellular homeostasis include APP, Tau and APOE.

BBB Platform Technology

Our proprietary BBB platform technology is designed to effectively transport antibodies (antibody transport vehicle, or ATV) and enzymes (enzyme transport vehicle, or ETV) across the BBB. This technology is designed to engage specific BBB transport receptors, which are ubiquitously expressed

in brain capillaries and facilitate transport of proteins into the brain (Figure B). In a mouse model across three studies designed to show proof of concept for the ATV platform, an antibody engineered with our ATV technology has demonstrated an average 20-fold greater brain penetration than a control antibody not enabled by this technology. In addition, initial data from an ongoing study in nonhuman primates designed to show proof of concept for the ATV platform demonstrates a robust and sustained pharmacodynamic effect in the brain after intravenous dosing of an ATV-enabled antibody, while a standard antibody had minimal pharmacodynamic effect. The improvement in brain exposure may enable therapeutically relevant concentrations of our ATV antibody product candidates in the brain, making them potentially superior to traditional monoclonal antibody therapeutics.

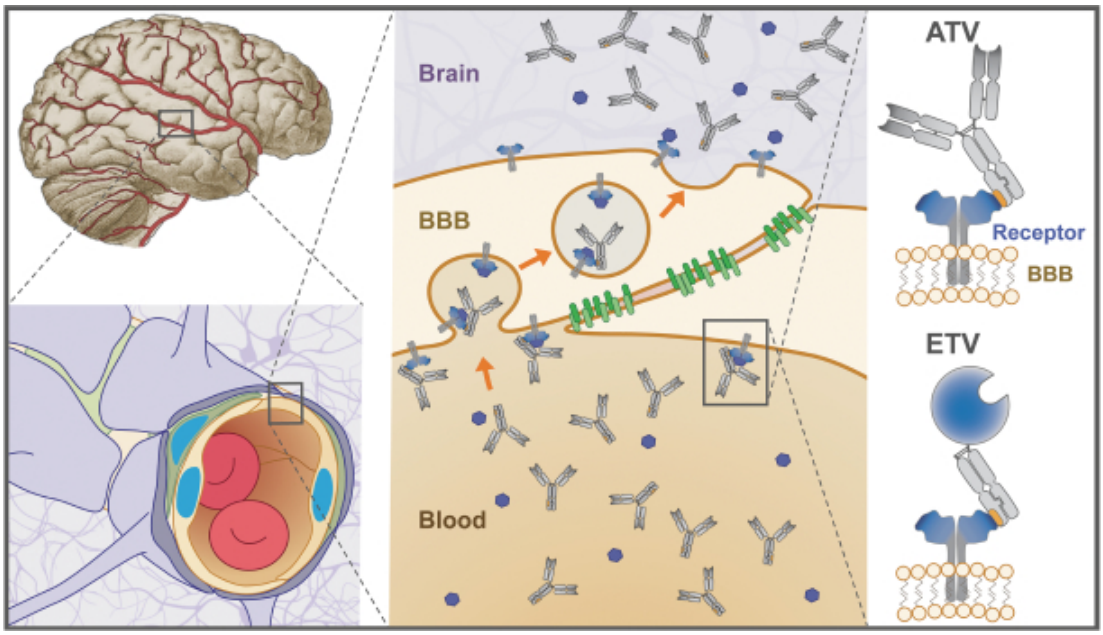


Figure B: Engineering brain delivery. Schematic of the ATV and ETV technologies, designed to cross the BBB through receptor-mediated transcytosis, leveraging endogenous receptors expressed on endothelial cells in the vasculature of the brain.

Biomarkers

As part of our strategy, we are developing proprietary reagents and assays to enable biomarkers for each of our core programs. These biomarkers, which are relevant for both animal models and human trials, are critical for patient selection, predicting and measuring target engagement, supporting dose selection and enabling decisions on progression of product candidates to the next phase of development. We have identified target engagement biomarkers for all six of our core programs. When practicable, we are developing patient selection biomarkers for our programs to enable identification of patients with the relevant disease biology and stage of disease likely to benefit from targeted therapy in order to increase the likelihood of success of clinical trials. Ultimately, by reducing the number of patients that are likely to experience a low treatment response, we expect to positively impact market acceptance of these targeted therapies driven by high and meaningful response rates within the targeted population as defined by the patient selection biomarkers. In certain indications, regulatory approval may limit the market of a product candidate to target patient populations when patient selection biomarkers are used.

In these indications, regulatory authorities may require us to run additional clinical trials prior to expanding the label for approval that includes a broader patient population.

Our Programs

We have a focused yet diversified portfolio that currently consists of six core and five seed programs. Our most advanced program targets LRRK2 for the treatment of Parkinson's disease and has a product candidate currently in Phase 1 development. Our next most advanced program targets RIPK1 for the treatment of Alzheimer's disease and ALS and currently has a product candidate in IND-enabling studies with a CTA filing planned for early 2018. In addition, we have four core programs in preclinical development that use our proprietary BBB platform technology.

Program Target	Drug Candidate	Therapeutic Modality	Disease Indication	Preclinical Development	Clinical Development			Biomarker		
					Phase I	Phase II	Phase III	Preclinical Target Engagement	Clinical Target Engagement	Patient Selection
Lysosomal Function Pathway										
LRRK2	DNL201	Small Molecule	Parkinson's disease	Phase 1				✓	✓	✓
	DNL151	Small Molecule	Parkinson's disease	IND-Enabling						
Alpha-Synuclein	ATV:aSyn	Antibody	Parkinson's disease, DLB, MSA	Preclinical				✓	●	●
Iduronate 2-sulfatase	ETV:IDS	Enzyme	MPS II (Hunter Syndrome)	Preclinical				✓	✓	✓
Glial Biology Pathway										
RIPK1	DNL747	Small Molecule	Alzheimer's disease, ALS	IND-Enabling				✓	✓	●
TREM2	ATV:TREM2	Antibody	Alzheimer's disease	Preclinical				✓	●	●
Cellular Homeostasis Pathway										
BACE1/TAU	ATV:BACE1/Tau	Antibody	Alzheimer's disease	Preclinical				✓	✓	✓

ATV : Antibody Transport Vehicle
ETV : Enzyme Transport Vehicle
ALS: Amyotrophic Lateral Sclerosis
DLB : Dementia with Lewy Bodies
MPS II: Mucopolysaccharidosis type II
MSA: Multiple System Atrophy

✓ Validated Biomarker
● Biomarker in Development

Our lead LRRK2 product candidates, DNL201 and DNL151, are potent, selective and brain penetrant small molecule inhibitors of LRRK2. LRRK2 regulates lysosomal genesis and function, which is impaired in Parkinson's disease and may be restored by LRRK2 inhibition. Mutations in the LRRK2 gene are the most frequent genetic cause of Parkinson's disease and a major driver of lysosomal dysfunction, which contributes to the formation of Lewy body protein aggregates and neurodegeneration. DNL201 is currently in a single and multiple ascending dose study in healthy volunteers. The FDA placed DNL201 on a partial clinical hold in order to impose an exposure cap on our Phase 1 study based on preclinical toxicity study findings. With the current exposure cap, we are able to dose to an exposure that we believe will be sufficient to inhibit LRRK2 50% on average over the dosing period and should effectively normalize LRRK2 kinase activity. If the exposure cap is not lifted in our Phase 1 clinical trial, we will not be able to evaluate doses and exposures that would potentially achieve higher degrees of LRRK2 kinase inhibition, which may negatively impact the development of DNL201. We expect data from this study in the first half of 2018. We submitted a CTA for DNL151 to the Netherlands Health Authority in October 2017 and it was accepted in November 2017. After completion of the Phase 1 clinical trials for DNL201 and DNL151, we plan to progress one of DNL201 or DNL151 into a Phase 1b study in LRRK2 mutation-carrying Parkinson's disease patients.

Our lead RIPK1 product candidate, DNL747, is a potent, selective and brain penetrant small molecule inhibitor of RIPK1 for Alzheimer's disease and ALS. Microglia are the resident immune cells of the brain and play a significant role in neurodegeneration. RIPK1 activation in microglia results in production of a number of pro-inflammatory cytokines that can cause tissue damage. Preliminary data from our GLP toxicity studies, including our 28-day GLP safety studies in cynomolgus monkeys and

rats, support advancing DNL747 to clinical testing. Immune-mediated histopathology findings were observed in our 28-day GLP study in cynomolgus monkeys, but we believe the projected safety margins will allow us to achieve DNL747 exposures that allow us to explore a robust pharmacodynamic range in humans. We plan to submit a CTA for DNL747 in early 2018 and initiate a Phase 1 clinical trial in healthy volunteers in the first half of 2018.

Our four other core programs all leverage our proprietary BBB platform technology to deliver antibody-based or enzyme-based therapies to the brain. Our three antibody programs are against known targets including aSyn, TREM2 and a bispecific therapeutic agent against both BACE1 and Tau. Our BACE1 and Tau program is an example of combination therapy, which we believe holds significant promise in developing effective therapies in neurodegenerative diseases. We believe each of these programs has characteristics that may allow for them to be best in class. Our fourth program is an enzyme replacement therapy for MPS II patients in which we deliver IDS to the brain. Neurodegeneration is a hallmark of MPS II patients that is not addressed by current enzyme replacement therapies, which fail to reach the brain.

We have development and commercialization rights to all of our core programs.

Risks Associated with Our Business

Our business is subject to numerous risks and uncertainties that you should consider before investing in our company. These risks are described more fully in the section titled “Risk Factors” in this prospectus. These risks include, but are not limited to, the following:

- We are in the early stages of clinical drug development and have a very limited operating history and no products approved for commercial sale.
- We have incurred significant net losses in each period since our inception and anticipate that we will continue to incur net losses for the foreseeable future.
- Drug development is a highly uncertain undertaking and involves a substantial degree of risk. We have never generated any revenue from product sales, and we may never generate revenue or be profitable.
- If we fail to obtain additional financing, we may be unable to complete the development and, if approved, commercialization of our product candidates.
- We are heavily dependent on the successful development of our BBB platform technology and the product candidates currently in our core programs, which are in the early stages of preclinical and clinical development.
- We may not be successful in our efforts to continue to create a pipeline of product candidates or to develop commercially successful products.
- We have concentrated our research and development efforts on the treatment of neurodegenerative diseases, a field that has seen limited success in drug development.
- We may encounter substantial delays in our clinical trials, or may not be able to conduct or complete our clinical trials on the timelines we expect, if at all.
- We face significant competition in an environment of rapid technological and scientific change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer, more advanced or more effective than ours.
- The regulatory approval processes of the FDA, EMA and comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable.

- We expect to depend on collaborations with third parties for the research, development and commercialization of certain of the product candidates we may develop.
- If we are unable to obtain and maintain patent protection for any product candidates we develop or for our BBB platform technology, our competitors could develop and commercialize products or technology similar or identical to ours.
- Our rights to develop and commercialize our BBB platform technology and product candidates are subject, in part, to the terms and conditions of licenses granted to us by others.

Corporate Information

We were incorporated in Delaware in 2013. Our principal executive offices are located at 151 Oyster Point Blvd., 2nd Floor, South San Francisco, California 94080. Our telephone number is (650) 866-8548. Our website address is www.denalitherapeutics.com. Information contained on our website is not incorporated by reference into this prospectus, and it should not be considered to be part of this prospectus.

We use Denali Therapeutics®, the Denali Therapeutics logo, and other marks as trademarks in the United States and other countries. This prospectus contains references to our trademarks and service marks and to those belonging to other entities. Solely for convenience, trademarks and trade names referred to in this prospectus, including logos, artwork and other visual displays, may appear without the ® or ™ symbols, but such references are not intended to indicate in any way that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other entities' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, any other entity.

Implications of Being an Emerging Growth Company

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, as amended, or JOBS Act. We will remain an emerging growth company until the earliest to occur of: the last day of the fiscal year in which we have more than $1.07 billion in annual revenue; the date we qualify as a "large accelerated filer," with at least $700 million of equity securities held by non-affiliates; the issuance, in any three-year period, by us of more than $1.0 billion in non-convertible debt securities; and the last day of the fiscal year ending after the fifth anniversary of our initial public offering. As a result of this status, we have taken advantage of reduced reporting requirements in this prospectus and may elect to take advantage of other reduced reporting requirements in our future filings with the SEC. In particular, in this prospectus, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. In addition, the JOBS Act provides that an emerging growth company may take advantage of an extended transition period for complying with new or revised accounting standards, delaying the adoption of these accounting standards until they would apply to private companies. We have irrevocably elected not to avail ourselves of this exemption and, as a result, upon completion of this offering we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies that are not emerging growth companies.

THE OFFERING

Common stock offered by us	8,333,333 shares
Common stock to be outstanding after this offering	82,423,920 shares (or 83,673,920 shares if the underwriters exercise their option to purchase additional shares in full)
Underwriters' option to purchase additional shares of common stock from us	1,250,000 shares
Use of proceeds	We estimate that the net proceeds from our issuance and sale of 8,333,333 shares of our common stock in this offering will be approximately $136.0 million, assuming an initial public offering price of $18.00 per share, which is the midpoint of the estimated initial public offering price range set forth on the cover page of this prospectus, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional shares in full, we estimate that our net proceeds will be approximately $156.9 million. We currently anticipate that we will use the net proceeds from this offering, together with our existing resources, through 2019 as follows: (1) to fund the costs of Phase 1 trials in healthy volunteers for each of DNL201 and DNL151 and a Phase 1b study in LRRK2 mutation-carrying Parkinson's disease patients, as well as preparation for a potential future Phase 2 clinical trial; (2) to fund the costs to advance our RIPK1 program through Phase 1 and early Phase 2 clinical development, substantially represented by the planned Phase 1 clinical trial in healthy volunteers, including a cohort in Alzheimer's disease patients, for DNL747, a Phase 2a clinical trial in ALS patients and a Phase 2a clinical trial in Alzheimer's disease patients; (3) to optimize and broaden our ATV and ETV platform technologies and to advance our four core antibody and enzyme replacement programs through preclinical development and IND-enabling activities; (4) if we exercise our option to acquire all outstanding shares of F-star Gamma, to fund the initial exercise payments; and (5) the remainder to fund seed programs, general research and development activities, working capital and other general corporate activities. See the section titled "Use of Proceeds" for additional information.
Proposed NASDAQ Global Select Market trading symbol	"DNLI"

The number of shares of our common stock to be outstanding after this offering is based on the 74,090,587 shares of our common stock outstanding as of September 30, 2017 (including convertible preferred stock on an as-converted basis, as well as 1,764,705 shares of our Series B-2 convertible preferred stock issued after September 30, 2017), and excludes the following:

- 6,179,687 shares of common stock issuable upon exercise of options to purchase shares of our common stock outstanding as of September 30, 2017, at a weighted-average exercise price of $3.06 per share;
- 194,000 shares of common stock issuable upon exercise of options to purchase shares of our common stock that were granted after September 30, 2017, at a weighted-average exercise price of $11.64 per share;
- 81,164 shares of common stock to be issued in connection with our acquisition of Incro Pharmaceuticals;
- 7,328,456 shares of common stock reserved for future issuance under our stock-based compensation plans, consisting of:
  - 118,456 shares of common stock reserved for future issuance under our 2015 Stock Incentive Plan, as amended, or our 2015 Plan, which shares will be added to the shares to be reserved under our 2017 Equity Incentive Plan, or our 2017 Plan;
  - 6,210,000 shares of common stock reserved for future issuance under our 2017 Plan (excluding the 118,456 shares to be transferred from our 2015 Plan), which will become effective in connection with this offering, and any additional shares that become available under our 2017 Plan pursuant to provisions thereof that automatically increase the share reserve under the plan each year, as more fully described in the section titled “Executive Compensation—Employee Benefit and Stock Plans;” and
  - 1,000,000 shares of common stock reserved for future issuance under our 2017 Employee Stock Purchase Plan, or ESPP, which will become effective in connection with this offering, and any additional shares that become available under our ESPP pursuant to provisions thereof that automatically increase the share reserve under the plan each year, as more fully described in the section titled “Executive Compensation—Employee Benefit and Stock Plans.”

Unless otherwise indicated, this prospectus reflects and assumes the following:

- a 4-for-1 reverse stock split of our common stock and convertible preferred stock to be effected prior to the completion of this offering;
- no exercise of outstanding options;
- no exercise by the underwriters of their option to purchase up to an additional 1,250,000 shares of our common stock from us;
- the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 60,365,020 shares of our common stock, which will occur immediately prior to the closing of this offering; and
- the filing and effectiveness of our amended and restated certificate of incorporation and the effectiveness of our amended and restated bylaws, which will occur immediately prior to the closing of this offering.

Certain of our existing stockholders, including one that beneficially owns more than 5% of our outstanding common stock, have indicated an interest in purchasing an aggregate of $50.0 million or

more in shares of our common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no shares in this offering to any of these stockholders, or any of these stockholders may determine to purchase more, less or no shares in this offering. The underwriters will receive the same underwriting discounts and commissions on any shares purchased by these stockholders as they will on any other shares sold to the public in this offering.

SUMMARY CONSOLIDATED FINANCIAL DATA

The following tables summarize our consolidated financial data for the periods and as of the dates indicated. We have derived the consolidated statements of operations and comprehensive loss data for the years ended December 31, 2015 and 2016 from our audited consolidated financial statements included elsewhere in this prospectus. The consolidated statements of operations and comprehensive loss data for the nine months ended September 30, 2016 and 2017 and the balance sheet data as of September 30, 2017 have been derived from our unaudited interim condensed consolidated financial statements included elsewhere in this prospectus and have been prepared in accordance with generally accepted accounting principles in the United States of America on the same basis as the annual audited consolidated financial statements and, in the opinion of management, the unaudited data reflects all adjustments, consisting only of normal recurring adjustments, necessary for the fair presentation of the financial information in those statements. Our historical results are not necessarily indicative of results that may be expected in the future, and results for the nine months ended September 30, 2017 are not necessarily indicative of the results to be expected for the full year ending December 31, 2017. You should read the following summary consolidated financial data together with our consolidated financial statements and the related notes appearing elsewhere in this prospectus and the information in the sections titled “Selected Consolidated Financial Data” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations.”

	Year Ended December 31,		Nine Months Ended September 30,	
	2015	2016	2016	2017
	(in thousands, except share and per share amounts)			
Consolidated Statements of Operations and Comprehensive Loss Data:				
Operating expenses:				
Research and development	$ 11,571	$ 75,702	$ 58,972	$ 55,989
General and administrative	5,108	11,731	8,685	10,611
Total operating expenses	16,679	87,433	67,657	66,600
Loss from operations	(16,679)	(87,433)	(67,657)	(66,600)
Interest income (expense), net	(109)	781	359	1,302
Net loss	(16,788)	(86,652)	(67,298)	(65,298)
Other comprehensive income (loss)	—	(373)	(131)	136
Comprehensive loss	$ (16,788)	$ (87,025)	$ (67,429)	$ (65,162)
Net loss per share, basic and diluted (1)	$ (5.58)	$ (13.49)	$ (11.43)	$ (6.77)
Weighted-average number of shares outstanding, basic and diluted (1)	3,006,379	6,424,720	5,888,385	9,643,686
Pro forma net loss per share, basic and diluted (unaudited) (1)		$ (1.77)		$ (0.96)
Pro forma weighted-average common shares outstanding, basic and diluted (unaudited) (1)		48,924,244		68,244,028

(1) See the consolidated statements of operations and Note 12 to our consolidated financial statements, and the condensed consolidated statements of operations and Note 9 to our unaudited condensed consolidated financial statements, for further details on the calculation of net

loss per share, basic and diluted, and the weighted-average number of shares used in the computation of the per share amounts and unaudited pro forma information.

	As of September 30, 2017		
	Actual	Pro Forma (1)	Pro Forma As Adjusted (2)
		(in thousands) (unaudited)	
Consolidated Balance Sheet Data:			
Cash, cash equivalents and marketable securities	$ 190,776	$ 220,676	$ 356,676
Working capital (3)	178,089	207,989	343,989
Total assets	210,309	240,209	376,209
Total liabilities	17,172	17,172	17,172
Convertible preferred stock	348,673	—	—
Accumulated deficit	(168,810)	(168,810)	(168,810)
Total stockholders' equity (deficit)	(155,536)	223,037	359,037

(1) The pro forma balance sheet data in the table above reflects the conversion of our outstanding shares of our convertible preferred stock into 60,365,020 shares of our common stock, which will occur immediately prior to the closing of this offering and the filing and effectiveness of our amended and restated certificate of incorporation. This includes the impact to assets and stockholders' equity of 1,764,705 shares issuable upon conversion of our Series B-2 convertible preferred stock.

(2) The pro forma as adjusted balance sheet data in the table above reflects the pro forma adjustments described in footnote (1) above plus the sale and issuance by us of shares of our common stock in this offering, based upon the assumed initial public offering price of $18.00 per share, which is the midpoint of the estimated offering price range set forth on the cover page of this prospectus, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. A $1.00 increase (decrease) in the assumed initial public offering price of $18.00 per share would increase (decrease) the pro forma as adjusted amount of each of cash, cash equivalents and marketable securities, working capital, total assets and total stockholders' equity (deficit) by approximately $7.8 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. An increase (decrease) of one million shares in the number of shares offered by us would increase (decrease) each of cash, cash equivalents and marketable securities, working capital, total assets and stockholders' equity (deficit) by approximately $16.7 million, assuming the assumed initial public offering price of $18.00 per share remains the same, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. The pro forma as adjusted information discussed above is illustrative only and will be adjusted based on the actual public offering price and other terms of this offering determined at pricing.

(3) We define working capital as current assets less current liabilities. See our condensed consolidated financial statements for further details regarding our current assets and current liabilities.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this prospectus, including our financial statements and the related notes and the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" in this prospectus, before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations.

Risks Related to Our Business, Financial Condition and Capital Requirements

We are in the early stages of clinical drug development and have a very limited operating history and no products approved for commercial sale, which may make it difficult to evaluate our current business and predict our future success and viability.

We are an early clinical-stage biopharmaceutical company with a limited operating history, focused on developing therapeutics for neurodegenerative diseases, including Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis, or ALS. We commenced operations in May 2015, have no products approved for commercial sale and have not generated any revenue. Drug development is a highly uncertain undertaking and involves a substantial degree of risk. We have only recently begun a Phase 1 clinical trial for our most advanced product candidate, DNL201, which is in our LRRK2 core program, and have not initiated clinical trials for any of our other current product candidates. To date, we have not initiated or completed a pivotal clinical trial, obtained marketing approval for any product candidates, manufactured a commercial scale product, or arranged for a third party to do so on our behalf, or conducted sales and marketing activities necessary for successful product commercialization. Our short operating history as a company makes any assessment of our future success and viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by early-stage biopharmaceutical companies in rapidly evolving fields, and we have not yet demonstrated an ability to successfully overcome such risks and difficulties. If we do not address these risks and difficulties successfully, our business will suffer.

We have incurred significant net losses in each period since our inception and anticipate that we will continue to incur net losses for the foreseeable future.

We have incurred net losses in each reporting period since our inception, including net losses of $86.7 million and $16.8 million for the years ended December 31, 2016 and 2015, respectively, and $65.3 million for the nine months ended September 30, 2017. As of September 30, 2017, we had an accumulated deficit of $168.8 million.

We have invested significant financial resources in research and development activities, including for our preclinical and clinical product candidates and our blood-brain barrier, or BBB, platform technology. We do not expect to generate revenue from product sales for several years, if at all. The amount of our future net losses will depend, in part, on the level of our future expenditures and our ability to generate revenue. Moreover, our net losses may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance.

We expect to continue to incur significant expenses and increasingly higher operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- continue our research and discovery activities;

- continue the development of our BBB platform technology;
- progress our current and any future product candidates through preclinical and clinical development;
- initiate and conduct additional preclinical, clinical or other studies for our product candidates;
- work with our contract manufacturers to scale up the manufacturing processes for our product candidates or, in the future, establish and operate a manufacturing facility;
- change or add additional contract manufacturers or suppliers;
- seek regulatory approvals and marketing authorizations for our product candidates;
- establish sales, marketing and distribution infrastructure to commercialize any products for which we obtain approval;
- acquire or in-license product candidates, intellectual property and technologies;
- make milestone, royalty or other payments due under any license or collaboration agreements;
- obtain, maintain, protect and enforce our intellectual property portfolio, including intellectual property obtained through license agreements;
- attract, hire and retain qualified personnel;
- provide additional internal infrastructure to support our continued research and development operations and any planned commercialization efforts in the future;
- experience any delays or encounter other issues related to our operations;
- meet the requirements and demands of being a public company; and
- defend against any product liability claims or other lawsuits related to our products.

Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

Drug development is a highly uncertain undertaking and involves a substantial degree of risk. We have never generated any revenue from product sales, and we may never generate revenue or be profitable.

We have no products approved for commercial sale and have not generated any revenue from product sales. We do not anticipate generating any revenue from product sales until after we have successfully completed clinical development and received regulatory approval for the commercial sale of a product candidate, if ever.

Our ability to generate revenue and achieve profitability depends significantly on many factors, including:

- successfully completing research and preclinical and clinical development of our product candidates;
- obtaining regulatory approvals and marketing authorizations for product candidates for which we successfully complete clinical development and clinical trials;
- developing a sustainable and scalable manufacturing process for our product candidates, including those that utilize our BBB platform technology, as well as establishing and

maintaining commercially viable supply relationships with third parties that can provide adequate products and services to support clinical activities and commercial demand of our product candidates;

- identifying, assessing, acquiring and/or developing new product candidates;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter;
- launching and successfully commercializing product candidates for which we obtain regulatory and marketing approval, either by collaborating with a partner or, if launched independently, by establishing a sales, marketing and distribution infrastructure;
- obtaining and maintaining an adequate price for our product candidates, both in the United States and in foreign countries where our products are commercialized;
- obtaining adequate reimbursement for our product candidates from payors;
- obtaining market acceptance of our product candidates as viable treatment options;
- addressing any competing technological and market developments;
- maintaining, protecting, expanding and enforcing our portfolio of intellectual property rights, including patents, trade secrets and know-how; and
- attracting, hiring and retaining qualified personnel.

Because of the numerous risks and uncertainties associated with drug development, we are unable to predict the timing or amount of our expenses, or when we will be able to generate any meaningful revenue or achieve or maintain profitability, if ever. In addition, our expenses could increase beyond our current expectations if we are required by the U.S. Food and Drug Administration, or FDA, or foreign regulatory agencies, to perform studies in addition to those that we currently anticipate, or if there are any delays in any of our or our future collaborators' clinical trials or the development of any of our product candidates. Even if one or more of our product candidates is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate and ongoing compliance efforts.

Even if we are able to generate revenue from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations. Revenue from the sale of any product candidate for which regulatory approval is obtained will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to get reimbursement at any price and whether we own the commercial rights for that territory. If the number of addressable patients is not as significant as we anticipate, the indication approved by regulatory authorities is narrower than we expect, or the reasonably accepted population for treatment is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our pipeline of product candidates or continue our operations and cause a decline in the value of our common stock, all or any of which may adversely affect our viability.

If we fail to obtain additional financing, we may be unable to complete the development and, if approved, commercialization of our product candidates.

Our operations have required substantial amounts of cash since inception. To date, we have financed our operations primarily through the sale of equity securities. We are currently advancing one

product candidate, DNL201, through clinical development and have several other product candidates in preclinical development, as well as early-stage research projects. Developing our product candidates is expensive, and we expect to continue to spend substantial amounts as we fund our early-stage research projects, continue preclinical development of our seed programs and, in particular, advance our core programs through preclinical development and clinical trials. Even if we are successful in developing our product candidates, obtaining regulatory approvals and launching and commercializing any product candidate will require substantial additional funding beyond the net proceeds of this offering.

As of September 30, 2017, we had $190.8 million in cash, cash equivalents and marketable securities. We estimate that our net proceeds from this offering will be approximately $136.0 million, assuming an initial public offering price of $18.00 per share, which is the midpoint of the estimated offering price range set forth on the cover page of this prospectus, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. We believe that our existing cash, cash equivalents and marketable securities will be sufficient to fund our projected operations through at least the next 12 months. Our estimate as to how long we expect our existing cash, cash equivalents and marketable securities to be available to fund our operations is based on assumptions that may be proved inaccurate, and we could use our available capital resources sooner than we currently expect. In addition, changing circumstances may cause us to increase our spending significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control. We may need to raise additional funds sooner than we anticipate if we choose to expand more rapidly than we presently anticipate.

We will require additional capital for the further development and, if approved, commercialization of our product candidates. Additional capital may not be available when we need it, on terms acceptable to us or at all. We have no committed source of additional capital. If adequate capital is not available to us on a timely basis, we may be required to significantly delay, scale back or discontinue our research and development programs or the commercialization of any product candidates, if approved, or be unable to continue or expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations and cause the price of our common stock to decline.

Due to the significant resources required for the development of our programs, and depending on our ability to access capital, we must prioritize development of certain product candidates. Moreover, we may expend our limited resources on programs that do not yield a successful product candidate and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Our current total portfolio consists of 11 programs. We designate certain programs as core programs and others as seed programs. Together, these programs require significant capital investment. We currently have six core programs which are at various stages of preclinical and early clinical development, and our seed programs are in the research, discovery and preclinical stages of development. We seek to maintain a process of prioritization and resource allocation to maintain an optimal balance between aggressively advancing lead programs and ensuring replenishment of our portfolio. We regularly review the designation of each program as core or seed, and terminate those programs which do not meet our development criteria, which we have done with three programs in the past two years.

Due to the significant resources required for the development of our programs, we must focus our programs on specific diseases and disease pathways and decide which product candidates to pursue and advance and the amount of resources to allocate to each. Our decisions concerning the allocation of research, development, collaboration, management and financial resources toward particular

product candidates or therapeutic areas may not lead to the development of any viable commercial product and may divert resources away from better opportunities. Similarly, our potential decisions to delay, terminate or collaborate with third parties in respect of certain programs may subsequently also prove to be suboptimal and could cause us to miss valuable opportunities. If we make incorrect determinations regarding the viability or market potential of any of our programs or product candidates or misread trends in the biopharmaceutical industry, in particular for neurodegenerative diseases, our business, financial condition and results of operations could be materially adversely affected. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases and disease pathways that may later prove to have greater commercial potential than those we choose to pursue, or relinquish valuable rights to such product candidates through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to invest additional resources to retain sole development and commercialization rights. We regularly review the designation of each program as core or seed, and terminate those programs which do not meet our development criteria.

Risks Related to the Discovery, Development and Commercialization of Our Product Candidates

Research and development of biopharmaceutical products is inherently risky. We are heavily dependent on the successful development of our BBB platform technology and the product candidates currently in our core programs, which are in the early stages of preclinical and clinical development. We cannot give any assurance that any of our product candidates will receive regulatory, including marketing, approval, which is necessary before they can be commercialized.

We are at an early stage of development of the product candidates currently in our programs and are further developing our BBB platform technology. To date, we have invested substantially all of our efforts and financial resources to identify, acquire intellectual property for, and develop our BBB platform technology and our programs, including conducting preclinical studies and early-stage clinical trials in our core programs, and providing general and administrative support for these operations. Our future success is dependent on our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize our product candidates, and we may fail to do so for many reasons, including the following:

- our product candidates may not successfully complete preclinical studies or clinical trials;
- our drug delivery platform technology designed to deliver large molecule therapeutics across the BBB may not be clinically viable;
- a product candidate may on further study be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- our competitors may develop therapeutics that render our product candidates obsolete or less attractive;
- our competitors may develop platform technologies to deliver large molecule therapeutics across the BBB that render our platform technology obsolete or less attractive;
- the product candidates and BBB platform technology that we develop may not be sufficiently covered by intellectual property for which we hold exclusive rights;
- the product candidates and BBB platform technology that we develop may be covered by third parties' patents or other intellectual property or exclusive rights;

- the market for a product candidate may change so that the continued development of that product candidate is no longer reasonable or commercially attractive;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all;
- if a product candidate obtains regulatory approval, we may be unable to establish sales and marketing capabilities, or successfully market such approved product candidate, to gain market acceptance; and
- a product candidate may not be accepted as safe and effective by patients, the medical community or third-party payors, if applicable.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations.

We may not be successful in our efforts to further develop our BBB platform technology and current product candidates. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates. Each of our product candidates is in the early stages of development and will require significant additional clinical development, management of preclinical, clinical, and manufacturing activities, regulatory approval, adequate manufacturing supply, a commercial organization, and significant marketing efforts before we generate any revenue from product sales, if at all.

We have never completed a clinical development program. In the past two years, we have discontinued the development of three programs prior to completion of preclinical development because we did not believe they met our criteria for potential clinical success. We currently have one product candidate, DNL201, in a Phase 1 clinical trial in healthy volunteers in the United States. None of our product candidates have advanced into late-stage development or a pivotal clinical trial and it may be years before any such trial is initiated, if at all. Further, we cannot be certain that any of our product candidates will be successful in clinical trials. For instance, in 2016, we initiated a Phase 1 clinical trial in a former RIPK1 inhibitor product candidate, DNL104, which we subsequently discontinued based on liver test abnormalities in some clinical trial healthy volunteer participants. We may in the future advance product candidates into clinical trials and terminate such trials prior to their completion.

If any of our product candidates successfully complete clinical trials, we generally plan to seek regulatory approval to market our product candidates in the United States, the European Union, or EU, and in additional foreign countries where we believe there is a viable commercial opportunity. We have never commenced, compiled or submitted an application seeking regulatory approval to market any product candidate. We may never receive regulatory approval to market any product candidates even if such product candidates successfully complete clinical trials, which would adversely affect our viability. To obtain regulatory approval in countries outside the United States, we must comply with numerous and varying regulatory requirements of such other countries regarding safety, efficacy, chemistry, manufacturing and controls, clinical trials, commercial sales, pricing, and distribution of our product candidates. We may also rely on our collaborators or partners to conduct the required activities to support an application for regulatory approval, and to seek approval, for one or more of our product candidates. We cannot be sure that our collaborators or partners will conduct these activities or do so within the timeframe we desire. Even if we (or our collaborators or partners) are successful in obtaining approval in one jurisdiction, we cannot ensure that we will obtain approval in any other jurisdictions. If we are unable to obtain approval for our product candidates in multiple jurisdictions, our revenue and results of operations could be negatively affected.

Even if we receive regulatory approval to market any of our product candidates, whether for the treatment of neurodegenerative diseases or other diseases, we cannot assure you that any such product candidate will be successfully commercialized, widely accepted in the marketplace or more effective than other commercially available alternatives.

Investment in biopharmaceutical product development involves significant risk that any product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval, and become commercially viable. We cannot provide any assurance that we will be able to successfully advance any of our product candidates through the development process or, if approved, successfully commercialize any of our product candidates.

We may not be successful in our efforts to continue to create a pipeline of product candidates or to develop commercially successful products. If we fail to successfully identify and develop additional product candidates, our commercial opportunity may be limited.

One of our strategies is to identify and pursue clinical development of additional product candidates. We currently have five seed programs, all of which are in the research, discovery and preclinical stages of development. Identifying, developing, obtaining regulatory approval and commercializing additional product candidates for the treatment of neurodegenerative diseases will require substantial additional funding beyond the net proceeds of this offering and is prone to the risks of failure inherent in drug development. We cannot provide you any assurance that we will be able to successfully identify or acquire additional product candidates, advance any of these additional product candidates through the development process, successfully commercialize any such additional product candidates, if approved, or assemble sufficient resources to identify, acquire, develop or, if approved, commercialize additional product candidates. If we are unable to successfully identify, acquire, develop and commercialize additional product candidates, our commercial opportunity may be limited.

We have concentrated our research and development efforts on the treatment of neurodegenerative diseases, a field that has seen limited success in drug development. Further, our product candidates are based on new approaches and novel technology, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval.

We have focused our research and development efforts on addressing neurodegenerative diseases. Collectively, efforts by biopharmaceutical companies in the field of neurodegenerative diseases have seen limited successes in drug development. There are few effective therapeutic options available for patients with Alzheimer's disease, Parkinson's disease, ALS and other neurodegenerative diseases. Our future success is highly dependent on the successful development of our BBB platform technology and our product candidates for treating neurodegenerative diseases. Developing and, if approved, commercializing our product candidates for treatment of neurodegenerative diseases subjects us to a number of challenges, including engineering product candidates to cross the BBB to enable optimal concentration of the therapeutic in the brain and obtaining regulatory approval from the FDA and other regulatory authorities who have only a limited set of precedents to rely on.

Our approach to the treatment of neurodegenerative diseases aims to identify and select targets with a genetic link to neurodegenerative diseases, identify and develop molecules that engage the intended target, identify and develop biomarkers, which are biological molecules found in blood, other bodily fluids or tissues that are signs of a normal or abnormal process or of a condition or disease, to select the right patient population and demonstrate target engagement, pathway engagement and impact on disease progression of our molecules, and engineer our molecules to cross the BBB and act directly in the brain. This strategy may not prove to be successful. We cannot be sure that our approach will yield satisfactory therapeutic products that are safe and effective, scalable, or profitable.

Moreover, public perception of drug safety issues, including adoption of new therapeutics or novel approaches to treatment, may adversely influence the willingness of subjects to participate in clinical trials, or if approved, of physicians to subscribe to novel treatments.

We may encounter substantial delays in our clinical trials, or may not be able to conduct or complete our clinical trials on the timelines we expect, if at all.

Clinical testing is expensive, time consuming, and subject to uncertainty. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. We cannot be sure that submission of an investigational new drug application, or IND, or a clinical trial application, or CTA, will result in the FDA or European Medicines Agency, or EMA, as applicable, allowing clinical trials to begin in a timely manner, if at all. Moreover, even if these trials begin, issues may arise that could suspend or terminate such clinical trials. A failure of one or more clinical trials can occur at any stage of testing, and our future clinical trials may not be successful. Events that may prevent successful or timely initiation or completion of clinical trials include:

- inability to generate sufficient preclinical, toxicology, or other *in vivo* or *in vitro* data to support the initiation or continuation of clinical trials;
- delays in confirming target engagement, patient selection or other relevant biomarkers to be utilized in preclinical and clinical product candidate development;
- delays in reaching a consensus with regulatory agencies on study design;
- delays in reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- delays in identifying, recruiting and training suitable clinical investigators;
- delays in obtaining required Institutional Review Board, or IRB, approval at each clinical trial site;
- imposition of a temporary or permanent clinical hold by regulatory agencies for a number of reasons, including after review of an IND or amendment, CTA or amendment, or equivalent application or amendment; as a result of a new safety finding that presents unreasonable risk to clinical trial participants; a negative finding from an inspection of our clinical trial operations or study sites; developments on trials conducted by competitors for related technology that raises FDA or EMA concerns about risk to patients of the technology broadly; or if the FDA or EMA finds that the investigational protocol or plan is clearly deficient to meet its stated objectives;
- delays in identifying, recruiting and enrolling suitable patients to participate in our clinical trials, and delays caused by patients withdrawing from clinical trials or failing to return for post-treatment follow-up;
- difficulty collaborating with patient groups and investigators;
- failure by our CROs, other third parties, or us to adhere to clinical trial requirements;
- failure to perform in accordance with the FDA's or any other regulatory authority's current good clinical practices, or cGCPs, requirements, or applicable EMA or other regulatory guidelines in other countries;
- occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;

- changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;
- the cost of clinical trials of our product candidates being greater than we anticipate;
- clinical trials of our product candidates producing negative or inconclusive results, which may result in our deciding, or regulators requiring us, to conduct additional clinical trials or abandon product development programs;
- transfer of manufacturing processes from our academic collaborators to larger-scale facilities operated by a contract manufacturing organization, or CMO, or by us, and delays or failure by our CMOs or us to make any necessary changes to such manufacturing process; and
- delays in manufacturing, testing, releasing, validating, or importing/exporting sufficient stable quantities of our product candidates for use in clinical trials or the inability to do any of the foregoing.

Any inability to successfully initiate or complete clinical trials could result in additional costs to us or impair our ability to generate revenue. In addition, if we make manufacturing or formulation changes to our product candidates, we may be required to or we may elect to conduct additional studies to bridge our modified product candidates to earlier versions. Clinical trial delays could also shorten any periods during which our products have patent protection and may allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the data safety monitoring board for such trial or by the FDA, EMA or any other regulatory authority, or if the IRBs of the institutions in which such trials are being conducted suspend or terminate the participation of their clinical investigators and sites subject to their review. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA, EMA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

Our most advanced product candidate, DNL201, which is currently in a Phase 1 clinical trial in healthy volunteers in the United States, is subject to a partial clinical hold issued by the FDA due to adverse clinical signs (e.g. severe hypoactivity and prostration) observed in our 10-day oral dose ranging pilot toxicity studies designed to define the maximum tolerated dose of DNL201 in rats. This partial clinical hold relates to the FDA's decision to impose an exposure cap in our Phase 1 healthy volunteer clinical trial. The partial clinical hold prohibits evaluation of DNL201 above a specific exposure level. The FDA may re-evaluate the exposure cap for this trial, and may potentially raise it, based on the safety and tolerability data generated by the trial as well as data supporting the monitorability of the effects of the trial. We cannot assure you that the FDA will deem our response to be a complete response or that it will determine to lift or change the exposure cap imposed, and ultimately lift this partial clinical hold. If the FDA does not lift or change the exposure cap currently imposed, this may negatively impact the development of DNL201 if we determine that we must achieve higher degrees of LRRK2 kinase inhibition than what can be achieved with the current exposure cap. If we make such determination and the FDA does not lift the exposure cap, we may be unable to continue or complete our clinical trial of DNL201. Any inability to continue or complete our clinical trial of DNL201, as a result of the partial clinical hold or otherwise, will delay or terminate our clinical development plans for DNL201, may require us to incur additional clinical development costs and could impair our ability to ultimately obtain FDA approval for DNL201. Furthermore, we proactively proposed

an interim exposure cap in our planned Phase 1 healthy volunteer clinical trial for DNL151. We observed toxicity at high doses in cynomolgus monkeys in our 28-day GLP safety study of our lead RIPK1 product candidate, DNL747, and we are in the process of completing our analysis of the data from such study. Adverse findings in such preclinical studies could result in the regulatory authorities imposing, or us proactively proposing, an exposure cap in our planned Phase 1 clinical trial for DNL747. We cannot assure you that DNL201, DNL151, DNL747 or our other product candidates will not be subject to new, partial or full clinical holds in the future.

We may in the future advance product candidates into clinical trials and terminate such trials prior to their completion, such as we did for DNL104, which could adversely affect our business.

Delays in the completion of any clinical trial of our product candidates will increase our costs, slow down our product candidate development and approval process and delay or potentially jeopardize our ability to commence product sales and generate revenue. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

We may encounter difficulties enrolling patients in our clinical trials, and our clinical development activities could thereby be delayed or otherwise adversely affected.

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the trial until its conclusion. We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons, including:

- the size and nature of the patient population;
- the patient eligibility criteria defined in the protocol, including biomarker-driven identification and/or certain highly-specific criteria related to stage of disease progression, which may limit the patient populations eligible for our clinical trials to a greater extent than competing clinical trials for the same indication that do not have biomarker-driven patient eligibility criteria;
- the size of the study population required for analysis of the trial's primary endpoints;
- the proximity of patients to a trial site;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- competing clinical trials for similar therapies or targeting patient populations meeting our patient eligibility criteria;
- clinicians' and patients' perceptions as to the potential advantages and side effects of the product candidate being studied in relation to other available therapies and product candidates;
- our ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will not complete such trials, for any reason.

Our clinical trials may fail to demonstrate substantial evidence of the safety and efficacy of our product candidates, which would prevent, delay or limit the scope of regulatory approval and commercialization.

Before obtaining regulatory approvals for the commercial sale of any of our product candidates, we must demonstrate through lengthy, complex and expensive preclinical studies and clinical trials that

our product candidates are both safe and effective for use in each target indication. For those product candidates that are subject to regulation as biological drug products, we will need to demonstrate that they are safe, pure, and potent for use in their target indications. Each product candidate must demonstrate an adequate risk versus benefit profile in its intended patient population and for its intended use.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies of our product candidates may not be predictive of the results of early-stage or later-stage clinical trials, and results of early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. The results of clinical trials in one set of patients or disease indications may not be predictive of those obtained in another. In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety issues, notwithstanding promising results in earlier trials. This is particularly true in neurodegenerative diseases, where failure rates historically have been higher than in many other disease areas. Most product candidates that begin clinical trials are never approved by regulatory authorities for commercialization.

We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. We cannot be certain that our current clinical trials or any other future clinical trials will be successful. Additionally, any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of our product candidates in those and other indications, which could have a material adverse effect on our business, financial condition and results of operations.

In addition, even if such clinical trials are successfully completed, we cannot guarantee that the FDA or foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit our product candidates for approval. To the extent that the results of the trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional trials in support of potential approval of our product candidates. Even if regulatory approval is secured for any of our product candidates, the terms of such approval may limit the scope and use of our product candidate, which may also limit its commercial potential.

We face significant competition in an environment of rapid technological and scientific change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer, more advanced or more effective than ours, which may negatively impact our ability to successfully market or commercialize any product candidates we may develop and ultimately harm our financial condition.

The development and commercialization of new drug products is highly competitive. Moreover, the neurodegenerative field is characterized by strong and increasing competition, and a strong emphasis on intellectual property. We may face competition with respect to any product candidates that we seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies, and other public and private research

organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization.

There are a number of large pharmaceutical and biotechnology companies that are currently pursuing the development of products for the treatment of the neurodegenerative disease indications for which we have research programs, including Alzheimer's disease, Parkinson's disease and ALS. Companies that we are aware are developing therapeutics in the neurodegenerative disease area include large companies with significant financial resources, such as AbbVie, AstraZeneca, Biogen, Celgene, Eli Lilly, GlaxoSmithKline, Johnson & Johnson, Novartis, Pfizer, Roche, Sanofi and Takeda. In addition to competition from other companies targeting neurodegenerative indications, any products we may develop may also face competition from other types of therapies, such as gene-editing therapies.

Many of our current or potential competitors, either alone or with their strategic partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any products that we may develop. Furthermore, currently approved products could be discovered to have application for treatment of neurodegenerative disease indications, which could give such products significant regulatory and market timing advantages over any of our product candidates. Our competitors also may obtain FDA, EMA or other regulatory approval for their products more rapidly than we may obtain approval for ours and may obtain orphan product exclusivity from the FDA for indications our product candidates are targeting, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, products or technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing any product candidates we may develop against competitors.

In addition, we could face litigation or other proceedings with respect to the scope, ownership, validity and/or enforceability of our patents relating to our competitors' products and our competitors may allege that our products infringe, misappropriate or otherwise violate their intellectual property. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize. See "Risks Related to Our Intellectual Property."

The manufacture of our product candidates, particularly those that utilize our BBB platform technology, is complex and we may encounter difficulties in production. If we or any of our third-party manufacturers encounter such difficulties, or fail to meet rigorously enforced regulatory standards, our ability to provide supply of our product candidates for clinical trials or our products for patients, if approved, could be delayed or stopped, or we may be unable to maintain a commercially viable cost structure.

The processes involved in manufacturing our drug and biological product candidates, particularly those that utilize our BBB platform technology, are complex, expensive, highly-regulated and subject to multiple risks. Additionally, the manufacture of biologics involves complex processes, including

developing cells or cell systems to produce the biologic, growing large quantities of such cells, and harvesting and purifying the biologic produced by them. As a result, the cost to manufacture a biologic is generally far higher than traditional small molecule chemical compounds, and the biologics manufacturing process is less reliable and is difficult to reproduce. Manufacturing biologics is highly susceptible to product loss due to contamination, equipment failure, improper installation or operation of equipment, vendor or operator error, inconsistency in yields, variability in product characteristics and difficulties in scaling the production process. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects and other supply disruptions. Further, as product candidates are developed through preclinical studies to late-stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives, and any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials.

In order to conduct clinical trials of our product candidates, or supply commercial products, if approved, we will need to manufacture them in small and large quantities. Our manufacturing partners may be unable to successfully increase the manufacturing capacity for any of our product candidates in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities. If our manufacturing partners are unable to successfully scale up the manufacture of our product candidates in sufficient quality and quantity, the development, testing and clinical trials of that product candidate may be delayed or become infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business. The same risks would apply to our internal manufacturing facilities, should we in the future decide to build internal manufacturing capacity. In addition, building internal manufacturing capacity would carry significant risks in terms of being able to plan, design and execute on a complex project to build manufacturing facilities in a timely and cost-efficient manner.

In addition, the manufacturing process for any products that we may develop is subject to FDA, EMA and foreign regulatory authority approval processes, and continuous oversight, and we will need to contract with manufacturers who can meet all applicable FDA, EMA and foreign regulatory authority requirements, including complying with current good manufacturing practices, or cGMPs, on an ongoing basis. If we or our third-party manufacturers are unable to reliably produce products to specifications acceptable to the FDA, EMA or other regulatory authorities, we may not obtain or maintain the approvals we need to commercialize such products. Even if we obtain regulatory approval for any of our product candidates, there is no assurance that either we or our CMOs will be able to manufacture the approved product to specifications acceptable to the FDA, EMA or other regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product, or to meet potential future demand. Any of these challenges could delay completion of clinical trials, require bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidate, impair commercialization efforts, increase our cost of goods, and have an adverse effect on our business, financial condition, results of operations and growth prospects.

If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any product candidates we may develop, we may not be successful in commercializing those product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing, or distribution of pharmaceutical products. To achieve commercial success for any approved product for which we retain sales and marketing responsibilities, we must either develop a sales and marketing

organization or outsource these functions to third parties. In the future, we may choose to build a focused sales, marketing, and commercial support infrastructure to sell, or participate in sales activities with our collaborators for, some of our product candidates if and when they are approved.

There are risks involved with both establishing our own commercial capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force or reimbursement specialists is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and other commercialization capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our commercialization personnel.

Factors that may inhibit our efforts to commercialize any approved product on our own include:

- our inability to recruit and retain adequate numbers of effective sales, marketing, reimbursement, customer service, medical affairs, and other support personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future approved products;
- the inability of reimbursement professionals to negotiate arrangements for formulary access, reimbursement, and other acceptance by payors;
- the inability to price our products at a sufficient price point to ensure an adequate and attractive level of profitability;
- restricted or closed distribution channels that make it difficult to distribute our products to segments of the patient population;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent commercialization organization.

If we enter into arrangements with third parties to perform sales, marketing, commercial support, and distribution services, our product revenue or the profitability of product revenue may be lower than if we were to market and sell any products we may develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to commercialize our product candidates or may be unable to do so on terms that are favorable to us. We may have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish commercialization capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates if approved.

Even if any product candidates we develop receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors, and others in the medical community necessary for commercial success.

The commercial success of any of our product candidates will depend upon its degree of market acceptance by physicians, patients, third-party payors, and others in the medical community. Even if any product candidates we may develop receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare payors, and others in the medical

community. The degree of market acceptance of any product candidates we may develop, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of such product candidates as demonstrated in pivotal clinical trials and published in peer-reviewed journals;
- the potential and perceived advantages compared to alternative treatments;
- the ability to offer our products for sale at competitive prices;
- the ability to offer appropriate patient access programs, such as co-pay assistance;
- the extent to which physicians recommend our products to their patients;
- convenience and ease of dosing and administration compared to alternative treatments;
- the clinical indications for which the product candidate is approved by FDA, EMA or other regulatory agencies;
- product labeling or product insert requirements of the FDA, EMA or other comparable foreign regulatory authorities, including any limitations, contraindications or warnings contained in a product's approved labeling;
- restrictions on how the product is distributed;
- the timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments;
- the strength of marketing and distribution support;
- sufficient third-party coverage or reimbursement; and
- the prevalence and severity of any side effects.

If any product candidates we develop do not achieve an adequate level of acceptance, we may not generate significant product revenue, and we may not become profitable.

Even if we are able to commercialize any product candidates, such products may become subject to unfavorable pricing regulations, third-party reimbursement practices, or healthcare reform initiatives, which would harm our business.

The regulations that govern marketing approvals, pricing, and reimbursement for new drugs vary widely from country to country. In the United States, recently enacted legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenue we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if any product candidates we may develop obtain marketing approval.

Our ability to successfully commercialize any products that we may develop also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers, and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance

organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Government authorities currently impose mandatory discounts for certain patient groups, such as Medicare, Medicaid and Veterans Affairs, or VA, hospitals, and may seek to increase such discounts at any time. Future regulation may negatively impact the price of our products, if approved. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. In order to get reimbursement, physicians may need to show that patients have superior treatment outcomes with our products compared to standard of care drugs, including lower-priced generic versions of standard of care drugs. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors and coverage and reimbursement levels for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time consuming and costly process that may require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the medicine is approved by the FDA, EMA or other comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved products we may develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize product candidates, and our overall financial condition.

If any of our product candidates that are small molecules obtain regulatory approval, additional competitors could enter the market with generic versions of such drugs, which may result in a material decline in sales of affected products.

Under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, a pharmaceutical manufacturer may file an abbreviated new drug application, or ANDA, seeking approval of a generic copy of an approved, small molecule innovator product. Under the Hatch-Waxman Act, a manufacturer may also submit a new drug application, or NDA, under section 505(b)(2) that references the FDA's prior approval of the small molecule innovator product. A 505(b)(2) NDA product may be for a new or improved version of the original innovator product. The Hatch-Waxman Act also provides for certain periods of regulatory exclusivity, which preclude FDA approval (or in some circumstances, FDA filing and reviewing) of an ANDA or 505(b)(2) NDA. These include, subject to certain exceptions, the period during which an FDA-approved drug is subject to orphan drug exclusivity. In

addition to the benefits of regulatory exclusivity, an innovator NDA holder may have patents claiming the active ingredient, product formulation or an approved use of the drug, which would be listed with the product in the FDA publication, “Approved Drug Products with Therapeutic Equivalence Evaluations,” known as the “Orange Book.” If there are patents listed in the Orange Book, a generic or 505(b)(2) applicant that seeks to market its product before expiration of the patents must include in the ANDA a “Paragraph IV certification,” challenging the validity or enforceability of, or claiming non-infringement of, the listed patent or patents. Notice of the certification must be given to the innovator, too, and if within 45 days of receiving notice the innovator sues to protect its patents, approval of the ANDA is stayed for 30 months, or as lengthened or shortened by the court.

Accordingly, if any of our small molecule product candidates are approved, competitors could file ANDAs for generic versions of our small molecule drug products or 505(b)(2) NDAs that reference our small molecule drug products, respectively. If there are patents listed for our small molecule drug products in the Orange Book, those ANDAs and 505(b)(2) NDAs would be required to include a certification as to each listed patent indicating whether the ANDA applicant does or does not intend to challenge the patent. We cannot predict which, if any, patents in our current portfolio or patents we may obtain in the future will be eligible for listing in the Orange Book, how any generic competitor would address such patents, whether we would sue on any such patents, or the outcome of any such suit.

We may not be successful in securing or maintaining proprietary patent protection for products and technologies we develop or license. Moreover, if any of our owned or in-licensed patents that are listed in the Orange Book are successfully challenged by way of a Paragraph IV certification and subsequent litigation, the affected product could immediately face generic competition and its sales would likely decline rapidly and materially. Should sales decline, we may have to write off a portion or all of the intangible assets associated with the affected product and our results of operations and cash flows could be materially and adversely affected. See “Risks Related to Our Intellectual Property.”

Our biologic, or large molecule, product candidates for which we intend to seek approval may face competition sooner than anticipated.

Even if we are successful in achieving regulatory approval to commercialize a product candidate faster than our competitors, our large molecule product candidates may face competition from biosimilar products. In the United States, our large molecule product candidates are regulated by the FDA as biologic products and we intend to seek approval for these product candidates pursuant to the biologics license application, or BLA, pathway. The Biologics Price Competition and Innovation Act of 2009, or BPCIA, created an abbreviated pathway for the approval of biosimilar and interchangeable biologic products. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as “interchangeable” based on its similarity to an existing brand product. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the original branded product was approved under a BLA. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our large molecule product candidates.

We believe that any of our large molecule product candidates approved as a biologic product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Moreover, the extent to which a

biosimilar product, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biologic products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing. In addition, a competitor could decide to forego the biosimilar approval path and submit a full BLA after completing its own preclinical studies and clinical trials. In such cases, any exclusivity to which we may be eligible under the BPCIA would not prevent the competitor from marketing its product as soon as it is approved.

In Europe, the European Commission has granted marketing authorizations for several biosimilar products pursuant to a set of general and product class-specific guidelines for biosimilar approvals issued over the past few years. In Europe, a competitor may reference data supporting approval of an innovative biological product, but will not be able to get it on the market until 10 years after the time of approval of the innovative product. This 10-year marketing exclusivity period will be extended to 11 years if, during the first eight of those 10 years, the marketing authorization holder obtains an approval for one or more new therapeutic indications that bring significant clinical benefits compared with existing therapies. In addition, companies may be developing biosimilar products in other countries that could compete with our products, if approved.

If competitors are able to obtain marketing approval for biosimilars referencing our large molecule product candidates, if approved, such products may become subject to competition from such biosimilars, with the attendant competitive pressure and potential adverse consequences. Such competitive products may be able to immediately compete with us in each indication for which our product candidates may have received approval.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk when and if we commercialize any products. For example, we may be sued if our product candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit testing and commercialization of our product candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased or interrupted demand for our products;
- injury to our reputation;
- withdrawal of clinical trial participants and inability to continue clinical trials;
- initiation of investigations by regulators;
- costs to defend the related litigation;
- a diversion of management’s time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;

- exhaustion of any available insurance and our capital resources;
- the inability to commercialize any product candidate; and
- a decline in our share price.

Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop, alone or with collaborators. Our insurance policies may have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

The regulatory approval processes of the FDA, EMA and comparable foreign regulatory authorities are lengthy, time consuming, and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, we will be unable to generate product revenue and our business will be substantially harmed.

The time required to obtain approval by the FDA, EMA and comparable foreign regulatory authorities is unpredictable, typically takes many years following the commencement of clinical trials, and depends upon numerous factors, including the type, complexity and novelty of the product candidates involved. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. Moreover, the FDA, EMA or other regulatory authorities may fail to approve companion diagnostics that we contemplate using with our therapeutic product candidates. We have not submitted for, or obtained regulatory approval for any product candidate, and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval.

Applications for our product candidates could fail to receive regulatory approval for many reasons, including but not limited to the following:

- the FDA, EMA or comparable foreign regulatory authorities may disagree with the design, implementation or results of our clinical trials;
- the FDA, EMA or comparable foreign regulatory authorities may determine that our product candidates are not safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use;
- the population studied in the clinical program may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval;
- we may be unable to demonstrate to the FDA or comparable foreign regulatory authorities that a product candidate's risk-benefit ratio when compared to the standard of care is acceptable;
- the FDA, EMA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;

- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA, BLA, or other submission or to obtain regulatory approval in the United States or elsewhere;
- we may be unable to demonstrate to the FDA, EMA or comparable foreign regulatory authorities that a product candidate's risk-benefit ratio for its proposed indication is acceptable;
- the FDA, EMA or comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA, EMA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in our failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations, and prospects.

Our product candidates may cause undesirable side effects or have other properties that could halt their clinical development, prevent their regulatory approval, limit their commercial potential, or result in significant negative consequences.

Adverse events or other undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay, or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, EMA or other comparable foreign regulatory authorities.

Our most advanced product candidate, DNL201, is currently our only clinical stage product candidate. In June 2017, we initiated a Phase 1 clinical trial of DNL201 in healthy volunteers in the United States and, to date, it has been well tolerated. However, adverse events and other side effects may result from higher dosing, repeated dosing and/or longer-term exposure to DNL201 and could lead to delays and/or termination of the development of this product candidate.

In 2016, we initiated a Phase 1 clinical trial in a former RIPK1 inhibitor product candidate, DNL104, which we subsequently discontinued based on liver function test abnormalities in some clinical trial healthy volunteer participants.

Drug-related side effects could affect patient recruitment, the ability of enrolled patients to complete the study, and/or result in potential product liability claims. We are required to maintain product liability insurance pursuant to certain of our license agreements. We may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business. In addition, regardless of merit or eventual outcome, product liability claims may result in impairment of our business reputation, withdrawal of clinical trial participants, costs due to related litigation, distraction of management's attention from our primary business, initiation of investigations by regulators, substantial monetary awards to patients or other claimants, the inability to commercialize our product candidates, and decreased demand for our product candidates, if approved for commercial sale.

Additionally, if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects or adverse events caused by such products, a number of potentially significant negative consequences could result, including but not limited to:

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the label;
- we may be required to change the way the product is administered or conduct additional clinical trials or post-approval studies;
- we may be required to create a Risk Evaluation and Mitigation Strategy plan, which could include a medication guide outlining the risks of such side effects for distribution to patients, a communication plan for healthcare providers, and/or other elements to assure safe use;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations, and prospects.

We may in the future conduct clinical trials for our product candidates outside the United States, and the FDA, EMA and applicable foreign regulatory authorities may not accept data from such trials.

We may in the future choose to conduct one or more of our clinical trials outside the United States, including in Europe. The acceptance of study data from clinical trials conducted outside the United States or another jurisdiction by the FDA, EMA or applicable foreign regulatory authority may be subject to certain conditions. In cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the United States population and United States medical practice; and (ii) the trials were performed by clinical investigators of recognized competence and pursuant to cGCP regulations. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory bodies have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA, EMA or any applicable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA, EMA or any applicable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in our product candidates not receiving approval or clearance for commercialization in the applicable jurisdiction.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our product candidates in other jurisdictions.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, but a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA or EMA grants marketing approval of a product candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods

different from those in the United States, including additional preclinical studies or clinical trials as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval.

Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we or any partner we work with fail to comply with the regulatory requirements in international markets or fail to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

Even if we obtain regulatory approval for a product candidate, our products will remain subject to extensive regulatory scrutiny.

If any of our product candidates are approved, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, and submission of safety, efficacy, and other post-market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities.

Manufacturers and manufacturers' facilities are required to comply with extensive requirements imposed by the FDA, EMA and comparable foreign regulatory authorities, including ensuring that quality control and manufacturing procedures conform to cGMP regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any NDA, BLA or marketing authorization application, or MAA. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

Any regulatory approvals that we receive for our product candidates will be subject to limitations on the approved indicated uses for which the product may be marketed and promoted or to the conditions of approval (including the requirement to implement a Risk Evaluation and Mitigation Strategy), or contain requirements for potentially costly post-marketing testing. We will be required to report certain adverse reactions and production problems, if any, to the FDA, EMA and comparable foreign regulatory authorities. Any new legislation addressing drug safety issues could result in delays in product development or commercialization, or increased costs to assure compliance. The FDA and other agencies, including the Department of Justice, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. We will have to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we may not promote our products for indications or uses for which they do not have approval. The holder of an approved NDA, BLA, or MAA must submit new or supplemental applications and obtain approval for certain changes to the approved product, product labeling, or manufacturing process. We could also be asked to conduct post-marketing clinical trials to verify the safety and efficacy of our products in general or in specific patient subsets. If original marketing approval was obtained via the accelerated approval pathway, we could be required to conduct a successful post-marketing clinical trial to confirm clinical benefit for our products. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of marketing approval.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, such regulatory agency may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things:

- issue warning letters that would result in adverse publicity;
- impose civil or criminal penalties;
- suspend or withdraw regulatory approvals;
- suspend any of our ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our contract manufacturers' facilities;
- seize or detain products; or
- require a product recall.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from our products. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected.

We plan to seek orphan drug designation for some product candidates, but we may be unable to obtain such designations or to maintain the benefits associated with orphan drug status, including market exclusivity, which may cause our revenue, if any, to be reduced.

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug or biologic. Orphan drug designation must be requested before submitting an NDA or BLA. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user-fee waivers. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. We plan to seek orphan drug designations for some product candidates and may be unable to obtain such designations.

If a product that has orphan drug designation subsequently receives the first FDA approval for a particular active ingredient for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other NDA or BLA applications to market the same drug or biologic for the same indication for seven years, except in limited circumstances such as a showing of clinical superiority to the product with orphan exclusivity or if FDA finds that the holder of the orphan exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan product to meet the needs of patients with the disease or condition for which the drug was designated. As a result, even if one of our product candidates receives orphan exclusivity, the FDA can still approve other drugs that have a different active ingredient for use in

treating the same indication or disease. Furthermore, the FDA can waive orphan exclusivity if we are unable to manufacture sufficient supply of our product.

Healthcare legislative measures aimed at reducing healthcare costs may have a material adverse effect on our business and results of operations.

Third-party payors, whether domestic or foreign, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the health care system that could impact our ability to sell our products profitably. In particular, in 2010, the Affordable Care Act, or ACA, was enacted, which, among other things, subjected biologic products to potential competition by lower-cost biosimilars, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program, extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations, subjected manufacturers to new annual fees and taxes for certain branded prescription drugs, and provided incentives to programs that increase the federal government's comparative effectiveness research. Recent changes in the U.S. administration could lead to repeal of or changes in some or all of the ACA, and complying with any new legislation or reversing changes implemented under the ACA could be time-intensive and expensive, resulting in a material adverse effect on our business. Until the ACA is fully implemented or there is more certainty concerning the future of the ACA, it will be difficult to predict its full impact and influence on our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in 2013, and will remain in effect through 2025 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012 further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at containing or lowering the cost of healthcare. We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

- the demand for our product candidates, if we obtain regulatory approval;
- our ability to receive or set a price that we believe is fair for our products;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous

coverage criteria, lower reimbursement, and new payment methodologies. This could lower the price that we receive for any approved product. Any denial in coverage or reduction in reimbursement from Medicare or other government-funded programs may result in a similar denial or reduction in payments from private payors, which may prevent us from being able to generate sufficient revenue, attain profitability or commercialize our product candidates, if approved.

Our employees, independent contractors, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of fraud, misconduct or other illegal activity by our employees, independent contractors, consultants, commercial partners and vendors. Misconduct by these parties could include intentional, reckless and negligent conduct that fails to: comply with the laws of the FDA, EMA and other comparable foreign regulatory authorities; provide true, complete and accurate information to the FDA, EMA and other comparable foreign regulatory authorities; comply with manufacturing standards we have established; comply with healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws; or report financial information or data accurately or to disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the United States, our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. In particular, research, sales, marketing, education and other business arrangements in the healthcare industry are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, educating, marketing and promotion, sales and commission, certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of business conduct and ethics, but it is not always possible to identify and deter misconduct by employees and third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

If we fail to comply with healthcare laws, we could face substantial penalties and our business, operations and financial conditions could be adversely affected.

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations will be subject to various federal and state fraud and abuse laws. The laws that may impact our operations include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;

- federal civil and criminal false claims laws and civil monetary penalty laws, including the False Claims Act, which impose criminal and civil penalties, including through civil “qui tam” or “whistleblower” actions, against individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid, or other third-party payors that are false or fraudulent or knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of these statutes or specific intent to violate them in order to have committed a violation;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization;
- the federal Physician Payment Sunshine Act, created under the ACA, and its implementing regulations, which require manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children’s Health Insurance Program to report annually to the U.S. Department of Health and Human Services under the Open Payments Program, information related to payments or other transfers of value made to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and
- analogous state and foreign laws and regulations, such as state and foreign anti-kickback, false claims, consumer protection and unfair competition laws which may apply to pharmaceutical business practices, including but not limited to, research, distribution, sales and marketing arrangements as well as submitting claims involving healthcare items or services reimbursed by any third-party payer, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government that otherwise restricts payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to file reports with states regarding pricing and marketing information, such as the tracking and reporting of gifts, compensations and other remuneration and items of value provided to healthcare professionals and entities; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could, despite our efforts to comply,

be subject to challenge under one or more of such laws. Efforts to ensure that our business arrangements will comply with applicable healthcare laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of any of our product candidates outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

If we or any contract manufacturers and suppliers we engage fail to comply with environmental, health, and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We and any contract manufacturers and suppliers we engage are subject to numerous federal, state, and local environmental, health, and safety laws, regulations, and permitting requirements, including those governing laboratory procedures; the generation, handling, use, storage, treatment, and disposal of hazardous and regulated materials and wastes; the emission and discharge of hazardous materials into the ground, air, and water; and employee health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. Under certain environmental laws, we could be held responsible for costs relating to any contamination at our current or past facilities and at third-party facilities. We also could incur significant costs associated with civil or criminal fines and penalties.

Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research, product development and manufacturing efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty, and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Our business activities may be subject to the Foreign Corrupt Practices Act, or FCPA, and similar anti-bribery and anti-corruption laws.

Our business activities may be subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate, including the U.K. Bribery Act. The FCPA generally prohibits offering, promising, giving, or authorizing others to give anything of value, either

directly or indirectly, to a non-U.S. government official in order to influence official action, or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the health care providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers are subject to regulation under the FCPA. Recently the Securities and Exchange Commission, or SEC, and Department of Justice have increased their FCPA enforcement activities with respect to biotechnology and pharmaceutical companies. There is no certainty that all of our employees, agents, contractors, or collaborators, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers, or our employees, the closing down of our facilities, requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs, and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our products in one or more countries and could materially damage our reputation, our brand, our international expansion efforts, our ability to attract and retain employees, and our business, prospects, operating results, and financial condition.

Risks Related to Our Reliance on Third Parties

We expect to depend on collaborations with third parties for the research, development and commercialization of certain of the product candidates we may develop. If any such collaborations are not successful, we may not be able to realize the market potential of those product candidates.

We anticipate seeking third-party collaborators for the research, development, and commercialization of certain of the product candidates we may develop. For example, we have a collaboration with F-star, among others, to further our development of product candidates and to enhance our research efforts directed to better understanding neurodegenerative diseases. Our likely collaborators for any other collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies, biotechnology companies and academic institutions. If we enter into any such arrangements with any third parties, we will likely have shared or limited control over the amount and timing of resources that our collaborators dedicate to the development or potential commercialization of any product candidates we may seek to develop with them. Our ability to generate revenue from these arrangements with commercial entities will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of any collaboration that we enter into.

Collaborations involving our research programs, or any product candidates we may develop, pose the following risks to us:

- collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not properly obtain, maintain, enforce, or defend intellectual property or proprietary rights relating to our product candidates or research programs or may use our proprietary information in such a way as to expose us to potential litigation or other intellectual property related proceedings, including proceedings challenging the scope, ownership, validity and enforceability of our intellectual property;
- collaborators may own or co-own intellectual property covering our product candidates or research programs that results from our collaboration with them, and in such cases, we may

not have the exclusive right to commercialize such intellectual property or such product candidates or research programs;

- we may need the cooperation of our collaborators to enforce or defend any intellectual property we contribute to or that arises out of our collaborations, which may not be provided to us;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development, or commercialization of our product candidates or research programs or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborators may decide to not pursue development and commercialization of any product candidates we develop or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials, or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates or research programs if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- collaborators with marketing and distribution rights to one or more product candidates may not commit sufficient resources to the marketing and distribution of such product candidates;
- we may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control;
- collaborators may undergo a change of control and the new owners may decide to take the collaboration in a direction which is not in our best interest;
- collaborators may become bankrupt, which may significantly delay our research or development programs, or may cause us to lose access to valuable technology, know-how or intellectual property of the collaborator relating to our products, product candidates or research programs;
- key personnel at our collaborators may leave, which could negatively impact our ability to productively work with our collaborators;
- collaborations may require us to incur short and long-term expenditures, issue securities that dilute our stockholders, or disrupt our management and business;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates or our BBB platform technology; and
- collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our development or commercialization program under such collaboration could be delayed, diminished, or terminated.

We may face significant competition in seeking appropriate collaborations. Recent business combinations among biotechnology and pharmaceutical companies have resulted in a reduced number

of potential collaborators. In addition, the negotiation process is time-consuming and complex, and we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop product candidates or bring them to market and generate product revenue.

If we enter into collaborations to develop and potentially commercialize any product candidates, we may not be able to realize the benefit of such transactions if we or our collaborator elects not to exercise the rights granted under the agreement or if we or our collaborator are unable to successfully integrate a product candidate into existing operations and company culture. In addition, if our agreement with any of our collaborators terminates, our access to technology and intellectual property licensed to us by that collaborator may be restricted or terminate entirely, which may delay our continued development of our product candidates utilizing the collaborator's technology or intellectual property or require us to stop development of those product candidates completely. We may also find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. Many of the risks relating to product development, regulatory approval, and commercialization described in this "Risk Factors" section also apply to the activities of our collaborators and any negative impact on our collaborators may adversely affect us.

We expect to rely on third parties to conduct our clinical trials and some aspects of our research and preclinical testing, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research, or testing.

We currently rely and expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions, and clinical investigators, to conduct some aspects of our research and preclinical testing and our clinical trials. Any of these third parties may terminate their engagements with us or be unable to fulfill their contractual obligations. If we need to enter into alternative arrangements, it would delay our product development activities.

Our reliance on these third parties for research and development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with cGCPs for conducting, recording, and reporting the results of clinical trials to assure that data and reported results are credible, reproducible and accurate and that the rights, integrity, and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database within certain timeframes. Failure to do so can result in fines, adverse publicity, and civil and criminal sanctions.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines, or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for any product candidates we may develop and will not be able to, or may be delayed in our efforts to, successfully commercialize our medicines.

We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or

marketing approval of any product candidates we may develop or commercialization of our medicines, producing additional losses and depriving us of potential product revenue.

We contract with third parties for the manufacture of materials for our research programs and preclinical studies and expect to continue to do so for clinical trials and for commercialization of any product candidates that we may develop. This reliance on third parties carries and may increase the risk that we will not have sufficient quantities of such materials, product candidates, or any medicines that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost, which could delay, prevent, or impair our development or commercialization efforts.

We do not have any manufacturing facilities. We currently rely on third-party manufacturers for the manufacture of our materials for preclinical studies and clinical trials and expect to continue to do so for preclinical studies, clinical trials and for commercial supply of any product candidates that we may develop.

We may be unable to establish any further agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- the possible breach of the manufacturing agreement by the third party;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us;
- reliance on the third party for regulatory compliance, quality assurance, safety, and pharmacovigilance and related reporting; and
- the inability to produce required volume in a timely manner and to quality standards.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in clinical holds on our trials, sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocations, seizures or recalls of product candidates or medicines, operating restrictions, and criminal prosecutions, any of which could significantly and adversely affect supplies of our medicines and harm our business, financial condition, results of operations, and prospects.

Any medicines that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply for any of our product candidates. If any one of our current contract manufacturers cannot perform as agreed, we may be required to replace that manufacturer and may incur added costs and delays in identifying and qualifying any such replacement. Furthermore, securing and reserving production capacity with contract manufacturers may result in significant costs.

Our current and anticipated future dependence upon others for the manufacture of any product candidates we may develop or medicines may adversely affect our future profit margins and our ability to commercialize any medicines that receive marketing approval on a timely and competitive basis.

We depend on third-party suppliers for key raw materials used in our manufacturing processes, and the loss of these third-party suppliers or their inability to supply us with adequate raw materials could harm our business.

We rely on third-party suppliers for the raw materials required for the production of our product candidates. Our dependence on these third-party suppliers and the challenges we may face in obtaining adequate supplies of raw materials involve several risks, including limited control over pricing, availability, quality and delivery schedules. As a small company, our negotiation leverage is limited and we are likely to get lower priority than our competitors who are larger than we are. We cannot be certain that our suppliers will continue to provide us with the quantities of these raw materials that we require or satisfy our anticipated specifications and quality requirements. Any supply interruption in limited or sole sourced raw materials could materially harm our ability to manufacture our product candidates until a new source of supply, if any, could be identified and qualified. We may be unable to find a sufficient alternative supply channel in a reasonable time or on commercially reasonable terms. Any performance failure on the part of our suppliers could delay the development and potential commercialization of our product candidates, including limiting supplies necessary for clinical trials and regulatory approvals, which would have a material adverse effect on our business.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for any product candidates we develop or for our BBB platform technology, our competitors could develop and commercialize products or technology similar or identical to ours, and our ability to successfully commercialize any product candidates we may develop, and our technology may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our BBB platform technology and any proprietary product candidates and other technologies we may develop. We seek to protect our proprietary position by in-licensing intellectual property and filing patent applications in the United States and abroad relating to our BBB platform technology, core programs and product candidates, as well as other technologies that are important to our business. Given that the development of our technology and product candidates is at an early stage, our intellectual property portfolio with respect to certain aspects of our technology and product candidates is also at an early stage. For example, we do not own or in-license any issued patents in the United States directed to the composition of matter of any of the antibodies or enzymes that we have thus far developed using our BBB platform technology or that cover the composition of matter of our DNL151 product candidate, which is in our LRRK2 core program. In addition, we do not own or in-license any issued patents covering the Fc domain portion of our BBB platform technology that binds to transferrin receptor, or any issued patents that cover our TREM2, aSyn, or IDS core programs. We have filed or intend to file patent applications on these aspects of our technology and core product candidates; however, there can be no assurance that any such patent applications will issue as granted patents. Furthermore, in some cases, we have only filed provisional patent applications on certain aspects of our technology and product candidates and each of these provisional patent applications is not eligible to become an issued patent until, among other things, we file a non-provisional patent application within 12 months of the filing date of the applicable provisional patent application. Any failure to file a non-provisional patent application within this timeline could cause us to lose the ability to obtain patent protection for the inventions disclosed in the associated provisional patent applications. Furthermore, in some cases, we may not be able to obtain issued claims covering compositions relating to our BBB platform technology, core programs and product candidates, as well as other technologies that are important to our business, and instead may need to rely on filing patent applications with claims covering a method of use and/or method of manufacture for protection of such BBB platform technology, core programs, product candidates and other technologies. There can be no assurance that any such patent applications will issue as granted

patents, and even if they do issue, such patent claims may be insufficient to prevent third parties, such as our competitors, from utilizing our technology. Any failure to obtain or maintain patent protection with respect to our BBB platform technology, core programs and product candidates could have a material adverse effect on our business, financial condition, results of operations, and prospects.

If any of our owned or in-licensed patent applications do not issue as patents in any jurisdiction, we may not be able to compete effectively.

Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our inventions, obtain, maintain, and enforce our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our owned and licensed patents. With respect to both in-licensed and owned intellectual property, we cannot predict whether the patent applications we and our licensors are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors or other third parties.

The patent prosecution process is expensive, time-consuming, and complex, and we may not be able to file, prosecute, maintain, enforce, or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output in time to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors, and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. In addition, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our inventions and the prior art allow our inventions to be patentable over the prior art. Furthermore, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we or our licensors were the first to make the inventions claimed in any of our owned or licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions.

If the scope of any patent protection we obtain is not sufficiently broad, or if we lose any of our patent protection, our ability to prevent our competitors from commercializing similar or identical technology and product candidates would be adversely affected.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights are highly uncertain. Our owned or in-licensed pending and future patent applications may not result in patents being issued which protect our BBB platform technology, product candidates or other technologies or which effectively prevent others from commercializing competitive technologies and product candidates.

Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if patent applications we license or own currently or in the future issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents that we own or in-license may be challenged, narrowed, circumvented, or invalidated by third parties. Consequently, we do not know whether our BBB platform technology, product candidates or other technologies will be protectable or

remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner which could materially adversely affect our business, financial condition, results of operations and prospects.

The issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. We or our licensors may be subject to a third party preissuance submission of prior art to the United States Patent and Trademark Office, or USPTO, or become involved in opposition, derivation, revocation, reexamination, post-grant and *inter partes* review, or interference proceedings or other similar proceedings challenging our owned or licensed patent rights. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable, our owned or in-licensed patent rights, allow third parties to commercialize our BBB platform technology, product candidates or other technologies and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Moreover, we, or one of our licensors, may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge our or our licensor's priority of invention or other features of patentability with respect to our owned or in-licensed patents and patent applications. Such challenges may result in loss of patent rights, loss of exclusivity, or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our BBB platform technology, product candidates and other technologies. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us.

In addition, given the amount of time required for the development, testing, and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Some of our owned and in-licensed patents and patent applications are, and may in the future be, co-owned with third parties. For example, we currently, and may in the future, co-own certain patents and patent applications relating to our BBB platform technology with F-star. In addition, certain of our licensors co-own the patents and patent applications we in-license with other third parties with whom we do not have a direct relationship. Our exclusive rights to certain of these patents and patent applications are dependent, in part, on inter-institutional or other operating agreements between the joint owners of such patents and patent applications, who are not parties to our license agreements. For example, under our license agreement with VIB, we license certain patents and patent applications co-owned by VIB and KU Leuven. Our rights to KU Leuven's interest in such patents and patent applications depends on an operating agreement between VIB and KU Leuven, pursuant to which VIB controls the licensing of such patents and patent applications. If our licensors do not have exclusive control of the grant of licenses under any such third-party co-owners' interest in such patents or patent applications or we are otherwise unable to secure such exclusive rights, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we may need the cooperation of any such co-owners of our patents in order to enforce such patents against third parties, and such cooperation may not be provided to us. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Our rights to develop and commercialize our BBB platform technology and product candidates are subject, in part, to the terms and conditions of licenses granted to us by others.

We are heavily reliant upon licenses to certain patent rights and proprietary technology from third parties that are important or necessary to the development of our BBB platform technology and product candidates. For example, in June 2016, we entered into an exclusive license agreement with Genentech pursuant to which we received an exclusive license to certain of Genentech's intellectual property relating to our LRRK2 program, including our DNL201 and DNL151 product candidates. In March 2017, we entered into an exclusive license agreement with VIB pursuant to which we received exclusive and non-exclusive licenses to certain patent rights and related know-how pertaining to antibodies that target BACE1. In addition, in August 2016, we entered into a collaboration with UK-based F-star, a biopharmaceutical company developing novel bispecific antibodies, focused on research and development of our BBB platform technology. The agreement with F-star includes certain non-exclusive licenses to F-star's modular antibody technology to research and develop certain antibodies, as well as options for us to obtain exclusive rights to develop and commercialize certain antibodies by exercising an option to obtain certain exclusive licenses or to buy-out all of the outstanding shares of F-star Gamma. See the section titled "Business—Licenses and Collaborations—F-star License and Collaboration Agreement" for additional information. However, we will not obtain exclusive rights to commercialize and exploit such antibodies unless we exercise our options to obtain such exclusive rights within specified periods of time. If we do not exercise our options with respect to a particular antibody in a timely manner or at all, or fail to satisfy any conditions upon which our options are contingent, F-star may offer such exclusive rights to other third parties. In addition, F-star may breach our agreement and attempt to license such patents and patent applications to other third parties, including our competitors, before or after we exercise our options. If we are unable to secure exclusive rights to F-star's modular antibody technology to commercialize and exploit our antibodies, our competitive position, business, financial condition, results of operations, and prospects may be materially harmed.

Our agreement with F-star and other license agreements may not provide exclusive rights to use the licensed intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products in the future. For example, F-star retains the right to use itself, and to license to others, its modular antibody technology for any purpose other than the targets and antibodies which we have agreed with F-star would or may be exclusively available to us. As a result, we may not be able to prevent competitors or other third parties from developing and commercializing competitive products that also utilizes technology that we have in-licensed.

In addition, subject to the terms of any such license agreements, we do not have the right to control the preparation, filing, prosecution and maintenance, and we may not have the right to control the enforcement, and defense of patents and patent applications covering the technology that we license from third parties. For example, under our agreements with F-star and Genentech, the licensors control prosecution and, in the case of F-star and in specified circumstances, enforcement of certain of the patents and patent applications licensed to us. We cannot be certain that our in-licensed patents and patent applications that are controlled by our licensors will be prepared, filed, prosecuted, maintained, enforced, and defended in a manner consistent with the best interests of our business. If our licensors fail to prosecute, maintain, enforce, and defend such patents, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated, our right to develop and commercialize our BBB platform technology and any of our product candidates that are subject of such licensed rights could be adversely affected, and we may not be able to prevent competitors from making, using and selling competing products. In addition, even where we have the right to control patent prosecution of patents and patent applications we have licensed to and from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensees, our licensors and their counsel that took place prior to the date upon which we assumed control over patent prosecution.

Furthermore, our owned and in-licensed patents may be subject to a reservation of rights by one or more third parties. For example, our license to certain intellectual property owned by Genentech is subject to certain research rights Genentech granted to third parties prior to our license agreement. In addition, certain of our in-licensed intellectual property relating to RIPK1 was funded in part by the U.S. government. As a result, the U.S. government may have certain rights to such intellectual property. When new technologies are developed with U.S. government funding, the U.S. government generally obtains certain rights in any resulting patents, including a non-exclusive license authorizing the U.S. government to use the invention or to have others use the invention on its behalf. The U.S. government's rights may also permit it to disclose the funded inventions and technology to third parties and to exercise march-in rights to use or allow third parties to use the technology we have licensed that was developed using U.S. government funding. The U.S. government may exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the government-funded technology, or because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U.S. industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States in certain circumstances and if this requirement is not waived. Any exercise by the U.S. government of such rights or by any third party of its reserved rights could have a material adverse effect on our competitive position, business, financial condition, results of operations, and prospects.

If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We have entered into license agreements with third parties and may need to obtain additional licenses from others to advance our research or allow commercialization of product candidates we may develop or our BBB platform technology. It is possible that we may be unable to obtain additional licenses at a reasonable cost or on reasonable terms, if at all. In that event, we may be required to expend significant time and resources to redesign our technology, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates or continue to utilize our existing BBB platform technology, which could harm our business, financial condition, results of operations, and prospects significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our current technology, including our BBB platform technology, manufacturing methods, product candidates, or future methods or products resulting in either an injunction prohibiting our manufacture or future sales, or, with respect to our future sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties, which could be significant.

In addition, each of our license agreements, and we expect our future agreements, will impose various development, diligence, commercialization, and other obligations on us. Certain of our license agreements also require us to meet development timelines, or to exercise commercially reasonable efforts to develop and commercialize licensed products, in order to maintain the licenses. In spite of our efforts, our licensors might conclude that we have materially breached our obligations under such license agreements and might therefore terminate the license agreements, thereby removing or limiting our ability to develop and commercialize products and technology covered by these license agreements. If these in-licenses are terminated, or if the underlying patents fail to provide the intended exclusivity, competitors or other third parties would have the freedom to seek regulatory approval of, and to market, products identical to ours and we may be required to cease our development and commercialization of certain of our product candidates or of our current BBB platform technology. Any

of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Moreover, disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, the agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects.

We may not be able to protect our intellectual property and proprietary rights throughout the world.

Filing, prosecuting, and defending patents on our BBB platform technology, product candidates and other technologies in all countries throughout the world would be prohibitively expensive, and the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as that in the United States. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property and proprietary rights generally. Proceedings to enforce our intellectual property and proprietary rights in foreign jurisdictions could result in substantial costs and divert our efforts and

attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment, and other requirements imposed by government patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees, and various other government fees on patents and applications will be due to be paid to the USPTO and various government patent agencies outside of the United States over the lifetime of our owned or licensed patents and applications. In certain circumstances, we rely on our licensing partners to pay these fees due to U.S. and non-U.S. patent agencies. The USPTO and various non-U.S. government agencies require compliance with several procedural, documentary, fee payment, and other similar provisions during the patent application process. We are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. In some cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in a partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market with similar or identical products or technology, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith America Invents Act, or the America Invents Act, enacted in September 2011, the United States transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013, but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain

that we or our licensors were the first to either (i) file any patent application related to our BBB platform technology, product candidates or other technologies or (ii) invent any of the inventions claimed in our or our licensor's patents or patent applications.

The America Invents Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. These include allowing third party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Therefore, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our owned or in-licensed patent applications and the enforcement or defense of our owned or in-licensed issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

Issued patents covering our BBB platform technology, product candidates and other technologies could be found invalid or unenforceable if challenged in court or before administrative bodies in the United States or abroad.

If we or one of our licensors initiated legal proceedings against a third party to enforce a patent covering our BBB platform technology, product candidates or other technologies, the defendant could counterclaim that such patent is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may raise claims challenging the validity or enforceability of our owned or in-licensed patents before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in the revocation of, cancellation of, or amendment to our patents in such a way that they no longer cover our BBB platform technology, product candidates or other technologies. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we or our licensing partners and the patent examiner were unaware during prosecution. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our BBB platform technology, product candidates or other

technologies. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations, and prospects.

If we do not obtain patent term extension and data exclusivity for any product candidates we may develop, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our owned or in-licensed U.S. patents may be eligible for limited patent term extension under the Hatch-Waxman Act. The Hatch-Waxman Act permit a patent term extension of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar extensions as compensation for patent term lost during regulatory review processes are also available in certain foreign countries and territories, such as in Europe under a Supplementary Patent Certificate. However, we may not be granted an extension in the United States and/or foreign countries and territories because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is shorter than what we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations and prospects could be materially harmed.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

We or our licensors may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in-licensed patents, trade secrets, or other intellectual property as an inventor or co-inventor. For example, we or our licensors may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our BBB platform technology, product candidates or other technologies. Litigation may be necessary to defend against these and other claims challenging inventorship or our or our licensors' ownership of our owned or in-licensed patents, trade secrets or other intellectual property. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our BBB platform technology, product candidates and other technologies. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for our BBB platform technology, product candidates and other technologies, we also rely on trade secrets and confidentiality agreements to protect our unpatented know-how, technology, and other proprietary information and to maintain our competitive position. Trade secrets and know-how can be difficult to protect. We expect our trade secrets and know-how to over time be disseminated within the industry through independent development, the publication of journal articles describing the methodology, and the movement of personnel from academic to industry scientific positions.

We seek to protect these trade secrets and other proprietary technology, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors, and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants as well as train our employees not to bring or use proprietary information or technology from former employers to us or in their work, and remind former employees when they leave their employment of their confidentiality obligations. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. Despite our efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be materially and adversely harmed.

We may not be successful in obtaining, through acquisitions, in-licenses or otherwise, necessary rights to our BBB platform technology, product candidates or other technologies.

We currently have rights to intellectual property, through licenses from third parties, to identify and develop our BBB platform technology and product candidates. Many pharmaceutical companies, biotechnology companies, and academic institutions are competing with us in the field of neurodegeneration and BBB technology and may have patents and have filed and are likely filing patent applications potentially relevant to our business. In order to avoid infringing these third party patents, we may find it necessary or prudent to obtain licenses to such patents from such third party intellectual property holders. We may also require licenses from third parties for certain BBB technologies that we are evaluating for use with our current or future product candidates. In addition, with respect to any patents we co-own with third parties, we may require licenses to such co-owners' interest to such patents. However, we may be unable to secure such licenses or otherwise acquire or in-license any compositions, methods of use, processes, or other intellectual property rights from third parties that we identify as necessary for our current or future product candidates and our BBB platform technology. The licensing or acquisition of third party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may be subject to claims that our employees, consultants, or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.

Many of our employees, consultants, and advisors are currently or were previously employed at universities or other biotechnology or pharmaceutical companies, including our licensors, competitors

and potential competitors. Although we try to ensure that our employees, consultants, and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Third-party claims of intellectual property infringement, misappropriation or other violation against us, our licensors or our collaborators may prevent or delay the development and commercialization of our BBB platform technology, product candidates and other technologies.

The field of discovering treatments for neurodegenerative diseases, especially using BBB technology, is highly competitive and dynamic. Due to the focused research and development that is taking place by several companies, including us and our competitors, in this field, the intellectual property landscape is in flux, and it may remain uncertain in the future. As such, there may be significant intellectual property related litigation and proceedings relating to our owned and in-licensed, and other third party, intellectual property and proprietary rights in the future.

Our commercial success depends in part on our, our licensors' and our collaborators' ability to avoid infringing, misappropriating and otherwise violating the patents and other intellectual property rights of third parties. There is a substantial amount of complex litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, derivation and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. As discussed above, recently, due to changes in U.S. law referred to as patent reform, new procedures including inter partes review and post-grant review have been implemented. As stated above, this reform adds uncertainty to the possibility of challenge to our patents in the future.

Numerous U.S. and foreign issued patents and pending patent applications owned by third parties exist relating to BBB technology and in the fields in which we are developing our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our BBB platform technology, product candidates and other technologies may give rise to claims of infringement of the patent rights of others. We cannot assure you that our BBB platform technology, product candidates and other technologies that we have developed, are developing or may develop in the future will not infringe existing or future patents owned by third parties. We may not be aware of patents that have already been issued and that a third party, for example, a competitor in the fields in which we are developing our BBB platform technology, product candidates, and other technologies might assert are infringed by our current or future BBB platform technology, product candidates or other technologies, including claims to compositions, formulations, methods of manufacture or methods of use or treatment that cover our BBB platform technology, product

candidates or other technologies. It is also possible that patents owned by third parties of which we are aware, but which we do not believe are relevant to our BBB platform technology, product candidates or other technologies, could be found to be infringed by our BBB platform technology, product candidates or other technologies. In addition, because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our BBB platform technology, product candidates or other technologies may infringe.

Third parties may have patents or obtain patents in the future and claim that the manufacture, use or sale of our BBB platform technology, product candidates or other technologies infringes upon these patents. In the event that any third party claims that we infringe their patents or that we are otherwise employing their proprietary technology without authorization and initiates litigation against us, even if we believe such claims are without merit, a court of competent jurisdiction could hold that such patents are valid, enforceable and infringed by our BBB platform technology, product candidates or other technologies. In this case, the holders of such patents may be able to block our ability to commercialize the applicable product candidate or technology unless we obtain a license under the applicable patents, or until such patents expire or are finally determined to be held invalid or unenforceable. Such a license may not be available on commercially reasonable terms or at all. Even if we are able to obtain a license, the license would likely obligate us to pay license fees or royalties or both, and the rights granted to us might be nonexclusive, which could result in our competitors gaining access to the same intellectual property. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, we may be unable to commercialize our BBB platform technology, product candidates or other technologies, or such commercialization efforts may be significantly delayed, which could in turn significantly harm our business.

Defense of infringement claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of management and other employee resources from our business, and may impact our reputation. In the event of a successful claim of infringement against us, we may be enjoined from further developing or commercializing our infringing BBB platform technology, product candidates or other technologies. In addition, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties and/or redesign our infringing product candidates or technologies, which may be impossible or require substantial time and monetary expenditure. In that event, we would be unable to further develop and commercialize our BBB platform technology, product candidates or other technologies, which could harm our business significantly.

Engaging in litigation to defend against third parties alleging that we have infringed, misappropriated or otherwise violated their patents or other intellectual property rights is very expensive, particularly for a company of our size, and time-consuming. Some of our competitors may be able to sustain the costs of litigation or administrative proceedings more effectively than we can because of greater financial resources. Patent litigation and other proceedings may also absorb significant management time. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings against us could impair our ability to compete in the marketplace. The occurrence of any of the foregoing could have a material adverse effect on our business, financial condition or results of operations.

We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, which could be expensive, time consuming, and unsuccessful.

Competitors may infringe our patents or the patents of our licensing partners, or we may be required to defend against claims of infringement. In addition, our patents or the patents of our licensing partners also may become involved in inventorship, priority or validity disputes. To counter or defend against such claims can be expensive and time consuming. In an infringement proceeding, a

court may decide that a patent owned or in-licensed by us is invalid or unenforceable, the other party's use of our patented technology falls under the safe harbor to patent infringement under 35 U.S.C. §271(e)(1), or may refuse to stop the other party from using the technology at issue on the grounds that our owned and in-licensed patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our owned or in-licensed patents at risk of being invalidated or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions, or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors or other third parties may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our business, financial condition, results of operations and prospects.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make products that are similar to our product candidates or utilize similar technology but that are not covered by the claims of the patents that we license or may own;
- we, or our current or future licensors or collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent application that we license or own now or in the future;

- we, or our current or future licensors or collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or licensed intellectual property rights;
- it is possible that our current or future pending owned or licensed patent applications will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors or other third parties;
- our competitors or other third parties might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may harm our business; and
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to Our Operations

We are highly dependent on our key personnel, and if we are not successful in attracting, motivating and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract, motivate and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our management, particularly our Chief Executive Officer, Dr. Ryan Watts, and our scientific and medical personnel. The loss of the services provided by any of our executive officers, other key employees, and other scientific and medical advisors, and our inability to find suitable replacements, could result in delays in the development of our product candidates and harm our business.

We conduct our operations at our facility in South San Francisco, California, in a region that is headquarters to many other biopharmaceutical companies and many academic and research institutions. Competition for skilled personnel is intense and the turnover rate can be high, which may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all. We expect that we may need to recruit talent from outside of our region, and doing so may be costly and difficult.

To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided restricted stock and stock option grants that vest over time. The value to employees of these equity grants that vest over time may be significantly affected by movements in our stock price that are beyond our control, and may at any time be insufficient to counteract more lucrative offers from other companies. Although we have employment agreements with our key employees, these employment agreements provide for at-will employment, which means that any of our employees could leave our employment at any time, with or without notice. We do not maintain “key man” insurance policies on the lives of all of these individuals or the lives of any of our other employees. If we are unable to attract and incentivize quality personnel on acceptable terms, or at all, it may cause our business and operating results to suffer.

We will need to grow the size and capabilities of our organization, and we may experience difficulties in managing this growth.

As of September 30, 2017, we had approximately 125 employees, all of whom were full-time. As our development plans and strategies develop, and as we transition into operating as a public company, we must add a significant number of additional managerial, operational, financial, and other personnel. Future growth will impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, retaining, and motivating additional employees;
- managing our internal development efforts effectively, including the clinical and FDA review process for our current and future product candidates, while complying with our contractual obligations to contractors and other third parties;
- expanding our operational, financial and management controls, reporting systems, and procedures; and
- managing increasing operational and managerial complexity.

Our future financial performance and our ability to continue to develop and, if approved, commercialize our product candidates will depend, in part, on our ability to effectively manage any future growth. Our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to manage these growth activities. Our ability to successfully manage our expected growth is uncertain given the fact that all of our executive officers have joined us since February 2015. This lack of long-term experience working together as a company may adversely impact our senior management team's ability to effectively manage our business and growth.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors and consultants to provide certain services. There can be no assurance that the services of these independent organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by consultants is compromised for any reason, our clinical trials may be extended, delayed, or terminated, and we may not be able to obtain regulatory approval of our product candidates or otherwise advance our business. There can be no assurance that we will be able to manage our existing consultants or find other competent outside contractors and consultants on economically reasonable terms, if at all.

If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop our product candidates and, accordingly, may not achieve our research, development, and commercialization goals.

If we engage in acquisitions or strategic partnerships, this may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities, and subject us to other risks.

We have in the past engaged in acquisitions and we may engage in various acquisitions and strategic partnerships in the future, including licensing or acquiring complementary products, intellectual property rights, technologies, or businesses. Any acquisition or strategic partnership may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of indebtedness or contingent liabilities;

- the issuance of our equity securities which would result in dilution to our stockholders;
- assimilation of operations, intellectual property, products and product candidates of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing product programs and initiatives in pursuing such an acquisition or strategic partnership;
- retention of key employees, the loss of key personnel, and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and regulatory approvals; and
- our inability to generate revenue from acquired intellectual property, technology and/or products sufficient to meet our objectives or even to offset the associated transaction and maintenance costs.

In addition, if we undertake such a transaction, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense.

Our internal computer systems, or those used by our third-party research institution collaborators, CROs or other contractors or consultants, may fail or suffer security breaches.

Despite the implementation of security measures, our internal computer systems and those of our future CROs and other contractors and consultants may be vulnerable to damage from computer viruses and unauthorized access. Although to our knowledge we have not experienced any such material system failure or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed, ongoing or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on our third-party research institution collaborators for research and development of our product candidates and other third parties for the manufacture of our product candidates and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or systems, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidates could be delayed.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations, and those of our third-party research institution collaborators, CROs, CMOs, suppliers, and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics, and other natural or man-made disasters or business interruptions, for which we are partly uninsured. In addition, we rely on our third-party research institution collaborators for conducting research and development of our product candidates, and they may be affected by government shutdowns or withdrawn funding. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We rely on third party manufacturers to produce and process our product candidates. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption.

All of our operations including our corporate headquarters are located in a single facility in South San Francisco, California. Damage or extended periods of interruption to our corporate, development or research facilities due to fire, natural disaster, power loss, communications failure, unauthorized entry or other events could cause us to cease or delay development of some or all of our product candidates. Although we maintain property damage and business interruption insurance coverage on these facilities, our insurance might not cover all losses under such circumstances and our business may be seriously harmed by such delays and interruption.

Our business is subject to economic, political, regulatory and other risks associated with international operations.

Our business is subject to risks associated with conducting business internationally. Some of our suppliers and collaborative relationships are located outside the United States. Accordingly, our future results could be harmed by a variety of factors, including:

- economic weakness, including inflation, or political instability in particular non-U.S. economies and markets;
- differing and changing regulatory requirements in non-U.S. countries;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- difficulties in compliance with non-U.S. laws and regulations;
- changes in non-U.S. regulations and customs, tariffs and trade barriers;
- changes in non-U.S. currency exchange rates and currency controls;
- changes in a specific country's or region's political or economic environment;
- trade protection measures, import or export licensing requirements or other restrictive actions by U.S. or non-U.S. governments;
- negative consequences from changes in tax laws;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- difficulties associated with staffing and managing international operations, including differing labor relations;
- potential liability under the FCPA or comparable foreign laws; and
- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

These and other risks associated with our planned international operations may materially adversely affect our ability to attain profitable operations.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

As of December 31, 2016, we had federal net operating loss carryforwards of approximately $65.4 million, which will begin to expire in 2035. Under Sections 382 and 383 of the United States

Internal Revenue Code of 1986, as amended, or the Code, if a corporation undergoes an "ownership change" (generally defined as a greater than 50-percentage-point cumulative change (by value) in the equity ownership of certain stockholders over a rolling three-year period), the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change taxable income or taxes may be limited. As a result of our most recent private placements and other transactions that have occurred since our incorporation, we may have experienced, and, in connection with this offering, may experience, such an ownership change. We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which are outside our control. As a result, our ability to use our pre-change net operating loss carryforwards and other pre-change tax attributes to offset post-change taxable income or taxes may be subject to limitation.

Risks Related to This Offering and Ownership of Our Common Stock

We do not know whether a market will develop for our common stock or what the market price of our common stock will be, and, as a result, it may be difficult for you to sell your shares of our common stock.

Before this offering, there was no public trading market for our common stock. If a market for our common stock does not develop or is not sustained, it may be difficult for you to sell your shares of common stock at an attractive price or at all. We cannot predict the prices at which our common stock will trade. It is possible that in one or more future periods our results of operations and progression of our product pipeline may not meet the expectations of public market analysts and investors, and, as a result of these and other factors, the price of our common stock may fall.

The market price of our common stock may be volatile, which could result in substantial losses for investors purchasing shares in this offering.

The initial public offering price for our common stock will be determined through negotiations with the underwriters. This initial public offering price may differ from the market price of our common stock after the offering. As a result, you may not be able to sell your common stock at or above the initial public offering price. Some of the factors that may cause the market price of our common stock to fluctuate include:

- the success of existing or new competitive products or technologies;
- the timing and results of clinical trials for our current product candidates and any future product candidates that we may develop;
- commencement or termination of collaborations for our product development and research programs;
- failure or discontinuation of any of our product development and research programs;
- failure to develop our BBB platform technology;
- results of preclinical studies, clinical trials, or regulatory approvals of product candidates of our competitors, or announcements about new research programs or product candidates of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents, or other proprietary rights;
- the recruitment or departure of key personnel;

- the level of expenses related to any of our research programs, clinical development programs, or product candidates that we may develop;
- the results of our efforts to develop additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines, or recommendations by securities analysts;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders, or other stockholders;
- expiration of market standoff or lock-up agreements;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry, and market conditions; and
- the other factors described in this “Risk Factors” section.

In recent years, the stock market in general, and the market for pharmaceutical and biotechnology companies in particular, has experienced significant price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. Broad market and industry factors may seriously affect the market price of our common stock, regardless of our actual operating performance. These fluctuations may be even more pronounced in the trading market for our stock shortly following this offering. Following periods of such volatility in the market price of a company’s securities, securities class action litigation has often been brought against that company. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future. Securities litigation could result in substantial costs and divert management’s attention and resources from our business.

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock will rely in part on the research and reports that industry or financial analysts publish about us or our business. We do not currently have and may never obtain research coverage by industry or financial analysts. If no or few analysts commence coverage of us, the trading price of our stock could decrease. Even if we do obtain analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

A significant portion of our total outstanding shares is restricted from immediate resale but may be sold into the market in the near future, which could cause the market price of our common stock to decline significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, upon the expiration of the market standoff and lock-up agreements, the early release of these agreements, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. After this offering and after giving effect to the conversion of all outstanding shares of our convertible

preferred stock into 60,365,020 shares of our common stock upon the closing of this offering (including 1,764,705 additional shares of our common stock issuable upon conversion of our Series B-2 convertible preferred stock issued after September 30, 2017), we will have 82,423,920 shares of common stock outstanding based on 13,725,567 shares of our common stock outstanding as of September 30, 2017. Of these shares, the 8,333,333 shares we are selling in this offering may be resold in the public market immediately, unless purchased by our affiliates. The remaining 74,090,587 shares, or 89.9% of our outstanding shares after this offering, are currently prohibited or otherwise restricted under securities laws, market standoff agreements entered into by our stockholders with us or lock-up agreements entered into by our stockholders with the underwriters; however, subject to applicable securities law restrictions and excluding shares of restricted stock that will remain unvested, these shares will be able to be sold in the public market beginning 180 days after the date of this prospectus. The representatives may, in their sole discretion, release all or some portion of the shares subject to lock-up agreements at any time and for any reason. In addition, 505,731 shares of unvested restricted stock were issued and outstanding as of September 30, 2017 will become available for sale immediately upon the vesting of such shares, as applicable, and the expiration of any applicable market standoff or lock-up agreements. Shares issued upon the exercise of stock options outstanding under our equity incentive plans or pursuant to future awards granted under those plans will become available for sale in the public market to the extent permitted by the provisions of applicable vesting schedules, any applicable market standoff and lock-up agreements, and Rule 144 and Rule 701 under the Securities Act of 1933, as amended, or the Securities Act. See the section titled “Shares Eligible for Future Sale” for additional information.

Moreover, after this offering, holders of an aggregate of 64,913,502 shares of our common stock will have rights, subject to conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also plan to register all shares of common stock that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance and once vested, subject to volume limitations applicable to affiliates and the lock-up agreements described in the section titled “Underwriting” in this prospectus. If any of these additional shares are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

You will incur immediate and substantial dilution as a result of this offering.

If you purchase common stock in this offering, you will incur immediate and substantial dilution of $13.64 per share, representing the difference between the assumed initial public offering price of $18.00 per share, which is the midpoint of the estimated offering price range set forth on the cover page of this prospectus, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, and our pro forma net tangible book value per share after giving effect to this offering and the automatic conversion of all outstanding shares of our convertible preferred stock upon the closing of this offering. As of September 30, 2017, there were 6,179,687 shares subject to outstanding options with a weighted-average exercise price of $3.06 per share. To the extent that these outstanding options are ultimately exercised or the underwriters exercise their option to purchase additional shares, you will incur further dilution. See the section titled “Dilution” for a further description of the dilution you will experience immediately after this offering.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

We may seek additional capital through a combination of public and private equity offerings, debt financings, strategic partnerships and alliances and licensing arrangements. We, and indirectly, our stockholders, will bear the cost of issuing and servicing such securities. Because our decision to issue

debt or equity securities in any future offering will depend on market conditions and other factors beyond our control, we cannot predict or estimate the amount, timing or nature of any future offerings. To the extent that we raise additional capital through the sale of equity or debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. The incurrence of indebtedness would result in increased fixed payment obligations and could involve restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. Additionally, any future collaborations we enter into with third parties may provide capital in the near term but limit our potential cash flow and revenue in the future. If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms unfavorable to us.

Insiders will continue to have substantial influence over us after this offering, which could limit your ability to affect the outcome of key transactions, including a change of control.

After this offering, our directors, executive officers, holders of more than 5% of our outstanding stock and their respective affiliates will beneficially own shares representing approximately 84.2% of our outstanding common stock. As a result, these stockholders, if they act together, will be able to influence our management and affairs and all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions. This concentration of ownership may have the effect of delaying or preventing a change in control of our company and might affect the market price of our common stock.

Certain of our existing stockholders, including one that beneficially owns more than 5% of our outstanding common stock, have indicated an interest in purchasing an aggregate of $50.0 million or more in shares of our common stock in this offering at the initial public offering price. The previously discussed ownership percentage upon completion of this offering does not reflect the potential purchase of any shares in this offering by such stockholders.

We are an “emerging growth company,” and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For so long as we remain an emerging growth company, we are permitted and plan to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or SOX Section 404, not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor’s report providing additional information about the audit and the financial statements, reduced disclosure obligations regarding executive compensation, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. As a result, the information we provide stockholders will be different than the information that is available with respect to other public companies. In this prospectus, we have not included all of the executive compensation related information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock, and our stock price may be more volatile.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an

emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards, and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

We will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an emerging growth company, we will incur significant legal, accounting, and other expenses that we did not incur as a private company. The SOX, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of NASDAQ, and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. We expect that we will need to hire additional accounting, finance, and other personnel in connection with our becoming, and our efforts to comply with the requirements of being, a public company, and our management and other personnel will need to devote a substantial amount of time towards maintaining compliance with these requirements. These requirements will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that the rules and regulations applicable to us as a public company may make it more difficult and more expensive for us to obtain director and officer liability insurance, which could make it more difficult for us to attract and retain qualified members of our board of directors. We are currently evaluating these rules and regulations and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to SOX Section 404, we will be required to furnish a report by our management on our internal control over financial reporting beginning with our second filing of an Annual Report on Form 10-K with the SEC after we become a public company. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with SOX Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants, adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented, and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by SOX Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

If we are unable to maintain effective internal controls, our business, financial position and results of operations could be adversely affected.

As a public company, we will be subject to reporting and other obligations under the Securities Exchange Act of 1934, as amended, or the Exchange Act, including the requirements of SOX

Section 404, which require annual management assessments of the effectiveness of our internal control over financial reporting. However, our auditors will not be required to formally attest to the effectiveness of our internal control over financial reporting pursuant to SOX Section 404 until we are no longer an emerging growth company if we continue to take advantage of the exemptions available to us through the JOBS Act.

The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation to meet the detailed standards under the rules. During the course of its testing, our management may identify material weaknesses or deficiencies which may not be remedied in time to meet the deadline imposed by the Sarbanes-Oxley Act of 2002. These reporting and other obligations place significant demands on our management and administrative and operational resources, including accounting resources.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the United States. Any failure to maintain effective internal controls could have an adverse effect on our business, financial position and results of operations.

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

We cannot specify with certainty the particular uses of the net proceeds we will receive from this offering. Our management will have broad discretion in the application of the net proceeds, including for any of the purposes described in the section titled “Use of Proceeds” in this prospectus. Our management may spend a portion or all of the net proceeds from this offering in ways that our stockholders may not desire or that may not yield a favorable return. The failure by our management to apply these funds effectively could harm our business, financial condition, results of operations and prospects. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

We do not expect to pay any dividends for the foreseeable future. Investors in this offering may never obtain a return on their investment.

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any dividends to holders of our common stock in the foreseeable future. Instead, we plan to retain any earnings to maintain and expand our existing operations. In addition, any future credit facility may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not purchase our common stock.

Delaware law and provisions in our amended and restated certificate of incorporation and bylaws that will become effective upon the closing of this offering might discourage, delay, or prevent a change in control of our company or changes in our management and, therefore, depress the trading price of our common stock.

Provisions in our amended and restated certificate of incorporation and bylaws that will become effective upon the closing of this offering may discourage, delay, or prevent a merger, acquisition, or other change in control that stockholders may consider favorable, including transactions in which you

might otherwise receive a premium for your shares of our common stock. These provisions may also prevent or frustrate attempts by our stockholders to replace or remove our management. Therefore, these provisions could adversely affect the price of our common stock. Among other things, our charter documents will:

- establish that our board of directors is divided into three classes, Class I, Class II and Class III, with each class serving staggered three year terms;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- provide that our directors may only be removed for cause;
- eliminate cumulative voting in the election of directors;
- authorize our board of directors to issues shares of preferred stock and determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval;
- provide our board of directors with the exclusive right to elect a director to fill a vacancy or newly created directorship;
- permit stockholders to only take actions at a duly called annual or special meeting and not by written consent;
- prohibit stockholders from calling a special meeting of stockholders;
- require that stockholders give advance notice to nominate directors or submit proposals for consideration at stockholder meetings;
- authorize our board of directors, by a majority vote, to amend the bylaws; and
- require the affirmative vote of at least 66 2/3% or more of the outstanding shares of common stock to amend many of the provisions described above.

In addition, Section 203 of the General Corporation Law of the State of Delaware, or DGCL, prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

Any provision of our amended and restated certificate of incorporation, amended and restated bylaws, or Delaware law that has the effect of delaying or preventing a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our capital stock and could also affect the price that some investors are willing to pay for our common stock.

Our amended and restated certificate of incorporation that will become effective upon the closing of this offering provides that the Court of Chancery of the State of Delaware and the federal district courts of the United States of America will be the exclusive forums for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, or employees.

Our amended and restated certificate of incorporation that will become effective upon the closing of this offering provides that the Court of Chancery of the State of Delaware is the exclusive forum for:

- any derivative action or proceeding brought on our behalf;

- any action asserting a claim of breach of fiduciary duty;
- any action asserting a claim against us arising under the DGCL, our amended and restated certificate of incorporation, or our amended and restated bylaws; and
- any action asserting a claim against us that is governed by the internal-affairs doctrine.

Our amended and restated certificate of incorporation further provides that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act.

These exclusive-forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees, which may discourage lawsuits against us and our directors, officers, and other employees. If a court were to find either exclusive-forum provision in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving the dispute in other jurisdictions, which could seriously harm our business.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements. All statements other than statements of historical facts contained in this prospectus, including statements regarding our future results of operations and financial position, business strategy, product candidates, planned preclinical studies and clinical trials, research and development costs, regulatory approvals, timing and likelihood of success, as well as plans and objectives of management for future operations, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that are in some cases beyond our control and may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “would,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “potential” or “continue” or the negative of these terms or other similar expressions. Forward-looking statements contained in this prospectus include, but are not limited to, statements about:

- the success, cost and timing of our development activities, preclinical studies and clinical trials, and in particular the development of our BBB platform technology, core programs and biomarkers;
- the extent to which any dosing limitations that we are subject to may affect the success of our product candidates;
- the impact of pre-clinical findings on our ability to achieve exposures of our product candidates that allow us to explore a robust pharmacodynamic range of these candidates in humans;
- the expected potential benefits of strategic collaboration agreements and our ability to attract collaborators with development, regulatory and commercialization expertise;
- the timing or likelihood of regulatory filings and approvals;
- our ability to obtain and maintain regulatory approval of our product candidates, and any related restrictions, limitations and/or warnings in the label of any approved product candidate;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;
- the terms and conditions of licenses granted to us and our ability to license additional intellectual property relating to our product candidates and BBB platform technology;
- our ability to obtain funding for our operations, including funding necessary to develop and commercialize our product candidates;
- our plans and ability to establish sales, marketing and distribution infrastructure to commercialize any product candidates for which we obtain approval;
- future agreements with third parties in connection with the commercialization of our product candidates;
- the size and growth potential of the markets for our product candidates, if approved for commercial use, and our ability to serve those markets;
- the rate and degree of market acceptance of our product candidates;
- existing regulations and regulatory developments in the United States and foreign countries;

- potential claims relating to our intellectual property and third-party intellectual property;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- the pricing and reimbursement of our product candidates, if approved;
- the success of competing products or platform technologies that are or may become available;
- our ability to attract and retain key managerial, scientific and medical personnel;
- the accuracy of our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our financial performance;
- our expectations regarding the period during which we qualify as an emerging growth company under the JOBS Act; and
- our anticipated use of the proceeds from this offering.

We have based these forward-looking statements largely on our current expectations and projections about our business, the industry in which we operate, and financial trends that we believe may affect our business, financial condition, results of operations and prospects, and these forward-looking statements are not guarantees of future performance or development. These forward-looking statements speak only as of the date of this prospectus and are subject to a number of risks, uncertainties and assumptions described in the section titled “Risk Factors” and elsewhere in this prospectus. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein until after we distribute this prospectus, whether as a result of any new information, future events or otherwise.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and you are cautioned not to unduly rely upon these statements.

MARKET, INDUSTRY AND OTHER DATA

This prospectus contains estimates, projections and other information concerning our industry, our business and the markets for our product candidates. We obtained the industry, market and similar data set forth in this prospectus from our own internal estimates and research and from academic and industry research, publications, surveys and studies conducted by third parties, including governmental agencies. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. While we believe that the data we use from third parties are reliable, we have not separately verified these data. Further, while we believe our internal research is reliable, such research has not been verified by any third party. You are cautioned not to give undue weight to any such information, projections and estimates.

In some cases, we do not expressly refer to the sources from which data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires.

The sources of industry and market data contained in this prospectus are listed below:

(1) *Science*, “RIPK1 Mediates Axonal Degeneration by Promoting Inflammation and Necroptosis in ALS,” Volume 353, Issue 6299, August 5, 2016

(2) The Alzheimer’s Association, “2017 Alzheimer’s Disease Facts and Figures”

(3) The Alzheimer’s Association, “Fact Sheet,” March 2017

(4) The National MPS Society, “MPS II”

(5) The Parkinson’s Disease Foundation, “Statistics on Parkinson’s”

(6) The ALS Association, “Facts You Should Know”

(7) The Michael J. Fox Foundation for Parkinson’s Research, “LRRK2 Kinase Inhibitors of Different Structural Classes Induce Abnormal Accumulation of Lamellar Bodies in Type II Pneumocytes in Non-Human Primates but are Reversible and Without Pulmonary Functional Consequences”

(8) The World Health Organization, “Dementia Fact Sheet,” May 2017

USE OF PROCEEDS

We estimate that the net proceeds from our issuance and sale of 8,333,333 shares of our common stock in this offering will be approximately $136.0 million, assuming an initial public offering price of 18.00 per share, which is the midpoint of the estimated offering price range set forth on the cover page of this prospectus, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional shares in full, we estimate that our net proceeds will be approximately $156.9 million.

A $1.00 increase (decrease) in the assumed initial public offering price of 18.00 per share would increase (decrease) the aggregate net proceeds to us from this offering by approximately $7.8 million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, each increase (decrease) of 1.0 million shares in the number of shares offered by us would increase (decrease) the net proceeds to us from this offering by approximately $16.7 million, assuming that the assumed initial public offering price remains the same, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. We do not expect that a change in the initial public offering price or the number of shares by these amounts would have a material effect on our uses of the proceeds from this offering, although it may accelerate the time at which we will need to seek additional capital.

The principal purposes of this offering are to obtain additional capital to support our operations, establish a public market for our common stock and facilitate our future access to the public capital markets. We currently anticipate that we will use the net proceeds from this offering, together with our existing resources, through 2019 as follows:

- approximately $20 to $25 million to fund the costs of Phase 1 trials in healthy volunteers for each of DNL201 and DNL151 and a Phase 1b study in LRRK2 mutation-carrying Parkinson's disease patients, as well as preparation for a potential future Phase 2 clinical trial;
- approximately $30 to $35 million to fund the costs to advance our RIPK1 program through Phase 1 and early Phase 2 clinical development, substantially represented by the planned Phase 1 clinical trial in healthy volunteers, including a cohort in Alzheimer's disease patients, for DNL747 and a Phase 2a clinical trial in ALS patients and a Phase 2a clinical trial in Alzheimer's disease patients;
- approximately $45 to $50 million to optimize and broaden our ATV and ETV platform technologies and to advance our four core antibody and enzyme replacement programs through preclinical development and IND-enabling activities;
- if we exercise our option to acquire all outstanding shares of F-star Gamma, in the aggregate, approximately $18.0 million to $50.0 million to fund the initial exercise payments; and
- the remainder to fund seed programs, general research and development activities, working capital and other general corporate activities.

We believe opportunities may exist from time to time to expand our current business through license or acquisitions of, or investments in, complementary businesses, products or technologies. While we currently have no agreements or commitments to complete any such transaction at this time, we may use a portion of the net proceeds for these purposes.

The net proceeds from this offering, together with our cash, cash equivalents and marketable securities, will not be sufficient for us to fund any of our product candidates through regulatory approval, and we will need to raise additional capital to complete the development and

commercialization of our product candidates. We expect to finance our incremental cash needs through a combination of equity offerings, debt financings and potential licenses and collaboration agreements. This expected use of net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development, the status of and results from clinical trials, as well as any collaborations that we may enter into with third parties for our programs, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds. We cannot specify with certainty all of the particular uses for the net proceeds to be received upon the closing of this offering.

Pending use of the proceeds as described above, we intend to invest the proceeds in a variety of capital preservation investments, including interest-bearing, investment-grade instruments and U.S. government securities.

DIVIDEND POLICY

We have not declared or paid any cash dividends on our capital stock since our inception. We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future. Payment of future cash dividends, if any, will be at the discretion of our board of directors after taking into account various factors, including our financial condition, operating results, current and anticipated cash needs, the requirements and contractual restrictions of then-existing debt instruments and other factors that our board of directors deems relevant.

CAPITALIZATION

The following table sets forth our cash, cash equivalents and marketable securities and capitalization as of September 30, 2017, as follows:

- on an actual basis;
- on a pro forma basis to reflect (1) the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 60,365,020 shares of common stock upon the closing of this offering (this includes the impact to assets and stockholders' equity of those additional shares issuable upon conversion of our Series B-2 convertible preferred stock) and (2) the filing and effectiveness of our amended and restated certificate of incorporation, which will occur immediately prior to the closing of this offering, as if such conversion had occurred on September 30, 2017; and
- on a pro forma as adjusted basis to further reflect our issuance and sale of 8,333,333 shares of common stock in this offering at an assumed initial public offering price of $18.00 per share, which is the midpoint of the estimated offering price range set forth on the cover page of this prospectus, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this information in conjunction with our consolidated financial statements and the related notes and the sections titled "Selected Consolidated Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" that are included elsewhere in this prospectus.

	As of September 30, 2017		
	Actual	Pro Forma	Pro Forma As Adjusted [1]
	(in thousands, except share and per share amounts)		
Cash, cash equivalents and marketable securities	$ 190,776	$ 220,676	$ 356,676
Convertible preferred stock, par value $0.01 per share; 63,288,466 shares authorized, 58,600,315 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	$ 348,673	$ —	$ —
Stockholder's equity (deficit):			
Preferred stock, par value $0.01 per share; no shares authorized, issued and outstanding, actual; 40,000,000 shares authorized, no shares issued and outstanding, pro forma and pro forma as adjusted	—	—	—
Common stock, par value $0.01 per share; 83,587,362 shares authorized, 13,725,567 shares issued and outstanding, actual; 400,000,000 shares authorized, 74,090,587 shares issued and outstanding, pro forma; 400,000,000 shares authorized, 82,423,920 shares issued and outstanding, pro forma as adjusted	424	1,028	1,111
Additional paid-in capital	13,087	391,056	526,973
Accumulated other comprehensive loss	(237)	(237)	(237)
Accumulated deficit	(168,810)	(168,810)	(168,810)
Total stockholders' equity (deficit)	(155,536)	223,037	359,037
Total capitalization	$ 193,137	$ 223,037	$ 359,037

(1) Each $1.00 increase (decrease) in the assumed initial public offering price of $18.00 per share, which is the midpoint of the estimated offering price range set forth on the cover page of this prospectus, would increase (decrease) our pro forma as adjusted cash, cash equivalents and marketable securities, additional paid-in capital, total stockholders' equity (deficit) and total capitalization by approximately $7.8 million, assuming that the number of shares of common stock offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. Each increase (decrease) of 1.0 million shares in the number of shares of common stock offered by us would increase (decrease) our pro forma as adjusted cash, cash equivalents and marketable securities, additional paid-in capital, total stockholders' equity (deficit) and total capitalization by approximately $16.7 million, assuming the assumed initial public offering price of $18.00 per share, which is the midpoint of the estimated offering price range set forth on the cover page of this prospectus, remains the same, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. The pro forma as adjusted information discussed above is illustrative only and will be adjusted based on the actual public offering price and other terms of this offering determined at pricing.

The number of shares of common stock that will be outstanding after this offering is based on 74,090,587 shares of common stock outstanding as of September 30, 2017 (including our convertible preferred stock on an as-converted basis, as well as 1,764,705 shares of our Series B-2 convertible preferred stock issued after September 30, 2017), and excludes the following:

- 6,179,687 shares of common stock issuable upon exercise of options to purchase shares of our common stock outstanding as of September 30, 2017, at a weighted-average exercise price of $3.06 per share;
- 194,000 shares of common stock issuable upon exercise of options to purchase shares of our common stock that were granted after September 30, 2017, at a weighted-average exercise price of $11.64 per share;
- 81,164 shares of common stock to be issued in connection with our acquisition of Incro Pharmaceuticals;
- 7,328,456 shares of common stock reserved for future issuance under our stock-based compensation plans, consisting of:
  - 118,456 shares of common stock reserved for future issuance under our 2015 Stock Incentive Plan, or 2015 Plan, which shares will be added to the shares to be reserved under our 2017 Equity Incentive Plan, or 2017 Plan;
  - 6,210,000 shares of common stock reserved for future issuance under our 2017 Plan (excluding the 118,456 shares to be transferred from our 2015 Plan), which will become effective in connection with this offering, and any additional shares that become available under our 2017 Plan pursuant to provisions thereof that automatically increase the share reserve under the plan each year, as more fully described in the section titled "Executive Compensation—Employee Benefit and Stock Plans;" and
  - 1,000,000 shares of common stock reserved for future issuance under our 2017 Employee Stock Purchase Plan, or ESPP, which will become effective in connection with this offering, and any additional shares that become available under our ESPP pursuant to provisions thereof that automatically increase the share reserve under the plan each year, as more fully described in the section titled "Executive Compensation—Employee Benefit and Stock Plans."

DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted immediately to the extent of the difference between the initial public offering price per share of our common stock and the pro forma as adjusted net tangible book value per share of our common stock immediately after this offering.

Our historical net tangible book value (deficit) as of September 30, 2017 was $(155.5) million, or $(11.33) per share of our common stock. Our historical net tangible book value (deficit) is the amount of our total tangible assets less our total liabilities and convertible preferred stock, which is not included within our stockholders' equity (deficit). Historical net tangible book value per share represents historical net tangible book value (deficit) divided by the number of shares of our common stock outstanding as of September 30, 2017.

Our pro forma net tangible book value as of September 30, 2017 was $223.0 million, or $3.01 per share of our common stock. Pro forma net tangible book value represents the amount of our total tangible assets less our total liabilities, after giving effect to the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 60,365,020 shares of common stock upon the completion of this offering. This includes the impact to assets and stockholders' equity of 1,764,705 shares issuable upon conversion of our Series B-2 convertible preferred stock. Pro forma net tangible book value per share represents pro forma net tangible book value divided by the total number of shares outstanding as of September 30, 2017, after giving effect to the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 60,365,020 shares of our common stock upon the completion of this offering (including 1,764,705 shares issuable upon conversion of our Series B-2 convertible preferred stock).

After giving further effect to our sale of 8,333,333 shares of common stock in this offering at the assumed initial public offering price of $18.00 per share, which is the midpoint of the estimated offering price range set forth on the cover page of this prospectus, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of September 30, 2017 would have been approximately $359.0 million, or approximately $4.36 per share. This represents an immediate increase in pro forma as adjusted net tangible book value per share of $1.35 to our existing stockholders and an immediate dilution in pro forma as adjusted net tangible book value per share of approximately $13.64 to new investors purchasing common stock in this offering. Dilution per share to new investors purchasing common stock in this offering is determined by subtracting pro forma as adjusted net tangible book value per share after this offering from the assumed initial public offering price per share paid by new investors.

The following table illustrates this dilution on a per share basis:

Assumed initial public offering price per share		$18.00
Historical net tangible book value (deficit) per share as of September 30, 2017	$(11.33)	
Pro forma increase in net tangible book value (deficit) per share as of September 30, 2017	$ 14.34	
Pro forma net tangible book value per share as of September 30, 2017	$ 3.01	
Increase in pro forma as adjusted net tangible book value per share attributable to new investors purchasing shares in this offering	$ 1.35	
Pro forma as adjusted net tangible book value per share after this offering		$ 4.36
Dilution per share to new investors purchasing shares in this offering		$13.64

Each $1.00 increase (decrease) in the assumed initial public offering price of $18.00 per share, which is the midpoint of the estimated offering price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted net tangible book value per share after this offering by $0.09 per share and the dilution to new investors purchasing common stock in this offering by $0.91 per share, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. An increase of 1.0 million shares in the number of shares offered by us would increase the pro forma as adjusted net tangible book value per share after this offering by $0.15 and decrease the dilution per share to new investors participating in this offering by $0.15, assuming no change in the assumed initial public offering price and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. A decrease of 1.0 million shares in the number of shares offered by us would decrease the pro forma as adjusted net tangible book value per share after this offering by $0.15 and increase the dilution per share to new investors participating in this offering by $0.15, assuming no change in the assumed initial public offering price and after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

If the underwriters exercise their option to purchase 1,250,000 additional shares of common stock in this offering in full at the assumed initial public offering price of $18.00 per share, which is the midpoint of the estimated offering price range set forth on the cover of this prospectus, and assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, the pro forma as adjusted net tangible book value per share after this offering would be $0.19 per share, and the dilution in pro forma as adjusted net tangible book value per share to new investors purchasing common stock in this offering would be $0.19 per share.

The following table summarizes, on a pro forma as adjusted basis, as of September 30, 2017, the number of shares of common stock purchased from us on an as converted to common stock basis (including 1,764,705 shares issuable upon conversion of our Series B-2 convertible preferred stock), the total consideration paid, or to be paid, and the weighted-average price per share paid, or to be paid, by existing stockholders and by new investors in this offering at the assumed initial public offering price of $18.00 per share, which is the midpoint of the estimated offering price range set forth on the cover page of this prospectus, before deducting underwriting discounts and commissions and estimated offering expenses payable by us.

	Shares Purchased		Total Consideration		Weighted Average Price Per Share
	Number	Percent	Amount	Percent	
Existing stockholders before this offering	74,090,587	90%	$381,051	74%	$ 5.14
Investors participating in this offering	8,333,333	10	136,000	26	16.32
Total	82,423,920	100%	$517,051	100%	

The table above assumes no exercise of the underwriters' option to purchase 1,250,000 additional shares in this offering. If the underwriters' option to purchase additional shares is exercised in full, the number of shares of our common stock held by existing stockholders would be reduced to 89% of the total number of shares of our common stock outstanding after this offering, and the number of shares of common stock held by new investors participating in the offering would be increased to 11% of the total number of shares outstanding after this offering.

Each $1.00 increase (decrease) in the assumed initial public offering price of $18.00 per share, which is the midpoint of the estimated offering price range set forth on the cover page of this

prospectus, would increase (decrease) the total consideration paid by new investors by $8.3 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same. An increase (decrease) of 1.0 million shares in the number of shares offered by us would increase (decrease) the total consideration paid by new investors by $18.0 million, assuming no change in the assumed initial public offering price.

The number of shares of common stock that will be outstanding after this offering is based on 74,090,587 shares of common stock outstanding as of September 30, 2017 (including convertible preferred stock on an as-converted basis, as well as 1,764,705 shares of our Series B-2 convertible preferred stock issued after September 30, 2017), and excludes the following:

- 6,179,687 shares of common stock issuable upon exercise of options to purchase shares of our common stock outstanding as of September 30, 2017, at a weighted-average exercise price of $3.06 per share;
- 194,000 shares of common stock issuable upon exercise of options to purchase shares of our common stock that were granted after September 30, 2017, at a weighted-average exercise price of $11.64 per share;
- 81,164 shares of common stock to be issued in connection with our acquisition of Incro Pharmaceuticals;
- 7,328,456 shares of common stock reserved for future issuance under our stock-based compensation plans, consisting of:
    - 118,456 shares of common stock reserved for future issuance under our 2015 Plan, which shares will be added to the shares to be reserved under our 2017 Plan;
    - 6,210,000 shares of common stock reserved for future issuance under our 2017 Plan (excluding the 118,456 shares to be transferred from our 2015 Plan), which will become effective in connection with this offering, and any additional shares that become available under our 2017 Plan pursuant to provisions thereof that automatically increase the share reserve under the plan each year, as more fully described in the section titled “Executive Compensation—Employee Benefit and Stock Plans;” and
    - 1,000,000 shares of common stock reserved for future issuance under our ESPP, which will become effective in connection with this offering, and any additional shares that become available under our ESPP pursuant to provisions thereof that automatically increase the share reserve under the plan each year, as more fully described in the section titled “Executive Compensation—Employee Benefit and Stock Plans.”

Certain of our existing stockholders, including one that beneficially owns more than 5% of our outstanding common stock, have indicated an interest in purchasing an aggregate of $50.0 million or more in shares of our common stock in this offering at the initial public offering price. The foregoing discussion does not reflect the potential purchase of any shares in this offering by these existing stockholders.

To the extent that any outstanding options are exercised or new options are issued under the equity benefit plans, or we issue additional shares of common stock or convertible securities in the future, there will be further dilution to investors participating in this offering.

SELECTED CONSOLIDATED FINANCIAL DATA

The following tables summarize our selected consolidated financial data for the periods and as of the dates indicated. We have derived our selected consolidated statements of operations and comprehensive loss data for the years ended December 31, 2015 and 2016, and the consolidated balance sheets data as of December 31, 2015 and 2016, from our audited consolidated financial statements and related notes included elsewhere in this prospectus. We have derived the selected consolidated statements of operations and comprehensive loss data for the nine months ended September 30, 2016 and 2017, and the consolidated balance sheet data as of September 30, 2017, from our unaudited interim condensed consolidated financial statements and related notes included elsewhere in this prospectus. The unaudited interim condensed consolidated financial statements have been prepared on the same basis as the audited consolidated financial statements and reflect, in the opinion of management, all adjustments, which include only normal, recurring adjustments that are necessary to present fairly the unaudited interim condensed consolidated financial statements. Our historical results are not necessarily indicative of the results that may be expected in the future, and the results for the nine months ended September 30, 2017, are not necessarily indicative of results to be expected for the full year or any other period. You should read the consolidated financial and other data below in conjunction with the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and related notes included elsewhere in this prospectus.

	Year Ended December 31,		Nine Months Ended September 30,	
	2015	2016	2016	2017
	(in thousands, except share and per share amounts)			
Consolidated Statements of Operations and Comprehensive Loss Data:				
Operating expenses:				
Research and development	$ 11,571	$ 75,702	$ 58,972	$ 55,989
General and administrative	5,108	11,731	8,685	10,611
Total operating expenses	16,679	87,433	67,657	66,600
Loss from operations	(16,679)	(87,433)	(67,657)	(66,600)
Interest income (expense), net	(109)	781	359	1,302
Net loss	(16,788)	(86,652)	(67,298)	(65,298)
Other comprehensive income (loss)	—	(373)	(131)	136
Comprehensive loss	$ (16,788)	$ (87,025)	$ (67,429)	$ (65,162)
Net loss per share, basic and diluted (1)	$ (5.58)	$ (13.49)	$ (11.43)	$ (6.77)
Weighted average number of shares outstanding, basic and diluted (1)	3,006,379	6,424,720	5,888,385	9,643,686
Pro forma net loss per share, basic and diluted (unaudited) (1)		$ (1.77)		$ (0.96)
Pro forma weighted-average common shares outstanding, basic and diluted (unaudited) (1)		48,924,244		68,244,028

(1) See the consolidated statements of operations and Note 12 to our consolidated financial statements, and the condensed consolidated statements of operations and Note 9 to our unaudited condensed consolidated financial statements, for further details on the calculation of net

loss per share, basic and diluted, and the weighted-average number of shares used in the computation of the per share amounts and unaudited pro forma information.

	As of December 31,		As of September 30,
	2015	2016	2017
	(in thousands)		
Consolidated Balance Sheets Data:			
Cash, cash equivalents and marketable securities	$ 30,740	$ 250,911	$ 190,776
Working capital (1)	29,950	172,849	178,089
Total assets	36,683	271,067	210,309
Total liabilities	4,009	16,548	17,172
Convertible preferred stock	48,308	348,673	348,673
Accumulated deficit	(16,860)	(103,512)	(168,810)
Total stockholders' deficit	(15,634)	(94,154)	(155,536)

(1) We define working capital as current assets less current liabilities. See our consolidated financial statements and condensed consolidated financial statements for further details regarding our current assets and current liabilities.

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with the section titled "Selected Consolidated Financial Data" and our consolidated financial statements and the related notes to those statements included elsewhere in this prospectus. This discussion and analysis and other parts of this prospectus contain forward-looking statements based upon current beliefs, plans and expectations related to future events and our future financial performance that involve risks, uncertainties and assumptions, such as statements regarding our intentions, plans, objectives, expectations, forecasts and projections. Our actual results and the timing of selected events could differ materially from those anticipated in these forward-looking statements as a result of several factors, including those set forth under the section titled "Risk Factors" and elsewhere in this prospectus. You should carefully read the "Risk Factors" to gain an understanding of the important factors that could cause actual results to differ materially from our forward-looking statements. Please also see the section titled "Special Note Regarding Forward-Looking Statements."

Overview

Our goal is to discover and develop therapeutics to defeat degeneration.

Our strategy is guided by three overarching principles:

- **Genetic Pathway Potential**: We select our therapeutic targets and disease pathways based on genes that, when mutated, cause, or are major risk factors for, neurodegenerative diseases, which we refer to as degenogenes.
- **Engineering Brain Delivery**: We engineer our product candidates to cross the BBB and act directly in the brain.
- **Biomarker-Driven Development**: We discover, develop and utilize biomarkers to select the right patient population and demonstrate target engagement, pathway engagement and impact on disease progression of our product candidates.

Our total portfolio currently consists of eleven programs. To prioritize the allocation of our resources, we designate certain programs as core programs and others as seed programs, and we currently have six core programs and five seed programs. Our core programs are at various stages of clinical and preclinical development. Our most advanced core programs are our LRRK2 inhibitor program to address Parkinson's disease and our RIPK1 inhibitor program to address Alzheimer's disease and ALS. The two most advanced product candidates in our LRRK2 program, DNL201 and DNL151, are potent, selective and brain penetrant small molecule LRRK2 inhibitor product candidates for Parkinson's disease. DNL201 is currently in a Phase 1 clinical trial in healthy volunteers in the United States. DNL151 has completed IND-enabling preclinical studies. We submitted a CTA for DNL151 to the Netherlands Health Authority in October 2017 and it was accepted in November 2017. The most advanced product candidate in our RIPK1 inhibitor program, DNL747, is a potent, selective and brain penetrant small molecule RIPK1 inhibitor product candidate for ALS and Alzheimer's disease. DNL747 is in IND-enabling preclinical studies and we plan to submit a CTA in early 2018.

We have also developed proprietary drug delivery platform technology designed to deliver large molecules across the BBB. We are currently optimizing and broadening this platform technology. Our ATV and ETV platforms are modular BBB delivery technologies for large molecule therapeutics, including antibodies, enzyme and other proteins. We plan to have multiple product candidates that utilize our ATV or ETV platforms enter clinical development in 2019 and 2020, including molecules targeting aSyn, IDS, TREM2, BACE1 and Tau.

To complement our internal capabilities, we have entered into arrangements with biopharmaceutical companies, patient-focused data companies, numerous leading academic institutions and foundations to gain access to new product candidates, enable and accelerate the development of our existing programs and deepen our scientific understanding of certain areas of biology. We rely on third-party contract manufacturers to manufacture and supply our preclinical and clinical materials to be used during the development of our product candidates. We currently do not need commercial manufacturing capacity.

Since we commenced operations in May 2015, we have devoted substantially all of our resources to discovering, acquiring and developing product candidates, building our BBB platform technology and assembling our core capabilities in neurodegenerative disease pathways. Key operational and financing milestones include:

- In May 2015, we commenced operations and began assembling a team with deep scientific, clinical, business and leadership experience and expertise.
- In May 2015, we entered into a preferred stock purchase agreement, which was subsequently amended, pursuant to which we raised aggregate proceeds of $219.3 million from issuances of our Series A-1 convertible preferred stock and Series A-2 convertible preferred stock in multiple closings between May 2015 and June 2016.
- In June 2015, in order to acquire certain patent rights and a product candidate, we acquired Incro Pharmaceuticals, or Incro, for $1.5 million, which consisted of $0.9 million in assumed liabilities and $0.6 million in shares of our common stock. In September 2016, following the satisfaction of certain milestones, we issued an additional $5.3 million in shares of common stock in connection with this acquisition.
- In June 2016, we entered into an exclusive license agreement with Genentech for the rights to certain patents, other intellectual property and a product candidate to expand and further progress our LRRK2 program.
- In June 2016, we amended our preferred stock purchase agreement, pursuant to which we raised an additional $130.0 million in proceeds from issuances of our Series B-1 convertible preferred stock in multiple closings between June 2016 and August 2016.
- In August 2016, we entered into a license and collaboration agreement with F-star. The goal of the collaboration is the development of certain constant Fc domains of an antibody with non-native antigen binding activity, or Fcabs, to enhance delivery of therapeutics across the BBB into the brain. In connection with the entry into the license and collaboration agreement, we purchased an option to acquire all outstanding shares of F-star Gamma pursuant to a pre-negotiated buy-out option agreement.
- In April 2017, we filed an IND with the FDA for our most advanced therapeutic product candidate, DNL201, and we initiated a Phase 1 clinical trial of DNL201 in healthy volunteers in the United States in June 2017.
- In November 2017, we further amended our preferred stock purchase agreement, pursuant to which we raised an additional $30.0 million in gross proceeds from issuances of our Series B-2 convertible preferred stock in multiple closings.

We do not have any products approved for sale and have not generated any product revenue since our inception. To date, we have funded our operations primarily with proceeds from the sale and issuance of convertible preferred stock. From our inception through September 30, 2017, we have raised aggregate cash proceeds of $349.3 million from the issuance of our convertible preferred stock.

We have incurred significant operating losses to date and expect to continue to incur operating losses for the foreseeable future. Our ability to generate product revenue will depend on the successful

development and eventual commercialization of one or more of our product candidates. Our net losses were $86.7 million and $16.8 million for the years ended December 31, 2016 and 2015, respectively, and $65.3 million for the nine months ended September 30, 2017. As of September 30, 2017, we had an accumulated deficit of $168.8 million. We expect to continue to incur significant expenses and operating losses as we advance our LRRK2 and RIPK1 programs through preclinical and clinical trials; broaden and improve our BBB platform technology; acquire, discover, validate and develop additional product candidates; obtain, maintain, protect and enforce our intellectual property portfolio; and hire additional personnel. In addition, upon the completion of this offering we expect to incur additional costs associated with operating as a public company.

License and Collaboration Agreements

F-star

On August 24, 2016, we entered into a License and Collaboration Agreement, or the Collaboration Agreement, with F-star. The goal of the collaboration is the development of Fcabs to enhance delivery of therapeutics across the BBB into the brain. The collaboration leverages F-star's modular antibody technology and our expertise in the development of therapies for neurodegenerative diseases.

Under the terms of the Collaboration Agreement, we can nominate up to three Fcab targets, or Accepted Fcab Targets, within the first three years of the date of the Collaboration Agreement; and we have selected TfR as the first Accepted Fcab Target. With respect to each Accepted Fcab Target, we can nominate up to eight Fab targets, or Accepted Fab Targets, which are targets bound by the variable domains of an antibody or other therapeutic modalities, or Fabs. Under the terms of the Collaboration Agreement, we paid F-star Gamma an upfront fee of $5.5 million, which includes selection of the first Accepted Fcab Target under the Collaboration Agreement. We are obligated to pay a one-time fixed fee in the low single-digit millions for each additional Accepted Fcab Target we select, technical milestone payments for each Accepted Fcab Target, up to a maximum of $15.0 million in the aggregate for all Accepted Fcab Targets, and, at specified times, monthly exclusivity fees for Accepted Fcab Targets and Accepted Fab Targets, which may be eliminated in certain circumstances. We are also responsible for certain research costs incurred by F-star in conducting activities under each agreed development plan, for up to 24 months. These research costs for the agreed TfR development plan will be up to $2.1 million.

In connection with the entry into the Collaboration Agreement, we also purchased an option for an upfront option fee of $0.5 million, or the buy-out option, to acquire all of the outstanding shares of F-star Gamma pursuant to a pre-negotiated buy-out option agreement, or the Option Agreement. If we exercise this buy-out option, we will be required to make initial exercise payments ranging from, in the aggregate, approximately $18.0 million to $50.0 million, plus a payment for the estimated net cash held by F-star Gamma at the time of such exercise. In addition to these initial exercise payments, we would be required to make certain contingent payments upon the achievement of certain preclinical, clinical, regulatory and commercial milestones, up to a maximum amount of $447.0 million in the aggregate. The amount of the initial exercise and contingent payments varies based on whether F-star delivers an Fcab that meets pre-defined criteria, whether the Fcab has been identified solely by us or solely by F-star or jointly by us and F-star and the timing of our exercise of the buy-out option. Following exercise of the buy-out option, we will not be required to make any further milestone or royalty payments under the Collaboration Agreement.

We recognized the entire $5.5 million upfront fee in research and development expense for the year ended December 31, 2016. We recognized an additional $0.3 million of research and development expense related to the funding of F-star Gamma research costs during the year ended December 31, 2016.

Genentech

On June 17, 2016, we entered into an Exclusive License Agreement with Genentech. The agreement gives us access to Genentech's preclinical stage LRRK2 small molecule program, which can be used to enhance and further progress our in-house LRRK2 program for Parkinson's disease. As consideration, we paid an upfront fee of $8.5 million and a technology transfer fee of $1.5 million, both of which are included in research and development expense for the year ended December 31, 2016 as there is no alternative future use of the rights acquired in other research and development projects.

We may owe Genentech milestone payments upon the achievement of certain development, regulatory, and commercial milestones, up to a maximum of $315.0 million in the aggregate, as well as royalties on net sales of licensed products ranging from low to high single-digit percentages, with the exact royalty rate dependent on various factors, including (i) whether the compound incorporated in the relevant licensed product is a Genentech-provided compound or a compound acquired or developed by us, (ii) the date a compound was first discovered, derived or optimized by us, (iii) the existence of patent rights covering the relevant licensed product in the relevant country, (iv) the existence of orphan drug exclusivity covering a licensed product that is a Genentech-provided compound and (v) the level of annual net sales of the relevant licensed product. We also have the right to credit a certain amount of third-party royalty and milestone payments against royalty and milestone payments owed to Genentech, up to a maximum reduction of fifty percent. The first clinical milestone of $2.5 million became due upon first patient dosing in the Phase 1 clinical trial for DNL201. The full amount was recognized in research and development expense in the nine months ended September 30, 2017.

Unless earlier terminated, the agreement with Genentech will continue in effect until all of our royalty and milestone payment obligations to Genentech expire. Following expiration of the agreement, we will retain the licenses under the intellectual property Genentech licensed to us on a non-exclusive, royalty-free basis.

Components of Operating Results

Operating Expenses

Research and Development

Research and development activities account for a significant portion of our operating expenses. We record research and development expenses as incurred. Research and development expenses incurred by us for the discovery and development of our product candidates and BBB platform technology include:

- external research and development expenses, including:
  - expenses incurred under arrangements with third parties, such as CROs, preclinical testing organizations, CMOs, academic and non-profit institutions and consultants;
  - expenses to acquire technologies to be used in research and development that have not reached technological feasibility and have no alternative future use;
  - fees related to our license and collaboration agreements;
- personnel related expenses, including salaries, benefits and non-cash stock-based compensation expense; and
- other expenses, which include direct and allocated expenses for laboratory, facilities and other costs.

A portion of our research and development expenses are direct external expenses, which we track on a program-specific basis once a program has commenced a late-stage IND-enabling study.

Program expenses include expenses associated with our most advanced product candidates and the discovery and development of backup or next-generation molecules. We also track external expenses associated with our BBB platform technology. All external costs associated with earlier stage programs, or that benefit the entire portfolio, are tracked as a group. We do not track personnel or other operating expenses incurred for our research and development programs on a program-specific basis. These expenses primarily relate to salaries and benefits, stock-based compensation, facility expenses including depreciation and lab consumables.

At this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the development of, and obtain regulatory approval for, any of our product candidates. We are also unable to predict when, if ever, material net cash inflows will commence from sales or licensing of our product candidates. This is due to the numerous risks and uncertainties associated with drug development, including the uncertainty of:

- our ability to add and retain key research and development personnel;
- our ability to establish an appropriate safety profile with IND-enabling toxicology studies;
- our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize, our product candidates;
- our successful enrollment in and completion of clinical trials;
- the costs associated with the development of any additional product candidates we identify in-house or acquire through collaborations;
- our ability to discover, develop and utilize biomarkers to demonstrate target engagement, pathway engagement and the impact on disease progression of our molecules;
- our ability to establish agreements with third-party manufacturers for clinical supply for our clinical trials and commercial manufacturing, if our product candidates are approved;
- the terms and timing of any collaboration, license or other arrangement, including the terms and timing of any milestone payments thereunder;
- our ability to obtain and maintain patent, trade secret and other intellectual property protection and regulatory exclusivity for our product candidates if and when approved;
- our receipt of marketing approvals from applicable regulatory authorities;
- our ability to commercialize products, if and when approved, whether alone or in collaboration with others; and
- the continued acceptable safety profiles of the product candidates following approval.

A change in any of these variables with respect to the development of any of our product candidates would significantly change the costs, timing and viability associated with the development of that product candidate. We expect our research and development expenses to increase at least over the next several years as we continue to implement our business strategy, advance our current programs, expand our research and development efforts, seek regulatory approvals for any product candidates that successfully complete clinical trials, access and develop additional product candidates and incur expenses associated with hiring additional personnel to support our research and development efforts. In addition, product candidates in later stages of clinical development generally incur higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials.

General and Administrative

General and administrative expenses include personnel related expenses, such as salaries, benefits, travel and non-cash stock-based compensation expense, expenses for outside professional

services and allocated expenses. Outside professional services consist of legal, accounting and audit services and other consulting fees. Allocated expenses consist of rent expenses related to our office and research and development facility not otherwise included in research and development expenses.

We expect to incur additional expenses as a result of operating as a public company, including expenses related to compliance with the rules and regulations of the SEC and those of any national securities exchange on which our securities are traded, additional insurance expenses, investor relations activities and other administrative and professional services. We also expect to increase our administrative headcount when operating as a public company and as we advance our product candidates through clinical development, which will also likely require us to increase our general and administrative expenses.

Interest Income (Expense), Net

Interest income (expense), net, consists primarily of interest income and investment income earned on our cash, cash equivalents and marketable securities.

Results of Operations

Comparison of the Nine Months Ended September 30, 2016 and 2017

The following table sets forth the significant components of our results of operations (in thousands):

	Nine Months Ended September 30,		
	2016	2017	Change
Operating expenses:			
Research and development	$ 58,972	$ 55,989	$(2,983)
General and administrative	8,685	10,611	1,926
Total operating expenses	67,657	66,600	(1,057)
Loss from operations	(67,657)	(66,600)	1,057
Interest income, net	359	1,302	943
Net loss	$(67,298)	$(65,298)	$ 2,000

Research and development expenses. Research and development expenses were $59.0 million for the nine months ended September 30, 2016 compared to $56.0 million for the nine months ended September 30, 2017.

The following table summarizes our research and development expenses (in thousands):

	Nine Months Ended September 30,		
	2016	2017	Change
LRRK2 program external expenses (1)	$14,458	$11,803	$(2,655)
RIPK1 program external expenses (2)	15,611	7,379	(8,232)
BBB platform external expenses (3)	7,292	2,655	(4,637)
Other external research and development expenses	5,308	7,663	2,355
Personnel related expenses (4)	10,479	16,713	6,234
Other unallocated research and development expenses	5,824	9,776	3,952
Total research and development expenses	$58,972	$55,989	$(2,983)

(1) Payments under the license agreement with Genentech for an upfront payment and technology transfer fee totaling $10.0 million and a milestone payment of $2.5 million are included in the amounts for the nine months ended September 30, 2016 and 2017, respectively.
(2) The amount for the nine months ended September 30, 2016 includes $5.3 million in expenses related to contingent stock consideration issued in connection with our acquisition of Incro.
(3) The amount for the nine months ended September 30, 2016 includes $5.5 million in expenses related to a payment made under our license and collaboration agreement with F-star.
(4) Personnel related expenses include stock-based compensation expense of $1.6 million for the nine months ended September 30, 2016 and $1.9 million for the nine months ended September 30, 2017, reflecting an increase of $0.3 million.

The decrease in total research and development expenses of $3.0 million was primarily attributable to an $8.2 million decrease in RIPK1 program external expenses and a $4.6 million decrease in BBB platform external expenses. The decrease in RIPK1 is primarily due to the $5.3 million in upfront expenses incurred in the nine months ended September 30, 2016 related to contingent consideration in connection with our acquisition of Incro, and the termination of the clinical trial for DNL104 in April 2017. The decrease in BBB platform expenses is due to the payment of $5.5 million made under our license and collaboration agreement with F-star in the nine months ended September 30, 2016.

These decreases were partially offset by a $6.2 million increase in personnel related expenses due to an increase in our research and development headcount and a $4.0 million increase in other unallocated research and development expenses. The increase in other unallocated research and development expenses consisted of an increase in lab consumable expenses of $1.9 million and an increase in facilities related expenses of $2.1 million, attributable to increases in research and development headcount and the move to our new headquarters in August 2016 which allowed us to significantly increase our lab space capacity.

General and administrative expenses. General and administrative expenses were $8.7 million for the nine months ended September 30, 2016 compared to $10.6 million for the nine months ended September 30, 2017. The increase of $1.9 million was primarily attributable to a $0.8 million increase in patent expenses and professional services to support our ongoing operations and $0.2 million related to increased facilities expenses attributable to general and administrative expenses resulting from the move to our new headquarters in August 2016.

Interest income, net. Interest income, net was $0.4 million for the nine months ended September 30, 2016 compared to $1.3 million for the nine months ended September 30, 2017. We began investing our excess cash in marketable securities in June 2016. As such, the increase of $0.9 million reflects that the nine months ended September 30, 2016 includes less than four months of income from marketable securities, compared to the nine months ended September 30, 2017, which includes nine months of income from marketable securities.

Comparison of the Years Ended December 31, 2015 and 2016

The following table sets forth the significant components of our results of operations (in thousands):

	Year Ended December 31,		
	2015	2016	Change
Operating expenses:			
Research and development	$ 11,571	$ 75,702	$ 64,131
General and administrative	5,108	11,731	6,623
Total operating expenses	16,679	87,433	70,754
Loss from operations	(16,679)	(87,433)	(70,754)
Interest income (expense), net	(109)	781	890
Net loss	$(16,788)	$(86,652)	$(69,864)

Research and development expenses. Research and development expenses were $11.6 million for the year ended December 31, 2015 compared to $75.7 million for the year ended December 31, 2016.

The following table summarizes our research and development expenses (in thousands):

	Year Ended December 31,		
	2015	2016	Change
LRRK2 program external expenses (1)	$ 777	$ 16,770	$ 15,993
RIPK1 program external expenses (2)	2,256	19,106	16,850
BBB platform external expenses (3)	33	8,016	7,983
Other external research and development expenses	3,305	8,020	4,715
Personnel related expenses (4)	2,943	14,974	12,031
Other unallocated research and development expenses	2,257	8,816	6,559
Total research and development expenses	$ 11,571	$ 75,702	$ 64,131

(1) The amount for the year ended December 31, 2016 includes an upfront payment and technology transfer license payment to Genentech totaling $10.0 million.

(2) The amount for the years ended December 31, 2015 and 2016 include $1.5 million and $5.3 million in expenses related to initial and contingent stock consideration, respectively, both issued in connection with our acquisition of Incro.

(3) The amount for the year ended December 31, 2016 includes $5.5 million in expenses related to a payment made under our license and collaboration agreement with F-star.

(4) Personnel related expenses include stock-based compensation expense of $0.1 million in 2015 and $2.1 million in 2016, with the increase driven by higher headcount and a higher estimated fair value of our common stock.

The increase in research and development expenses of $64.1 million is a result of several factors. The increase was attributable to a $16.9 million increase in our RIPK1 program external expenses, a $16.0 million increase in our LRRK2 program external expenses, an $8.0 million increase in our BBB platform technology external expenses and a $12.0 million increase in personnel related expenses. In addition, the increase reflects the fact that the expenses in the year ended December 31, 2015 only include seven months of operations, as we commenced operations in May 2015.

The increase in our RIPK1 program external expenses is primarily attributable to the increased fair value and number of shares of our common stock issued during 2016 to former shareholders of Incro as contingent consideration for our acquisition of Incro, as well as the expenses incurred for the preparation for and initiation of the DNL104 Phase 1 clinical trial. The increase in our LRRK2 program external expenses is primarily attributable to an upfront payment and a technology transfer license payment to Genentech totaling $10.0 million in the year ended December 31, 2016, as well as increased external research services to progress DNL201 and other LRRK2 molecules into development. The increase in our BBB platform technology external expenses is primarily attributable to the $5.5 million upfront fee payment to F-star Gamma in the year ended December 31, 2016. The increase in personnel related expenses is attributable to a $10.0 million increase in salaries and benefits and a $2.0 million increase in stock-based compensation expense, both due primarily to an increase in our research and development headcount.

Furthermore, there was a $6.6 million increase in other unallocated research and development expenses. This was primarily composed of an increase in lab consumable expenses of $3.4 million and an increase in facilities related expenses of $2.7 million. These increases are partially attributable to the fact that these expenses include seven and twelve months of expenses in the years ended December 31, 2015 and 2016, respectively, and also reflect increases in research and development headcount and increased expenses related to the move to our new headquarters in August 2016.

General and administrative expenses. General and administrative expenses were $5.1 million for the year ended December 31, 2015 compared to $11.7 million for the year ended December 31, 2016. The increase of $6.6 million was primarily attributable to a $2.8 million increase in employee salaries and benefits as we expanded our headcount, a $2.5 million increase in patent and professional services to support our ongoing operations, a $0.5 million increase in stock-based compensation expense and $0.3 million related to increased facilities related expenses resulting from the move to our new headquarters in August 2016 and reflects the fact that the expenses in the year ended December 31, 2015 include only seven months of operations, as we commenced operations in May 2015.

Interest income (expense), net. Interest expense was $(0.1) million for the year ended December 31, 2015 compared to interest income of $0.8 million for the year ended December 31, 2016. The expense for the year ended December 31, 2015 represents interest expense on a $5.0 million promissory note outstanding from January 2015 until May 2015, at which time this note, along with the accrued interest, was converted into Series A-1 convertible preferred stock. The income for the year ended December 31, 2016 represents income from marketable securities earned in the period from June 2016 to December 2016, during which we invested our excess cash in marketable securities.

Liquidity and Capital Resources

Sources of Liquidity

From our inception through September 30, 2017, we have funded our operations primarily through the sale and issuance of our convertible preferred stock. From our inception through September 30, 2017, we raised aggregate cash proceeds of $349.3 million from the issuance of our convertible preferred stock. As of September 30, 2017, we had cash, cash equivalents and marketable securities in the amount of $190.8 million.

Future Funding Requirements

To date, we have not generated any revenue. We do not expect to generate any meaningful revenue unless and until we obtain regulatory approval of and commercialize any of our product

candidates or enter into collaborative agreements with third parties, and we do not know when, or if, either will occur. We expect to continue to incur significant losses for the foreseeable future, and we expect the losses to increase as we continue the development of, and seek regulatory approvals for, our product candidates, and begin to commercialize any approved products. We are subject to all of the risks typically related to the development of new product candidates, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. Moreover, following the completion of this offering, we expect to incur additional costs associated with operating as a public company. We anticipate that we will need substantial additional funding in connection with our continuing operations.

Until we can generate a sufficient amount of revenue from the commercialization of our product candidates or from collaborative agreements with third parties, if ever, we expect to finance our future cash needs through public or private equity or debt financings. Additional capital may not be available on reasonable terms, if at all. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our product candidates. If we raise additional funds through the issuance of additional debt or equity securities, it could result in dilution to our existing stockholders, increased fixed payment obligations and the existence of securities with rights that may be senior to those of our common stock. If we incur indebtedness, we could become subject to covenants that would restrict our operations and potentially impair our competitiveness, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. Additionally, any future collaborations we enter into with third parties may provide capital in the near term but limit our potential cash flow and revenue in the future. Any of the foregoing could significantly harm our business, financial condition and prospects.

Since our inception, we have incurred significant losses and negative cash flows from operations. We have an accumulated deficit of $168.8 million through September 30, 2017. We expect to incur substantial additional losses in the future as we conduct and expand our research and development activities. We believe that our existing cash, cash equivalents and marketable securities will be sufficient to enable us to fund our projected operations through at least the next 12 months.

The expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. However, we have based these estimates on assumptions that may prove to be wrong, and we could use our capital resources sooner than we expect.

The timing and amount of our operating expenditures will depend largely on:

- the timing and progress of preclinical and clinical development activities;
- the number and scope of preclinical and clinical programs we decide to pursue;
- the progress of the development efforts of third parties with whom we have entered into license and collaboration agreements;
- our ability to maintain our current research and development programs and to establish new research and development, license or collaboration arrangements;
- our ability and success in securing manufacturing relationships with third parties or, in the future, in establishing and operating a manufacturing facility;
- the costs involved in prosecuting, defending and enforcing patent claims and other intellectual property claims;
- the cost and timing of regulatory approvals;

- our efforts to enhance operational, financial and information management systems and hire additional personnel, including personnel to support development of our product candidates; and
- the costs and ongoing investments to in-license and/or acquire additional technologies.

A change in the outcome of any of these or other variables with respect to the development of any of our product candidates could significantly change the costs and timing associated with the development of that product candidate. Furthermore, our operating plans may change in the future, and we may need additional funds to meet operational needs and capital requirements associated with such operating plans.

Cash Flows

The following table sets forth a summary of the primary sources and uses of cash for each of the periods presented below (in thousands):

	Year Ended December 31,		Nine Months Ended September 30,	
	2015	2016	2016	2017
Cash used in operating activities	$(15,052)	$ (72,359)	$ (53,993)	$(58,299)
Cash provided by (used in) investing activities	(3,062)	(219,004)	(200,057)	53,983
Cash provided by financing activities	48,854	300,476	300,480	732
Net increase (decrease) in cash and cash equivalents	$ 30,740	$ 9,113	$ 46,430	$ (3,584)

Cash Used in Operating Activities

During the nine months ended September 30, 2017, cash used in operating activities was $58.3 million, which consisted of a net loss of $65.3 million, adjusted by non-cash charges of $6.1 million and cash provided by changes in our operating assets and liabilities of $0.9 million. The non-cash charges consisted primarily of stock-based compensation expense of $3.0 million and depreciation expense of $2.3 million. The change in our operating assets and liabilities was primarily due to an increase of $0.9 million in accrued and other current liabilities.

During the nine months ended September 30, 2016, cash used in operating activities was $54.0 million, which consisted of a net loss of $67.3 million, adjusted by non-cash charges of $8.5 million and cash provided by changes in our operating assets and liabilities of $4.8 million. The non-cash charges consisted primarily of the expense recognized for the estimated fair value of our common stock issued in connection with the acquisition of Incro of $5.3 million and stock-based compensation expense of $2.3 million. The change in our operating assets and liabilities was primarily due to an increase of $3.1 million in accrued and other liabilities and an increase of $1.6 million in accounts payable.

During the year ended December 31, 2016, cash used in operating activities was $72.4 million, which consisted of a net loss of $86.7 million, adjusted by non-cash charges of $10.0 million and cash provided by changes in our operating assets and liabilities of $4.3 million. The non-cash charges consisted primarily of the expense recognized for the fair value of our common stock issued in connection with the acquisition of Incro of $5.3 million and stock-based compensation expense of $3.0 million. The change in our operating assets and liabilities was primarily due to an increase of $5.4 million of accrued and other liabilities. Our accrued liabilities increased due to employee bonuses and general business expenses, reflective of our increased headcount and expenses. This was partially

offset by an increase in restricted cash of $0.5 million associated with the lease for our new headquarters and an increase of $0.5 million in prepaid expenses and other assets mainly associated with prepayments made for ongoing research and development being conducted by third-party service providers.

During the year ended December 31, 2015, cash used in operating activities was $15.1 million, which consisted of a net loss of $16.8 million, adjusted by non-cash charges of $1.3 million and cash provided by changes in our operating assets and liabilities of $0.4 million. The non-cash charges consisted primarily of the expense recognized for the fair value of our common stock issued in connection with the acquisition of Incro of $0.6 million, and stock-based compensation expense of $0.5 million. The change in our operating assets and liabilities was primarily due to an increase of $3.3 million of accounts payable, accrued and other liabilities. Our accrued liabilities increased due to employee bonuses and general business expenses, reflective of the increased headcount and expenses. This was partially offset by an increase in prepaid expenses and other assets of $2.7 million primarily associated with prepayments made for ongoing research and development being conducted by third-party service providers and the deferral of employee bonuses.

Cash Provided by (Used in) Investing Activities

During the nine months ended September 30, 2017, cash provided by investing activities was $54.0 million, which consisted of $102.4 million in proceeds from the maturity of marketable securities, partially offset by $46.7 million of purchases of short-term marketable securities and $1.8 million of capital expenditures to purchase property and equipment.

During the nine months ended September 30, 2016, cash used in investing activities was $200.1 million, which primarily consisted of $195.7 million of purchases of short-term marketable securities and $3.8 million of capital expenditures to purchase property and equipment.

During the year ended December 31, 2016, cash used in investing activities was $219.0 million, which consisted of $226.4 million of purchases of marketable securities, $6.1 million of capital expenditures to purchase property and equipment and $0.5 million of purchases of intangible assets, partially offset by $14.0 million in proceeds from the maturity of marketable securities.

During the year ended December 31, 2015, cash used in investing activities was $3.1 million, all of which related to capital expenditures to purchase property and equipment.

Cash Provided by Financing Activities

During the nine months ended September 30, 2017, cash provided by financing activities was $0.7 million, which consisted of net proceeds in connection with exercises of options to purchase common stock.

During the nine months ended September 30, 2016, cash provided by financing activities was $300.5 million, which primarily consisted of net proceeds from the issuances of shares of our convertible preferred stock.

During the years ended December 31, 2015 and 2016, cash provided by financing activities was $48.9 million and $300.5 million, respectively, which primarily consisted of net proceeds from the issuances of shares of our convertible preferred stock and convertible promissory note, which has since been converted to convertible preferred stock.

Since our inception through December 31, 2016, we have raised an aggregate of approximately $348.6 million in net proceeds, through the issuance of shares of our convertible preferred stock, net of

$0.7 million in issuance costs, which we have used to fund our operations. During 2016, net proceeds from our sale of Series A and Series B-1 convertible preferred stock were $300.4 million. During 2015, net proceeds from our sale of Series A-1 convertible preferred stock were $43.2 million and net proceeds from the sale and issuance of a convertible promissory note was $5.0 million.

Off-Balance Sheet Arrangements

We have not entered into any off-balance sheet arrangements. Our license and collaboration agreements with F-star represent a variable interest in a variable interest entity, or VIE, F-star Gamma. However, we do not consolidate F-star Gamma in our consolidated financial statements because we are not considered to be its primary beneficiary.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of December 31, 2016 (in thousands):

	Total	Less Than 1 Year	1-3 Years	3-5 Years	More Than 5 Years
Operating lease obligations (1)	$21,039	$ 2,510	$5,250	$5,574	$ 7,705
Total contractual obligations	$21,039	$ 2,510	$5,250	$5,574	$ 7,705

(1) We lease our former and current facilities under operating leases. In September 2015, we entered into a lease for our current laboratory and office space that commenced in August 2016 and expires in July 2024. The minimum lease payments above do not include any related common area maintenance charges or real estate taxes.

In the normal course of business, we enter into various firm purchase commitments primarily related to research and development activities. As of December 31, 2016, we had noncancelable purchase commitments of $1.0 million and contractual obligations under license agreements of $0.2 million.

Pursuant to certain license agreements, including our agreements with Genentech and F-star, we have obligations to make future milestone and royalty payments to other parties. Additionally, we have an option to acquire all outstanding shares of F-star Gamma for initial exercise payments ranging from $18.0 million to $50.0 million in the aggregate, plus the estimated net cash held by F-star Gamma at the time of such purchase. In addition to these initial exercise payments, we would be required to make certain contingent payments up to a maximum amount of $447.0 million in the aggregate. However, we are unable to estimate the timing or likelihood of achieving the milestones or of exercising the option to purchase the outstanding shares of F-star Gamma and, therefore, any related payments are not included in the table above.

Effective September 2017, we entered into a development and manufacturing services agreement, as amended, the DMSA or the Lonza agreement, with Lonza Sales AG, or Lonza, for the development and manufacture of biologic products. Under the DMSA, we will execute purchase orders based on project plans authorizing Lonza to provide development and manufacturing services with respect to certain of our antibody and enzyme products, and will pay for the services provided and batches delivered in accordance with the DMSA and project plan. Unless earlier terminated, the Lonza agreement will expire on September 6, 2022. As of September 30, 2017, we had not incurred any obligations or made any purchase commitments under the DMSA. In October 2017, we executed the first purchase order of up to $0.7 million, the activities under which will commence prior to the end of 2017.

Critical Accounting Policies and Significant Judgments and Estimates

This discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States, or GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. While our significant accounting policies are described in more detail in the notes to our consolidated financial statements included elsewhere in this prospectus, we believe that the following accounting policies are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates.

Research and Development Expenses

We record research and development expenses to operations as incurred. Research and development expenses represent costs incurred by us for the discovery and development of our product candidates and the development of our BBB platform technology and include: employee-related expenses, including salaries, benefits, travel and non-cash stock-based compensation expense; external research and development expenses incurred under arrangements with third parties, such as CROs, preclinical testing organizations, CMOs, academic and non-profit institutions and consultants; costs to acquire technologies to be used in research and development that have not reached technological feasibility and have no alternative future use; license fees; and other expenses, which include direct and allocated expenses for laboratory, facilities and other costs.

As part of the process of preparing financial statements, we are required to estimate and accrue expenses. A portion of our research and development expenses are external costs, which we track on a program-specific basis once a program has commenced a late-stage IND-enabling study. We record the estimated expenses of research and development activities conducted by third-party service providers based upon the estimated amount of services provided within research and development expense in the statements of operations and comprehensive loss. These services include the conduct of preclinical studies and clinical trials, contract manufacturing activities and consulting services. If the costs have been prepaid, this expense reduces the prepaid expenses in the balance sheet, and if not yet invoiced, the costs are included in accrued liabilities in the balance sheet. These costs are a significant component of our research and development expenses. We record amortization of prepaid expenses or accrued expenses for these costs based on the estimated amount of work completed and in accordance with agreements established with these third parties.

Costs for certain research and development activities are recognized based on an evaluation of the progress to completion of specific tasks. We estimate the amount of work completed through discussions with internal personnel and external service providers as to the progress or stage of completion of the services and the agreed-upon fee to be paid for such services. We make significant judgments and estimates in determining the accrued balance in each reporting period. As actual costs become known, we adjust our accrued estimates. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed may vary from our estimates and could result in us reporting amounts that are too high or too low in any particular period. Our accrued expenses are dependent, in part, upon the receipt of timely and accurate reporting from external clinical research organizations and other third-party

service providers. To date, we have not experienced material differences between our accrued expenses and actual expenses. However, due to the nature of estimates, we cannot assure you that we will not make changes to our estimates in the future as we become aware of additional information about the status or conduct of our clinical trials and other research activities.

Variable Interest Entities

We assess whether we are the primary beneficiary of a VIE at the inception of the arrangement and at each reporting date. This assessment is based on our power to direct the activities of the VIE that most significantly impact the VIE's economic performance and our obligation to absorb losses or the right to receive benefits from the VIE that could potentially be significant to the VIE.

Stock-Based Compensation

We have granted stock-based awards, consisting of stock options and restricted stock, to our employees, certain non-employee consultants and certain members of our board of directors. We measure stock-based compensation expense for restricted stock and stock options granted to our employees and directors on the date of grant and recognize the corresponding compensation expense of those awards over the requisite service period, which is generally the vesting period of the respective award. We account for stock-based compensation arrangements with non-employee consultants using a fair value approach. The estimated fair value of unvested options granted to non-employee consultants is remeasured at each reporting date through the date of final vesting. As a result, the noncash charge to operations for nonemployee options with vesting conditions is affected in each reporting period by changes in the estimated fair value of our common stock. We adjust for actual forfeitures as they occur.

We have also granted stock options that vest in conjunction with certain performance and market conditions to certain key employees. At each reporting date, we are required to evaluate whether the achievement of the performance or market condition is probable. Compensation expense is recorded over the appropriate service period based on our assessment of accomplishing each performance or market provision or the occurrence of other events that may have caused the awards to accelerate and vest. See the section titled "Executive Compensation" for additional information.

We estimate the fair value of stock options granted to our employees and directors on the grant date, and the resulting stock-based compensation expense, using the Black-Scholes option-pricing model. The Black-Scholes option-pricing model requires the use of highly subjective assumptions which determine the fair value of stock-based awards. These assumptions include:

- *Expected Term*. Our expected term represents the period that our stock-based awards are expected to be outstanding and is determined using the simplified method (based on the mid-point between the vesting date and the end of the contractual term), as we do not have sufficient historical data to use any other method to estimate expected term.
- *Expected Volatility*. As there has been no public market for our common stock to date, and as a result we do not have any trading history of our common stock, the expected volatility is estimated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. The comparable companies are chosen based on their similar size, stage in the life cycle or area of specialty.
- *Risk-Free Interest Rate*. The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of the stock option grants.

- *Expected Dividend*. We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we use an expected dividend yield of zero.

For options granted to non-employee consultants, the fair value of these options is also remeasured using the Black-Scholes option-pricing model reflecting the same assumptions as applied to employee options in each of the reported periods, other than the expected life, which is assumed to be the remaining contractual life of the option.

As there has been no public market for our common stock to date, the estimated fair value of our common stock has been determined by our board of directors, with input from management, considering our most recently available third-party valuations of common stock and our board of directors' assessment of additional objective and subjective factors that it believed were relevant, and factors that may have changed from the date of the most recent valuation through the date of the grant. These factors include, but are not limited to: our most recently available valuations of our common stock by an unrelated third party; the prices at which we sold shares of our convertible preferred stock to outside investors in arms-length transactions; the rights, preferences and privileges of our convertible preferred stock relative to those of our common stock; our results of operations, financial position and capital resources; current business conditions and projections; the lack of marketability of our common stock; the hiring of key personnel and the experience of management; the risk inherent in the development of our products; our stage of development and material risks related to its business; the fact that the option grants involve illiquid securities in a private company; and the likelihood of achieving a liquidity event, such as an initial public offering or sale, in light of prevailing market conditions.

We have periodically determined the estimated fair value of our common stock at various dates using contemporaneous valuations performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*, or the Practice Aid. The Practice Aid identifies various available methods for allocating enterprise value across classes and series of capital stock to determine the estimated fair value of common stock at each valuation date. In accordance with the Practice Aid, our board of directors considered the following methods:

- *Current Value Method.* Under the Current Value Method, or CVM, our value is determined based on our balance sheet. This value is then first allocated based on the liquidation preference associated with preferred stock issued as of the valuation date, and then any residual value is assigned to the common stock.
- *Option-Pricing Method.* Under the option-pricing method, or OPM, shares are valued by creating a series of call options with exercise prices based on the liquidation preferences and conversion terms of each equity class. The estimated fair values of the preferred and common stock are inferred by analyzing these options.
- *Probability-Weighted Expected Return Method.* The probability-weighted expected return method, or PWERM, is a scenario-based analysis that estimates value per share based on the probability-weighted present value of expected future investment returns, considering each of the possible outcomes available to us, as well as the economic and control rights of each share class.

Our common stock valuation as of May 31, 2015 was prepared using a hybrid between the CVM and OPM, the latter of which was based on the price at which we sold shares of our Series A-1 convertible preferred stock. The deemed fair value was determined by weighting these two methodologies differently resulting in an increased estimated fair value of our common stock for financial reporting purposes.

Our common stock valuations as of March 31, 2016, June 30, 2016, September 30, 2016, and December 31, 2016 were prepared using the back-solve method of OPM, which derives the implied equity value for one type of equity security from a contemporaneous transaction involving another type of security.

Our common stock valuations as of March 31, 2017, June 30, 2017 and September 30, 2017 were prepared using the hybrid method, which is a hybrid between the PWERM and OPM, consistent with how such hybrid method is described in the Practice Aid.

Our board of directors and management develop best estimates based on application of these approaches and the assumptions underlying these valuations, giving careful consideration to the advice from our third-party valuation expert. Such estimates involve inherent uncertainties and the application of significant judgment. As a result, if factors or expected outcomes change and we use significantly different assumptions or estimates, our equity-based compensation could be materially different. Following the closing of this offering, our board of directors will determine the fair market value of our common stock based on its closing price as reported on the date of grant on the primary stock exchange on which our common stock is traded.

The intrinsic value of all outstanding options as of September 30, 2017 was approximately $92.3 million, based on the assumed initial public offering price of $18.00 per share, which is the midpoint of the estimated initial public offering price range set forth on the cover page of this prospectus, of which approximately $9.3 million is related to vested options and approximately $83.0 million is related to unvested options.

JOBS Act

We are an emerging growth company under the JOBS Act. As an emerging growth company, we may delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have nonetheless irrevocably elected not to avail ourselves of this exemption and, as a result, upon completion of this offering we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

We will remain an emerging growth company until the earliest of (i) the last day of our first fiscal year in which we have total annual gross revenues of $1.07 billion or more, (ii) the date on which we are deemed to be a “large accelerated filer” under the rules of the SEC with at least $700.0 million of outstanding equity securities held by non-affiliates, (iii) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the previous three years, or (iv) the last day of our fiscal year following the fifth anniversary of the date of the completion of this offering.

Quantitative and Qualitative Disclosures About Market Risk

Interest Rate Sensitivity

We are exposed to market risk related to changes in interest rates. We had cash, cash equivalents and marketable securities of $190.8 million as of September 30, 2017, which consisted primarily of money market funds and marketable securities, largely composed of investment grade, short to intermediate term fixed income securities.

The primary objective of our investment activities is to preserve capital to fund our operations. We also seek to maximize income from our investments without assuming significant risk. To achieve our objectives, we maintain a portfolio of investments in a variety of securities of high credit quality and short-term duration, according to our board-approved investment charter.

Our investments are subject to interest rate risk and could fall in value if market interest rates increase. A hypothetical 10% relative change in interest rates during any of the periods presented would not have had a material impact on our consolidated financial statements.

Foreign Currency Sensitivity

The majority of our transactions occur in U.S. dollars. However, we do have certain transactions that are denominated in currencies other than the U.S. dollar, primarily the Euro, and we therefore are subject to foreign exchange risk. The fluctuation in the value of the U.S. dollar against the Euro affects the reported amounts of expenses, assets and liabilities associated with a limited number of preclinical and clinical activities. We do not currently engage in any hedging activity to reduce our potential exposure to currency fluctuations, although we may choose to do so in the future. A hypothetical 10% change in foreign exchange rates during any of the periods presented would not have had a material impact on our consolidated financial statements.

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, No. 2014–09, Revenue from Contracts with Customers (Topic 606), and further updated through ASU 2016-12, which amends the existing accounting standards for revenue recognition. ASU 2014–09 is based on principles that govern the recognition of revenue at an amount to which an entity expects to be entitled when products are transferred to customers. This guidance is effective for annual reporting periods, and interim periods within those years, beginning after December 15, 2017, for public entities and no later than for annual reporting periods beginning after December 15, 2018, for non–public entities. The new revenue standard may be applied retrospectively to each prior period presented or retrospectively with the cumulative effect recognized as of the date of adoption. While we continue to assess all potential impacts under ASU 2014-09, we do not believe adopting the new revenue recognition standard will materially impact the consolidated financial statements as we have not yet generated revenue.

In February 2016, the FASB issued ASU No. 2016-02, Leases (Topic 842), which supersedes the guidance in former ASC 840, Leases. The new standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than 12 months regardless of their classification. Leases with a term of 12 months or less will be accounted for similar to existing guidance for operating leases today. The standard is effective for interim and annual periods beginning after December 15, 2019, with early adoption permitted. The ASU is expected to impact our consolidated financial statements as we have certain operating lease arrangements for which we are the lessee. We are currently in the process of evaluating the impact the adoption of ASU 2016-02 will have on our consolidated financial position or results of operations. We expect that the adoption of this standard will result in the recognition of an asset for the right to use the leased facility on our consolidated balance sheet, as well as the recognition of a liability for the lease payments remaining on the lease. While the consolidated balance sheet presentation is expected to change, we do not expect a material change to our consolidated statement of operations.

In November 2016, the FASB issued ASU 2016-18, Statement of Cash Flows (Topic 230): Restricted Cash. The purpose of Update No. 2016-18 is to clarify guidance and presentation related to restricted cash in the statement of cash flows. The amendment requires beginning-of-period and end-of-period total amounts shown on the statement of cash flows to include cash and cash equivalents as

well as restricted cash and restricted cash equivalents. The update is effective for fiscal years beginning after December 15, 2017, including interim reporting periods within those fiscal years. Early adoption is permitted. We are currently evaluating the impact of adopting this standard on the consolidated financial statements and disclosures, but do not expect it to be material.

In May 2017, the FASB issued ASU 2017-09, Compensation—Stock Compensation (Topic 718): Scope of Modification Accounting, which clarifies when to account for a change to the terms or conditions of a share-based payment award as a modification. Under the new guidance, modification accounting is required only if the fair value, the vesting conditions, or the classification of the award (as equity or liability) changes as a result of the change in terms or conditions. It is effective for annual and interim periods beginning after December 15, 2017. Early adoption is permitted. We are currently evaluating the impact of adopting this standard on our consolidated financial statements and disclosures, but we do not expect it to have a significant impact.

FOUNDERS' VISION

We have embarked on a deeply personal journey to conquer neurodegenerative diseases. Collectively, these diseases represent one of the most significant medical challenges facing us today, impacting millions of people including our own families and friends. We are passionately dedicated to understanding these diseases. Our goal is nothing short of defeating neurodegeneration by harnessing the power of modern science and technology to discover and develop medicines that meaningfully improve the lives of patients and their families.

This is a formidable challenge and opportunity. Defeating degeneration – to us – is akin to summiting the tallest mountains. Hence the name Denali. For the longest time, mankind was unable to summit the highest peaks. But when the time was right, bold mountaineers succeeded, enabled by technological progress and a better understanding of the elements. We believe that the same is possible in neurodegeneration today.

We are well aware that we are taking on a major challenge, yet we believe that success is within our reach. Recent genetic insights, better diagnostic tools and the ability to engineer medicines to cross the blood-brain barrier are crucial components in defeating degeneration. We have contributed to and experienced firsthand the advances that are made possible by following breakthrough science. We believe that the field of neurodegeneration is now at the inflection point where oncology was years ago when genetic discoveries revealed biological pathways responsible for cancer growth that resulted in powerful drug targets, and biomarkers enabled the diagnosis and selection of patients for targeted treatment approaches. Similar success is within reach in neurodegeneration.

Just like the mountaineers who set out to conquer the highest peaks, it takes a courageous team with a singular focus and unrelenting persistence to succeed. At Denali, we have assembled an outstanding team of driven and passionate scientists and drug developers, and a powerful network of collaborators in academia and industry.

The science is breaking open, and the time is right to discover and develop effective medicines for neurodegeneration. Every day matters. To patients, to their families and to society at large. We invite you to join us on our journey to the summit.

Ryan Watts, Ph.D. CEO and Co-Founder	Alexander Schuth, M.D. COO and Co-Founder	Marc Tessier-Lavigne, Ph.D. Director and Co-Founder

BUSINESS

Overview and Strategy

Our goal is to discover and develop therapeutics to defeat degeneration.

Neurodegeneration represents one of the most significant unmet medical needs of our time, with few effective therapeutic options available for patients with Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, or ALS, and other neurodegenerative diseases. The burden of these diseases to patients and society is massive.

We believe the time is right to make a strong and ambitious effort to defeat neurodegeneration. We believe that we can succeed in a field that has seen limited success in the past, because of our team of experienced and passionately dedicated scientists and drug developers, our focused scientific strategy, and our proprietary blood-brain barrier, or BBB, platform delivery technology. We are developing a broad portfolio of targeted therapeutic candidates for neurodegenerative diseases and have recently initiated our first clinical trials. We commenced operations in May 2015.

Historical challenges in developing effective therapeutics for patients with neurodegenerative diseases included a scarcity of therapeutic targets due to a limited understanding of disease biology, insufficient uptake of therapeutics into the brain because of the BBB and few available biomarkers for target engagement, diagnosis, patient selection and tracking disease progression. In recent years, however, significant progress in each of these areas has been made, greatly increasing the likelihood of success of developing effective therapeutics for neurodegenerative diseases.

Our scientific strategy is guided by three overarching principles. We believe that the application of these principles will significantly increase the probability of success and will accelerate the timing to bring effective therapeutics to patients with neurodegenerative diseases:

Genetic Pathway Potential	We use recent advances in understanding human genetics and cell biology in neurodegeneration to select our therapeutic targets, disease pathways and biomarkers. We focus on genes that, when mutated, cause, or are major risk factors for, neurodegenerative diseases, which we refer to as degenogenes. These degenogenes directly point to important disease pathways, and we have initially selected three such pathways for which we have built significant scientific expertise: lysosomal function, glial biology and cellular homeostasis.
Engineering Brain Delivery	We engineer our product candidates to cross the blood-brain barrier and act directly in the brain. This engineering is designed to enable optimal concentration of a therapeutic in the brain in order to improve therapeutic target engagement. For large molecule product candidates, such as antibodies and enzymes, we have engineered a proprietary BBB platform technology. For small molecule product candidates, which are synthetically created therapeutics, we design and test appropriate molecular architectures to optimize their exposure in the brain.
Biomarker-Driven Development	We discover, develop and utilize biomarkers to select the right patient population and demonstrate target engagement, pathway engagement and impact on disease progression of our product candidates. These biomarkers can be used as endpoints of efficacy in early clinical trials, with the goal of accelerating clinical development timelines. In addition, each of our therapeutic programs includes a patient selection strategy using biomarkers to identify and segment patients in order to increase the likelihood of success.

Our total portfolio currently consists of eleven programs. To prioritize the allocation of our resources, we designate certain programs as core programs and others as seed programs, and we currently have six core programs and five seed programs. Our core programs are at various stages of clinical and preclinical development, and we believe that each of these programs has the potential to result in either first-in-class or best-in-class products for neurodegenerative diseases.

In building and developing our portfolio, we are guided by the principles outlined above, which means that the therapeutic target or pathway for each program is genetically linked to neurodegenerative disease, our product candidates are being engineered to optimize brain delivery, and the clinical development plan will be enabled by biomarkers. We rigorously follow the science and employ the therapeutic modality that we believe is best suited to modulate the target pathway. Our product candidates currently include small molecules, antibodies and enzymes and may expand to include other modalities in the future.

To increase the probability of success, we make parallel investments in several product candidates and back-up candidates, and plan to advance only those candidates to the later stages of clinical development that show strong preclinical and early clinical data. We constantly strive to replenish, grow and optimize our portfolio through in-house discovery and external business development activities, in each case enabled by our strong internal research and development expertise and capabilities.

By developing a broad portfolio of product candidates, we can continuously apply learnings and tools across programs and leverage economies of scale in our research and development organization. Our target indications include diseases with large patient populations, such as Alzheimer's disease, as well as orphan indications, such as mucopolysaccharidosis type II, or MPS II, and ALS**.** We aim to increase the probability of success and accelerate clinical development timelines by using biomarkers and other tools to demonstrate an impact on relevant disease biology for proof of concept in early clinical trials.

We have development and commercialization rights to all of our core programs.

The following table summarizes key information about our core programs:

Program Target	Drug Candidate	Therapeutic Modality	Disease Indication	Preclinical Development	Clinical Development			Biomarker		
					Phase I	Phase II	Phase III	Preclinical Target Engagement	Clinical Target Engagement	Patient Selection
Lysosomal Function Pathway										
LRRK2	DNL201	Small Molecule	Parkinson's disease	Phase 1				✓	✓	✓
	DNL151	Small Molecule	Parkinson's disease	IND-Enabling						
Alpha-Synuclein	ATV:aSyn	Antibody	Parkinson's disease, DLB, MSA	Preclinical				✓	●	●
Iduronate 2-sulfatase	ETV:IDS	Enzyme	MPS II (Hunter Syndrome)	Preclinical				✓	✓	✓
Glial Biology Pathway										
RIPK1	DNL747	Small Molecule	Alzheimer's disease, ALS	IND-Enabling				✓	✓	●
TREM2	ATV:TREM2	Antibody	Alzheimer's disease	Preclinical				✓	●	●
Cellular Homeostasis Pathway										
BACE1/TAU	ATV:BACE1/Tau	Antibody	Alzheimer's disease	Preclinical				✓	✓	✓

ATV : Antibody Transport Vehicle
ETV : Enzyme Transport Vehicle
ALS: Amyotrophic Lateral Sclerosis
DLB : Dementia with Lewy Bodies
MPS II: Mucopolysaccharidosis type II
MSA: Multiple System Atrophy

✓ Validated Biomarker
● Biomarker in Development

Delivering therapeutics across the BBB has been a major obstacle to successful drug development in neurodegeneration, and is critical to enabling effective treatments. Protein

therapeutics, such as antibodies, have revolutionized the treatment of many diseases, but this class of medicines does not effectively cross the BBB and, therefore, currently has very limited therapeutic application to the treatment of neurodegenerative diseases. To address this limitation, we have developed proprietary drug delivery platform technologies, called ATV, or Antibody Transport Vehicle, and ETV, or Enzyme Transport Vehicle, designed to deliver large molecules across the BBB. We have achieved proof of concept for the ATV platform in a mouse model and have initial validating data from an ongoing study in nonhuman primates. We are currently optimizing and broadening this platform technology.

Our ATV and ETV platforms are modular BBB delivery technologies for large molecule therapeutics, including antibodies, enzyme and other proteins. Therapeutic candidates enabled by the ATV or ETV platforms are designed to engage specific BBB transport receptors, which are ubiquitously expressed in the brain capillaries and facilitate transport of proteins into the brain. In a mouse model across three studies designed to demonstrate proof of concept of the ATV platform, an antibody engineered with our ATV technology has demonstrated an average 20-fold greater brain penetration than a control antibody not enabled by this technology. In addition, initial data from an ongoing study in nonhuman primates designed to show proof of concept for the ATV platform demonstrates a robust and sustained pharmacodynamics, or PD, effect in the brain after intravenous dosing of an ATV-enabled antibody, while a standard antibody had minimal PD effect. The improvement in brain exposure may enable therapeutically relevant concentrations of our ATV antibody product candidates in the brain, making them potentially superior to traditional monoclonal antibody therapeutics.

We are currently developing several product candidates for multiple programs to advance to investigational new drug, or IND, enabling studies in preparation for human clinical trials. We plan to have multiple product candidates that utilize our ATV or ETV platforms enter clinical development in 2019 and 2020, including molecules targeting alpha-synuclein, or aSyn; iduronate 2-sulfatase, or IDS; triggering receptor expressed in myeloid cells 2, or TREM2; beta-secretase 1, or BACE1; and Tau.

We also follow a rigorous approach to designing small molecules to cross the BBB. DNL201 and DNL151, our small molecule inhibitors of leucine-rich repeat kinase 2, or LRRK2, and DNL747, our small molecule inhibitor of receptor interacting serine/threonine protein kinase 1, or RIPK1, have been specifically designed to cross the BBB.

LRRK2 is a degenogene that regulates lysosomal function, and mutations in LRRK2 are one of the most commonly known genetic causes of Parkinson’s disease. DNL201 is currently in a Phase 1 clinical trial. We submitted a CTA for DNL151 to the Netherlands Health Authority in October 2017 and it was accepted in November 2017. For DNL201, the FDA has allowed us to proceed with our Phase 1 clinical trial in healthy volunteers at doses that we believe will be sufficient to inhibit LRRK2 50% on average over the dosing period and should effectively normalize LRRK2 kinase activity. For exposures expected to be higher than this level, the FDA has issued a partial clinical hold on the DNL201 Phase 1 clinical trial, which the FDA may re-evaluate based on the safety and tolerability data generated by the study and data supporting the monitorability of the effects of DNL201.

RIPK1 is a regulator of microglial homeostasis and increased RIPK1 kinase activity drives neuroinflammation and cell necroptosis in immune cells and in the brain. RIPK1 inhibition has been shown to have beneficial effects in preclinical models of Alzheimer’s disease, ALS and other diseases. DNL747 is in IND-enabling preclinical studies and we plan to submit a CTA in early 2018.

We have assembled a team with deep scientific, clinical, business and leadership experience and expertise in biotechnology, and specifically in neurodegenerative diseases, who worked together at Genentech for many years prior to the founding of Denali. Our Co-Founder and Chief Executive Officer, Ryan J. Watts, Ph.D., is a world-leading drug developer and neuroscientist, with particular

expertise in BBB therapeutic delivery. Dr. Watts most recently led the neuroscience research team at Genentech and has led multiple discovery teams, including programs in Alzheimer's disease, Parkinson's disease and ALS. Our Co-Founder and Chief Operating Officer, Alexander O. Schuth, M.D., held various operational and leadership roles at Genentech for nearly ten years, including leading the partnering groups for neuroscience as well as technology innovation and diagnostics. Dr. Schuth has led more than 35 partnering transactions and a clinical stage development program. Our Co-Founder and director, Marc Tessier-Lavigne, Ph.D., is a world-leading neuroscientist, was formerly Chief Scientific Officer at Genentech and serves as President of Stanford University. Carole Ho, M.D., our Chief Medical Officer, brings over a decade of clinical development experience, most recently as Vice President, Non-Oncology Early Clinical Development at Genentech. Dr. Ho has overseen or contributed to more than ten IND filings and three drug approvals. Our Chief Financial Officer, Steve E. Krognes, brings over two decades of operational and corporate finance experience, most recently serving six years as Chief Financial Officer and member of the Executive Committee at Genentech. Mr. Krognes has led more than 40 strategic deals and led or contributed to several capital raising transactions.

Our leadership team is joined by approximately 125 employees, approximately two-thirds of whom hold Ph.D. or M.D. degrees. Together, they bring expertise across relevant disciplines, including neuroscience, BBB biology, genetics, oncology, immunology, translational science, antibody engineering, chemistry and biomarker development. Our development leadership team members have, collectively, led and contributed to more than 120 IND and clinical trial application, or CTA, filings. Our board of directors is comprised of several leaders from both academia and industry. Our directors include Vicki Sato, Ph.D. (Chair), retired Professor of Management at Harvard Business School, Doug Cole, M.D., Managing Director of Flagship Pioneering, Jay Flatley, Executive Chairman and retired Chief Executive Officer of Illumina, Robert T. Nelsen, co-founder and Managing Director of ARCH Venture Partners and David Schenkein, M.D., Chief Executive Officer of Agios Pharmaceuticals. Our directors collectively bring deep scientific knowledge and relevant industry experience.

Licenses and collaborations are central components of our strategy to build and advance our pipeline of product candidates. We have entered into arrangements with biopharmaceutical companies such as Genentech and F-star, numerous leading academic institutions such as Harvard University, Massachusetts General Hospital, Washington University in St. Louis, the University of California, San Diego and Vlaams Instituut voor Biotechnologie, foundations such as the Michael J. Fox Foundation, and patient-focused data companies such as 23andMe and Patients Like Me, to gain access to new product candidates, deepen our scientific understanding of certain areas of biology and enable and accelerate the development of our programs. We believe that accessing external innovation is important to our success and we plan to remain active in accessing external innovation through business development activities. Our goal is to be the most attractive partner for academic groups and companies in the field of neurodegeneration based on our singular focus, broad capabilities and ability to execute with scientific rigor and speed.

Our Approach to Defeating Neurodegeneration

Disease Overview

Neurodegenerative diseases are a collection of conditions defined by progressive nervous system dysfunction, degeneration and/or death of neurons causing cognitive decline, functional impairment and eventually death. Neurodegeneration represents one of the most significant unmet medical needs of our time, with the aging of the population and the lack of effective therapeutic options causing a rapid increase in the number of patients. The two most common neurodegenerative diseases are Alzheimer's disease, representing an estimated 60% to 70% of all dementias according to the World Health Organization, and Parkinson's disease. In the United States, 5.5 million people suffer from

Alzheimer's disease, as many as one million people suffer from Parkinson's disease (with 60,000 new patients being diagnosed each year), and more than 20,000 patients suffer from ALS, according to estimates from the Alzheimer's Association, the Parkinson's Disease Foundation, and the ALS Association, respectively.

The cost to society from neurodegenerative disease is massive. The direct costs of caring for individuals with Alzheimer's disease and other dementias in the United States will total an estimated $259 billion in 2017, and is projected to increase to $1.1 trillion by 2050, according to the Alzheimer's Association. In the United States, the total cost of care to patients suffering from Alzheimer's disease and other dementias far exceeds that of many other diseases, including cancer.

Genetic Pathway Potential

Advances in our understanding of the genetics, pathology and cell biology underlying chronic neurodegenerative diseases have identified pathways that trigger and/or contribute to disease onset and progression. Of particular importance is the progress in genetic sequencing where the dramatic reduction in the cost of deoxyribonucleic acid, or DNA, sequencing has recently contributed to the discovery of numerous genetic mutations that have been linked to neurodegeneration (Figure 1).

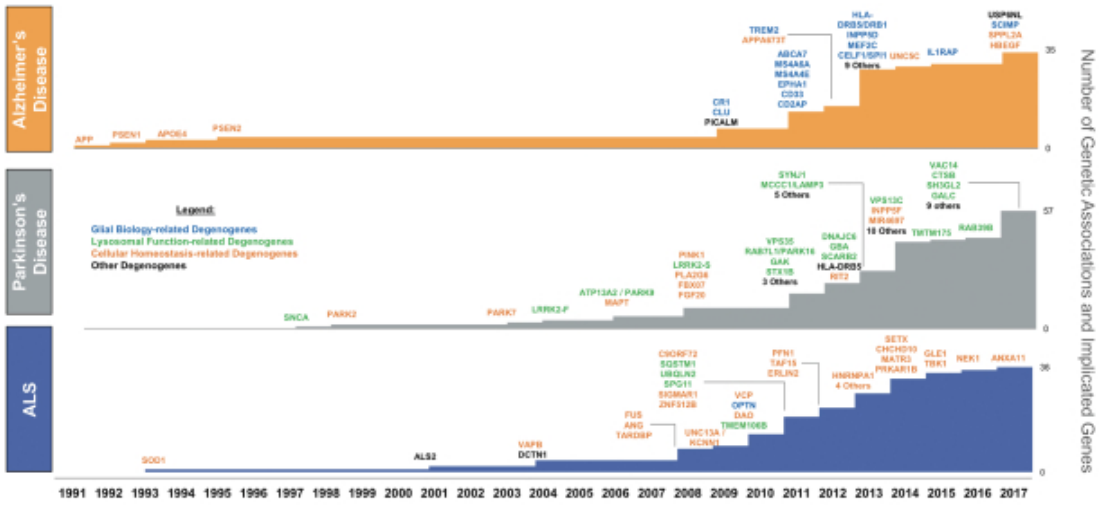
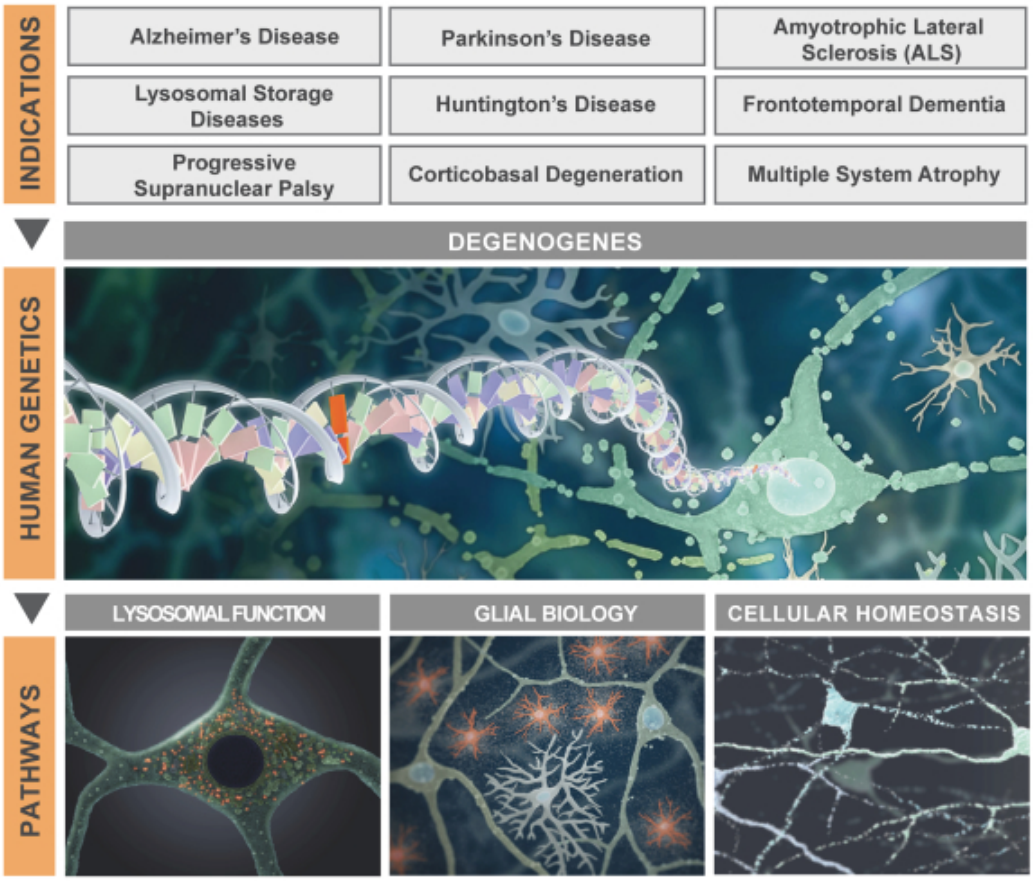


Figure 1: The number of associated genetic mutations linked to Alzheimer's disease, Parkinson's disease and ALS from 1991 to 2017. For genome-wide association studies, disease genes were selected based on genome-wide significance (p<5×10-8). Rare disease-causing and/or high penetrance mutations were included based on a p value of 1x10^-7 and replication in an independent cohort.

Human Genetics: Degenogenes

Prior to 2007, only a limited number of genetic mutations linked to Alzheimer's disease, Parkinson's disease and ALS had been identified. Since 2007, the number of genetic associations discovered in neurodegenerative diseases has grown rapidly, with more than 100 genes associated with these three neurodegenerative diseases collectively. The degenogenes directly point to important disease pathways that are disrupted in neurodegeneration, and are our scientific foundation for identifying and pursuing promising targets for drug development. We have chosen to initially focus on three such pathways: lysosomal function, glial biology and cellular homeostasis.



Disease Pathways

Lysosomal Function

The lysosomal system, the disposal and recycling compartment of the cell, is involved in the digestion and processing of proteins and lipids in brain cells. Dysfunction of the lysosomal system is associated with several neurodegenerative diseases, including Parkinson's disease and neurodegeneration in the context of lysosomal storage diseases, or LSDs. Degenogenes linked to lysosomal function include LRRK2, aSyn, and lysosomal enzymes, including IDS, and glucocerebrosidase, or GBA. Most LSDs result in rapid and aggressive neurodegeneration. We believe therapeutics designed to correct lysosomal dysfunction are a promising approach to broadly treat neurodegeneration.

Glial Biology

The human brain contains several types of glial cells, which are non-neuronal cells that maintain homeostasis, which is the ability of cellular or molecular pathways to seek and maintain a condition of equilibrium or stability within its internal environment when dealing with cellular stress and genetic variation, form myelin and support, protect and provide nutrition to neurons, and are critical to healthy brain function. A specific type of glial cells, microglial cells, which are macophages of the brain and spinal cord, act as the resident immune system in the brain. It has been recently discovered that

degenogenes implicate immune dysfunction in the brains of patients with Alzheimer's disease and other neurodegenerative diseases. These genes include TREM2 and numerous other genes that are highly expressed in inflamed microglia. We believe the impact of immune modulation in neurodegeneration is a promising approach to treating disease. Genetic and pathological data suggest that reversing defects in glial biology may significantly delay or halt the progression of some neurodegenerative diseases, such as Alzheimer's disease and ALS. Specifically, we and others have recently discovered that RIPK1, a kinase, which is an enzyme that catalyzes the addition of a phosphate group to substrates, usually proteins, downstream of the TNF receptor pathway, a highly validated biologic target in human disease, is overactive in inflamed microglia and several other cells in the brain. Blocking RIPK1 may reverse the hyper-inflamed nature of glia and restore normal function. Improving glial function and modulating the resident immune system in the brain represents a potentially attractive therapeutic strategy.

Cellular Homeostasis

Many degenogenes directly alter the homeostatic balance of brain cells. Specifically, defects in protein or ribonucleic acid, or RNA, homeostasis lead to the death of neurons and dysfunction of the nervous system. This includes spreading of protein aggregates resulting in proteinopathy, which is disease that results from disorders of protein synthesis, trafficking, folding, processing or degradation in cells, in Alzheimer's and Parkinson's diseases, and the aggregation of RNA binding proteins disrupting cellular stress response in Alzheimer's disease and ALS. The clearance of macromolecules in the brain is particularly susceptible to imbalances that result in aggregation and degeneration in nerve cells. For example, Alzheimer's disease pathology is characterized by the presence of amyloid plaques, which are accumulations of amyloid, or the complex proteins deposited in tissues that form the primary component of plaques characteristic of Alzheimer's disease, and neurofibrillary tangles, which are aggregates of hyperphosphorylated Tau protein that are a marker of Alzheimer's disease and other diseases known as tauopathies. Our approach is to create a bispecific antibody that targets both BACE1 and Tau, key proteins in the production of amyloid plaques and neurofibrillary tangles, which we believe has the potential for synergistic activity, restoring protein homeostasis with regards to the two most common Alzheimer's disease pathologies. We believe that therapies that correct defects in cellular homeostasis have the potential to halt or delay neurodegenerative disease progression.

Engineering Brain Delivery

The Blood-Brain Barrier Challenge

The human brain contains approximately 400 miles of blood vessels. These blood vessels are lined by closely linked endothelial cells to form the BBB, which protects the brain from toxins by regulating the transfer of proteins, nutrients and waste products. Delivery of therapeutics to the brain has been challenging as most small molecule drugs are actively excluded by efflux pumps, and brain uptake of therapeutic antibodies and recombinant enzymes is severely limited by their size. (Figure 2).

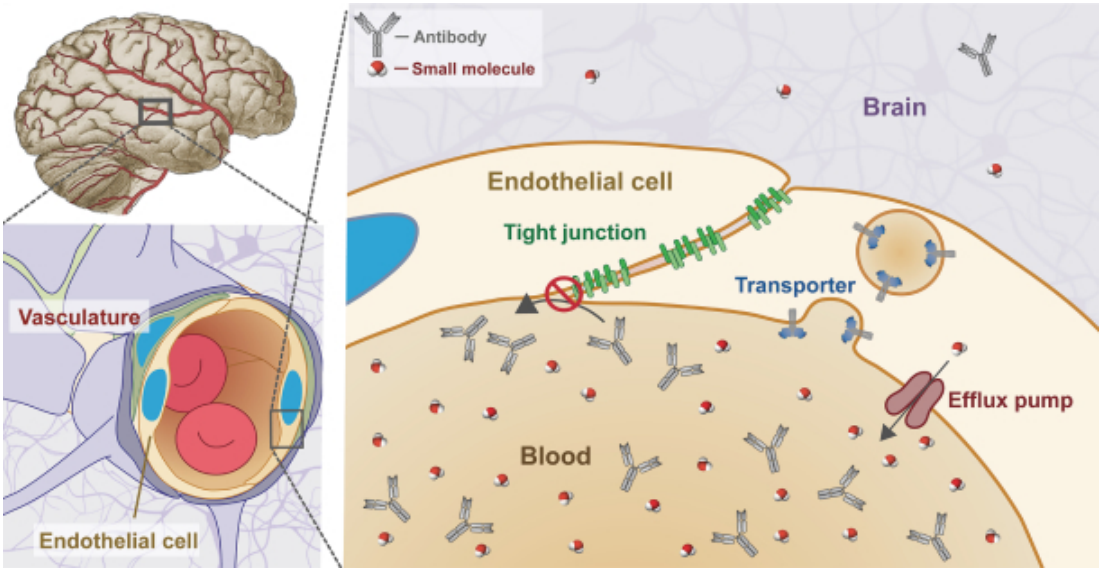


Figure 2. Schematic of the BBB. The specialized vessels of the brain represent a significant barrier for both small and large molecule therapeutics. Tight junctions between endothelial cells prevent the diffusion of large molecules while most small molecules are kept out of the brain by efflux pumps.

The protective nature of the BBB limits the passive uptake of small molecule and large molecule therapeutics in the brain. For example, the concentration of most therapeutic antibodies in the brain is only 0.1% of the concentration in the blood. We believe that this is one of the major reasons for the low success rates of clinical trials in neurodegenerative diseases to date. Engineering brain delivery of product candidates is critical to our success in developing effective therapeutics for patients with neurodegenerative diseases. Our product candidates are engineered to reach their intended targets in the brain at exposure levels that will provide a therapeutic effect, while having an acceptable safety profile. We do not plan to bring a product candidate into late-stage clinical testing unless it has shown sufficient brain concentration and target engagement in the brain in preclinical models and early-stage clinical trials.

Engineering Large Molecule Brain Delivery

For large molecules, including therapeutic antibodies and enzymes, we are developing proprietary platform technologies to actively transport these molecules across the BBB through receptor-mediated transcytosis, or RMT. RMT through the BBB is the process by which macromolecules in the blood bind to receptors on the endothelial cells that make up the BBB and are actively transported and released into the brain. Our large molecule transport vehicle, or TV, platform technology engineers BBB receptor binding into an Fc domain (Figure 3). We have selected transferrin receptor, or TfR, which is a highly-expressed BBB receptor that we believe has the ability to substantially improve brain uptake of therapeutic molecules. This construct can be integrated and fused to therapeutic molecules as described below, without disrupting the binding of transferrin to TfR.

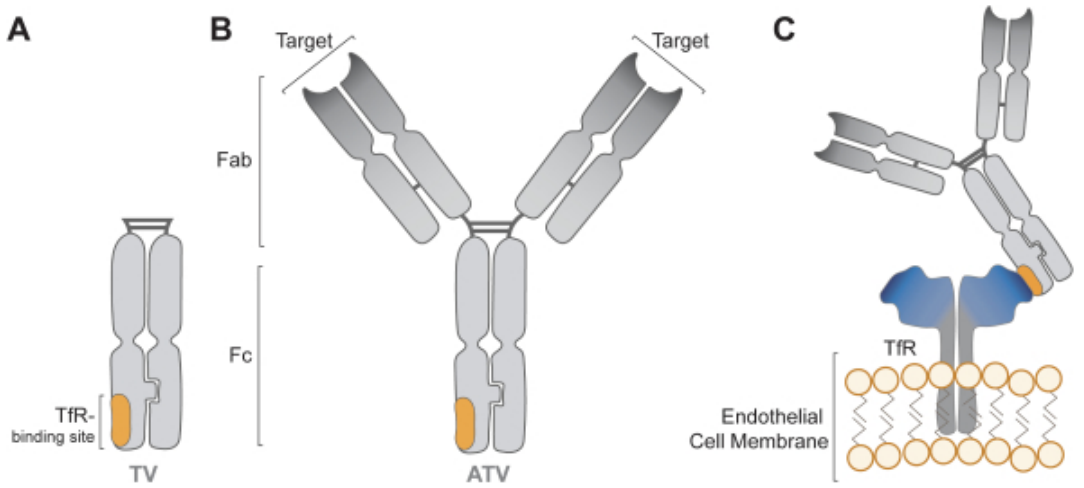


Figure 3. Schematic of the BBB large molecule Transport Vehicle (TV) technology. The TV platform technology contains BBB receptor (TfR) binding in the Fc domain (A). The TV can be fused to Fab arms constituting the Antibody Transport Vehicle (ATV) technology (B). ATVs bind to TfR, enabling TfR-mediated transcytosis and brain uptake (C).

Antibody Transport Vehicle

Our ATV platform technology utilizes the BBB receptor binding Fc domain to engineer bispecific and bivalent antibodies with improved brain delivery (Figure 4).

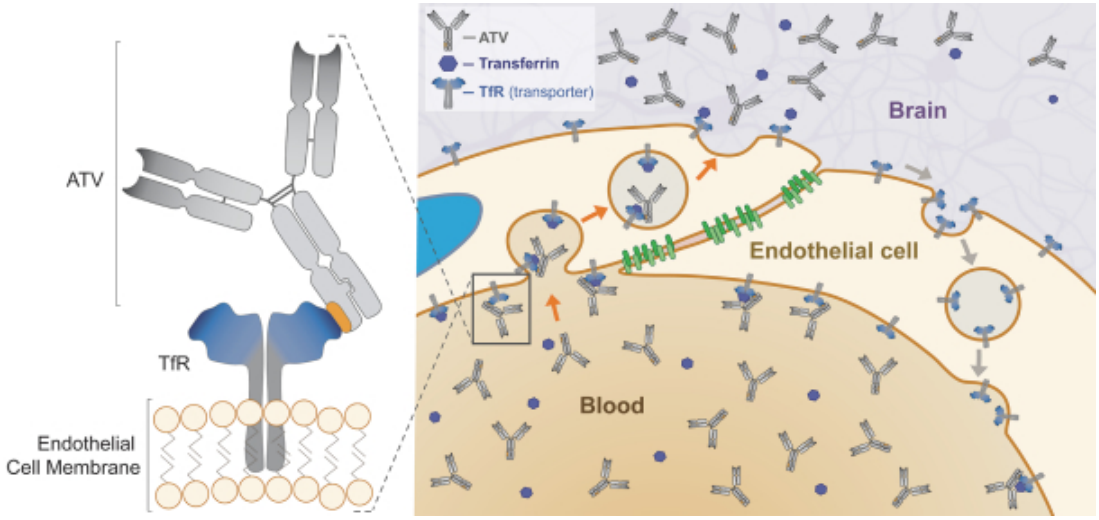


Figure 4. Schematic of receptor-mediated transport of ATV at the BBB. ATV molecules engage TfR on the blood vessel wall in the brain. Once bound, ATV is brought into vesicles that are transcytosed across the endothelial cell and released into the brain, thus substantially increasing antibody concentrations in brain. ATV binding to TfR does not disrupt the binding of transferrin to TfR.

We have achieved *in vivo* proof of concept for the ATV platform in mice whose genomes have been engineered to express a portion of the human TfR gene at a specific location, or human TfR knock-in mice, and we have generated initial validating data in an ongoing study in nonhuman primates.

In the human TfR knock-in-mouse model, we have completed three preclinical studies designed to demonstrate proof of concept for the ATV platform. Such studies have demonstrated an average 20-fold increased antibody uptake in the brain, compared to a control antibody (Figure 5).

As a result of a dramatic improvement in brain antibody uptake with the ATV, we observed a robust brain pharmacodynamic, or PD, response, which is the biochemical and physiological effect of a drug, as measured by reduction in levels of amyloid beta in brain. This represents a highly disease relevant proximal readout as amyloid beta levels are a primary driver of the amyloid plaque pathology in Alzheimer's disease. These data demonstrate that the brain concentrations achieved with the ATV platform are in excess of levels needed to mediate a therapeutic response. Without the ATV, the control antibody was unable to have a desired PD effect in the brain (Figure 5).

ATV-enabled antibodies also showed broad distribution in the brain, effectively crossing the BBB and associating with brain cells. Using brain imaging techniques, human IgG1 distribution was compared between a control anti-BACE1 antibody and ATV1:BACE1 (Figure 5). Images show robust localization of ATV1:BACE1 with cells in the brain after systemic delivery. These proof of concept data in a human TfR knock-in-mouse model demonstrate the ability of ATV to achieve therapeutic concentrations and broad distribution in brain.

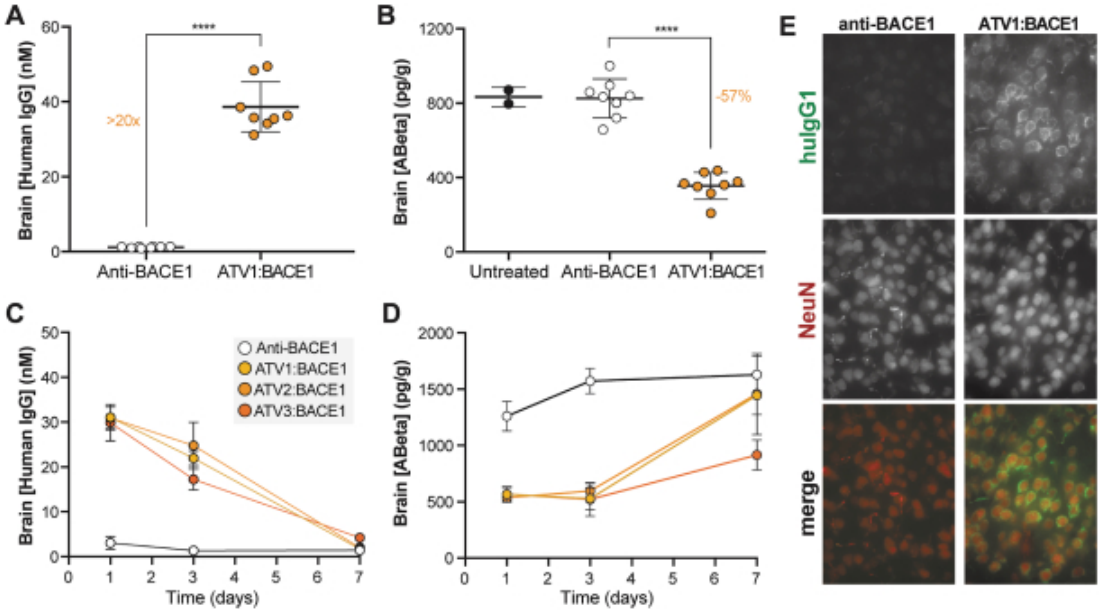


Figure 5: ATV therapeutics achieve robust brain uptake and pharmacodynamic activity in human TfR knock-in mice. Mice were injected with 50 mg/kg of anti-BACE1 or ATV1:BACE1. After 24 hours of circulation, brain antibody concentrations were compared between anti-BACE1 (1.2nM) and ATV1:BACE1 (38.6nM) (A). A significant reduction in brain Abeta levels (57%) was observed for mice injected with ATV:BACE1 compared to anti-BACE1, where no reduction was observed as compared to untreated mice (B). Mice were injected with 50 mg/kg of anti-BACE1, ATV1:BACE1, ATV2:BACE1 or ATV3:BACE1. All ATV:BACE1 variants show a significant increase in brain uptake at 1 and 3 days post-dose as compared to anti-BACE1 (C). Significant brain Abeta reduction was observed for all ATV:BACE1 variants at 1 and 3 days post-dose, and for ATV3:BACE1 at 7 days post-dose, as compared to anti-BACE1 (D). Immunohistochemistry staining of brain sections from mice injected with either anti-BACE1 or ATV1:BACE1 24 hours post-dose. Robust and broad neuronal distribution of systemically administered ATV1: BACE1, but not anti-BACE1 is observed (E). HulgG1 labels antibody; NeuN labels neurons; ** indicates p<0.0001.**

To further validate the ATV platform, we initiated an *in vivo* study in nonhuman primates with an ATV designed to bind to cynomolgus monkey TfR (ATV4:BACE1). Initial data from this ongoing study

demonstrates a robust and sustained brain PD response as measured from fluid taken from brains of living monkeys (Figure 6). When measuring drug activity in blood (plasma) versus brain (CSF), both anti-BACE1 and ATV4:BACE1 show robust activity in the blood, however only the ATV enabled antibody (ATV4:BACE1) demonstrated robust and sustained PD activity in the nonhuman primate brain. We believe these *in vivo* proof of concept data in nonhuman primates provide support for the translatability of the ATV platform for human studies.

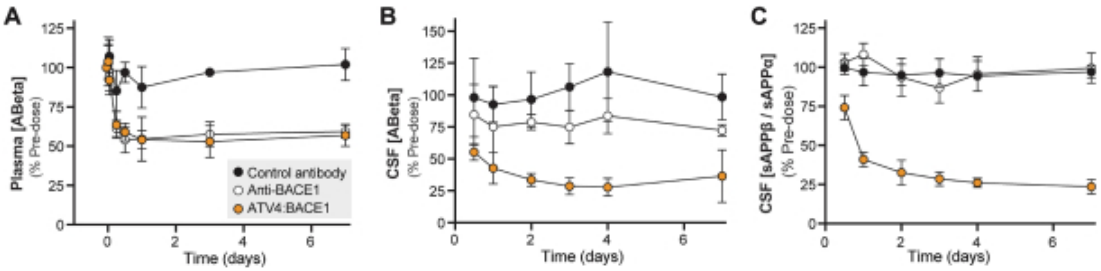


Figure 6. ATV therapeutics achieve CNS pharmacodynamic activity in nonhuman primates. Cynomolgus monkeys were systemically injected with 30 mg/kg of control antibody, anti-BACE1, or ATV4:BACE1. In plasma, anti-BACE1 and ATV4:BACE1 equally reduce Abeta levels (A). In CSF, a robust and sustained reduction in CSF Abeta (B) and soluble APPbeta/APPalpha ratio (C) was observed in monkeys injected with ATV4:BACE1 compared to control antibody. In contrast, anti-BACE1 has minimal impact on CSF Abeta and APPbeta/APPalpha levels (C).

Enzyme Transport Vehicle

Our ETV platform utilizes the same RMT approach as our ATV platform to deliver enzymes across the BBB. One potential application of this technology is the neurological component of LSDs. The ETV platform technology is an Fc enzyme fusion in which the TfR binding is engineered into the Fc domain (Figure 7). The high modularity of the platform make it uniquely well suited for delivery of enzymes across the BBB. The ETV enables different fusion formats with one or two enzymes. The characteristics of the ETV platform are also applicable to proteins and peptides that may be fused to the platform for other indications.

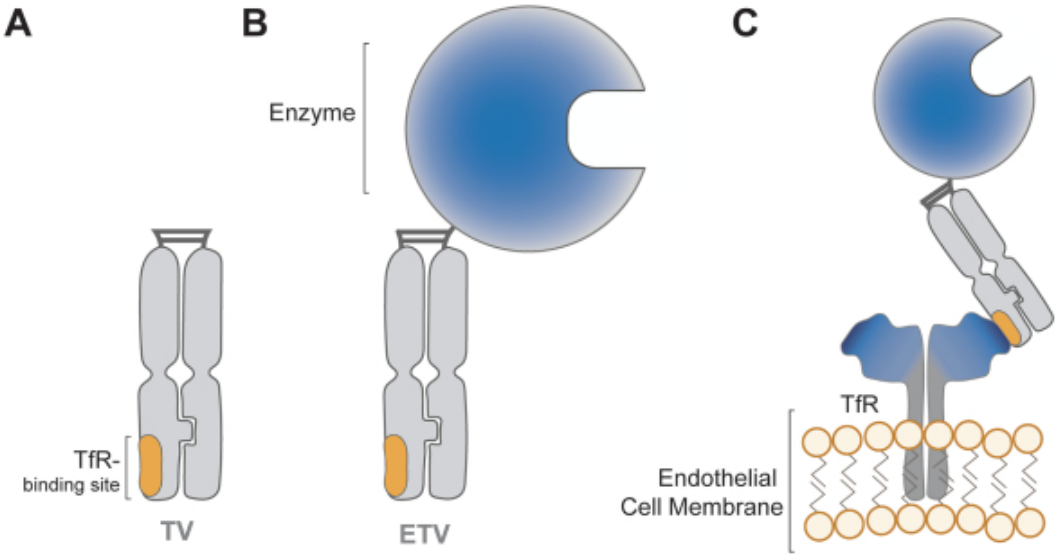


Figure 7: Engineering brain delivery using the ETV platform. The ETV platform technology contains BBB receptor (TfR) binding in the Fc domain (A) fused to an enzyme (B) to enable transport of enzymes into the brain through TfR-mediated transcytosis (C).

Platform Technology Development and Applications

We are advancing our ATV and ETV platforms through further preclinical studies in mice and non-human primates. We plan to commence IND-enabling studies with multiple preclinical product candidates in 2018 and initiate clinical trials in 2019. We are also combining our proprietary human TfR knock-in-mice model with disease-specific animal models in order to more precisely assess the potential of our ATV-enabled therapeutic candidates in relevant disease models. We expect that this will give us the ability to perform pharmacokinetic/pharmacodynamic, or PK/PD, and efficacy studies and to quantitatively demonstrate the advantages of antibodies and proteins delivered using our ATV platform technology.

To enable the development of our ATV and ETV platform technologies, we have entered into a strategic licensing and collaboration agreement with F-star. This collaboration gives us the ability to obtain exclusive access to an intellectual property portfolio covering engineering of the Fc region of antibodies for use with specific targets, such as the TfR. The collaboration enhances our own protein engineering capabilities by leveraging F-star's more than 10 years of experience in this area. Our collaboration is focused on TfR binding with the option to expand the collaboration to develop two additional BBB receptor targets.

We believe that our ATV and ETV platforms are also broadly applicable beyond neurodegeneration and LSDs to improve delivery of antibodies to treat other brain diseases, including cancer. We currently are not pursuing these additional indications, but we may do so independently or with partners in the future.

Engineering Small Molecule Brain Delivery

We are focused on engineering small molecule therapeutics that achieve exposure levels in the brain sufficient to bind to protein targets and drive a therapeutic effect. Efficacious orally administered small-molecule medicines for brain diseases must be readily absorbed from the gut into the blood and penetrate the BBB while avoiding transporter-mediated efflux (Figure 8). It has been estimated that approximately 98% of small molecule drugs do not cross the BBB.

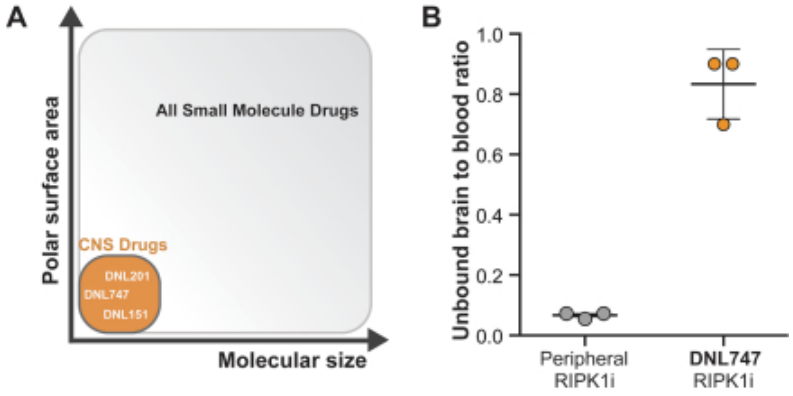


Figure 8: Generation of brain penetrant small molecules. The molecular properties compatible with CNS drugs are significantly more restricted than those generally used to design small molecule drugs, including tight restrictions on

molecular weight and total polar surface area (A). This figure is not to scale. An example of how molecular properties influence brain penetration is shown in (B), where our lead RIPK1 inhibitor DNL747 displays a brain to blood ratio of ~0.8 while a benchmark periphery-restricted RIPK1 inhibitor displays a ratio of ~0.05.

Our small molecule drug discovery scientists have many years of experience designing small molecules for brain diseases, including DNL151, one of our lead LRRK2 inhibitors, and DNL747, our lead RIPK1 inhibitor, both of which have demonstrated strong brain exposure and confirmed target engagement in preclinical studies.

Biomarker-Driven Development

Translational science is the process of gathering and interpreting data obtained from cellular and animal models to inform the design and expected clinical outcome of future patient studies. In the field of neurodegeneration, this has been particularly difficult due to a lack of validated biomarkers and predictive animal models to confirm drug exposure and target engagement in brain tissue, as well as clinical disease progression and response. Historically, many programs have advanced into late-stage clinical trials prior to demonstrating a relevant biologic response.

We define biomarker goals at every phase of development, including prior to the filing of an IND. As molecules transition from the discovery phase to early clinical development, we focus on refining our understanding of the relationship between the PK/PD response and modulation of target biology using target engagement and other relevant biomarkers. This integrated approach allows for the design of rigorous and informative pharmacology experiments.

In addition, we strive to develop a patient selection strategy guided by a genetic rationale and understanding of target biology for each of our programs. With this approach, we seek to increase the probability of success and make drug development more cost efficient by attempting to minimize avoidable errors in dose selection and study design that are impactful and costly in Phase 2 and Phase 3 clinical trials.

Approach to Target Engagement and Dose Selection

As part of our strategy, we are developing proprietary reagents, which are substances used to characterize or quantify a biological process or component, and assays, which are procedures to assess the amount or activity of a target entity, to enable biomarkers for each of our core programs. These biomarkers, which are relevant for both animal models and human trials, are critical for patient selection, predicting and measuring target engagement, supporting dose selection and enabling decisions on progression of product candidates to the next phase of development. Because potential targets of interest are in the brain, it is important to develop reagents that can assay specific biomarkers not only in the blood but also in the cerebrospinal fluid, or CSF, and the brain. By enabling biomarkers that are present in both animal models and humans, we are able to create a clinical strategy whereby measurements of exposure and target engagement in animals allows for better clinical translation and PK/PD modeling for human trials.

An example of this approach is reflected in our LRRK2 program. We developed validated assays of LRRK2 kinase activity that measure phosphorylation of LRRK2 at Serine 935, or pS935, or the phosphorylation of the LRRK2 substrate Rab10, or pRab10. In a preclinical monkey model, we have demonstrated that, following a single dose of a brain penetrant LRRK2 kinase inhibitor, there is a dose dependent reduction of LRRK2 kinase activity observed in the brain that is reflected in LRRK2 kinase inhibition in peripheral blood mononuclear cells, or PBMCs. Experiments such as this establish a relationship between peripheral (e.g. blood) and central (e.g. brain) target engagement, enabling the prediction of central target engagement in humans with measurements of blood and CSF drug exposure in conjunction with a peripheral assay for LRRK2 kinase activity.

Development of blood based assays potentially enables an assessment of target engagement in the clinic as early as first-in-human Phase 1 trials in healthy volunteer subjects. We have developed human assays using healthy control blood samples to assess performance of clinical candidates, and we regularly refine the reliability and quantitative rigor of our target engagement assays. After development of prototype assays, high sensitivity, high throughput, and quantitative platform based assays are developed for clinical use.

In the design of our Phase 1 trials, we plan to integrate our target engagement biomarker data with pharmacokinetic, or PK, analysis, which is the time course of drug absorption, distribution, metabolism and excretion, from both the plasma and CSF to determine the relationship between dose, time and drug response. We develop an integrated exposure response model that enables tailoring of the dose selection for future patient studies. This model relies on the quantitative PD biomarkers assessment enabled by the development and refinement of reliable assays, described above. We plan to progress product candidates that show robust target engagement at well-tolerated doses in early clinical development into our proof of concept trials.

We have identified target engagement biomarkers for all six of our core programs. When practicable, we are developing patient selection biomarkers for our programs to enable identification of patients with the relevant disease biology and stage of disease likely to benefit from targeted therapy in order to increase the likelihood of success of clinical trials. Ultimately, by reducing the number of patients that are likely to experience a low treatment response, we expect to positively impact market acceptance of these targeted therapies driven by high and meaningful response rates within the targeted population as defined by the patient selection biomarkers. In certain indications, regulatory approval may limit the market of a product candidate to target patient populations when patient selection biomarkers are used. In these indications, regulatory authorities may require us to run additional clinical trials prior to expanding the label for approval that includes a broader patient population.

We plan to leverage the target engagement biomarker data resulting from Phase 1 healthy volunteer studies to determine target engagement and guide dose selection in patients. We have invested in capabilities to obtain blood samples and other samples from patients with Alzheimer’s disease, Parkinson’s disease, and ALS to improve our prediction of relevant exposure-response relationships and support the design of future patient clinical trials. The data from these biomarker assessments using proprietary assays and PK analyses are critical to dose selection in the design of Phase 1b and Phase 2 clinical trials.

Approach to Pathway Engagement and Disease Progression

Our approach to building expertise in pathway biology enables identification of candidate pathway biomarkers that can be assessed in our clinical studies to understand pathway engagement and may serve as potential endpoints. An example of this approach is outlined in Figure 9. In this example, development of reagents for fluid biomarkers (for instance, Rabs) as well as imaging biomarkers (for instance, dopamine transporter imaging, or DAT) are being evaluated.

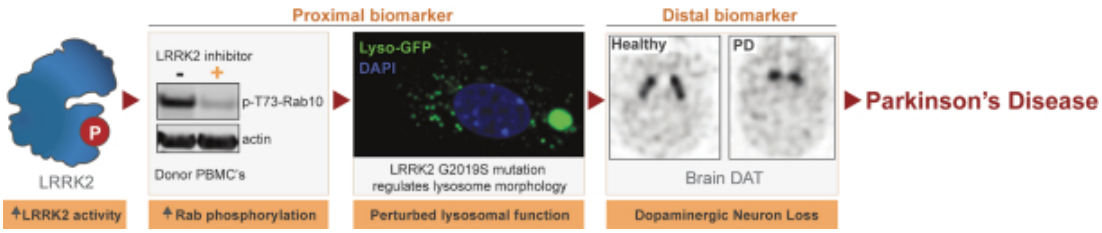


Figure 9: Example of strategic approach to generate biomarkers of LRRK2 target engagement (i.e., Rab phosphorylation), pathway modulation (i.e., lysosomal function) and disease modification (i.e. brain DAT imaging) to build evidence of relevant biologic activity that will impact clinical outcomes.

Approach to Patient Selection

In the past, the diagnosis of neurodegenerative diseases has generally relied on clinical diagnosis, without direct confirmation of pathology. This approach is inherently prone to errors, including misdiagnosis. The lack of pathology-confirming biomarkers has led to the enrollment of patients in clinical trials for neurodegenerative diseases who were very unlikely to respond to treatment, including patients who in fact did not have the disease being studied.

Our focus on degenogenes and the underlying biology of genetic pathways enables more precise selection of patients compared to relying only on a clinical diagnosis. For example, genotyping Parkinson's disease patients for LRRK2 mutations is a strategy for patient selection. Alzheimer's disease is likely a heterogeneous disease with different biology contributing to common downstream effects, including amyloid deposition in the brain. In Alzheimer's disease, understanding the biology of patient subsets defined by APOE4 genetic status as well as inflammatory biomarkers highlighted by Genome Wide Association Studies, provides hypotheses for development of novel biomarkers that can identify the subset of patients most likely to benefit from a particular therapeutic approach.

By utilizing biomarkers and genetic information, we can better target and select the best patient population for our clinical trials and product candidates.

Our Portfolio

As described above, our portfolio currently comprises six core programs and five seed programs. In addition, we continually evaluate additional targets for inclusion as seed programs, while we seek to maintain a rigorous process of prioritization and resource allocation to maintain an optimal balance between aggressively advancing lead programs and ensuring replenishment of the portfolio. We discuss our six core programs in further detail below.

Lysosomal Function Pathway Programs

LRRK2 Inhibitor Program

The two most advanced product candidates are potent, selective and brain penetrant small molecule LRRK2 inhibitor product candidates for Parkinson's disease. DNL201 is currently in a Phase 1 clinical trial. DNL151 has completed IND-enabling preclinical studies. We submitted a CTA for DNL151 to the Netherlands Health Authority in October 2017 and it was accepted in November 2017.

Therapeutic Rationale

Lysosomal dysfunction is a central pathology of Parkinson's disease. Genetic mutations in several proteins associated with Parkinson's disease, including LRRK2, GBA and aSyn, disrupt normal

lysosomal function and contribute to the formation of Lewy bodies, which are intracellular aggregates containing aSyn proteins, and neurodegeneration (Figure 10). LRRK2 regulates lysosomal function by phosphorylating Rab proteins, which control intracellular lysosomal trafficking (Figure 11). Mutations in the LRRK2 gene that cause Parkinson's disease increase both LRRK2 kinase activity and the phosphorylation of Rab proteins. Excessive phosphorylation of Rab proteins alters Rab localization and disrupts normal lysosomal movement and maturation. Inhibition of LRRK2 kinase activity with a LRRK2 kinase inhibitor reduces Rab phosphorylation and restores normal lysosomal morphology.

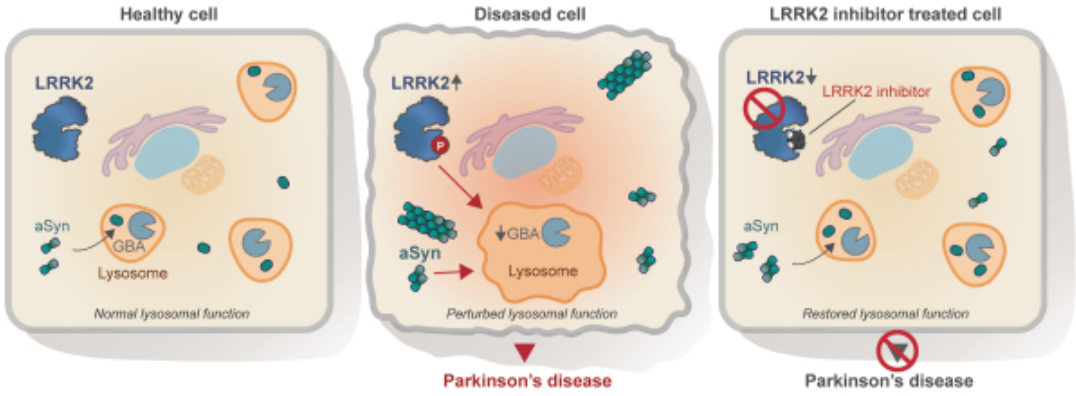


Figure 10: LRRK2 acts in healthy cells to maintain normal lysosomal function. Excessive LRRK2 activation or expression reduces lysosomal function and contributes to the progression of Parkinson's disease. Lysosomal dysfunction in Parkinson's disease can also be caused by high levels of aSyn and by loss of function of GBA. LRRK2 inhibition can restore normal lysosomal function and reduce toxicity in Parkinson's disease models.

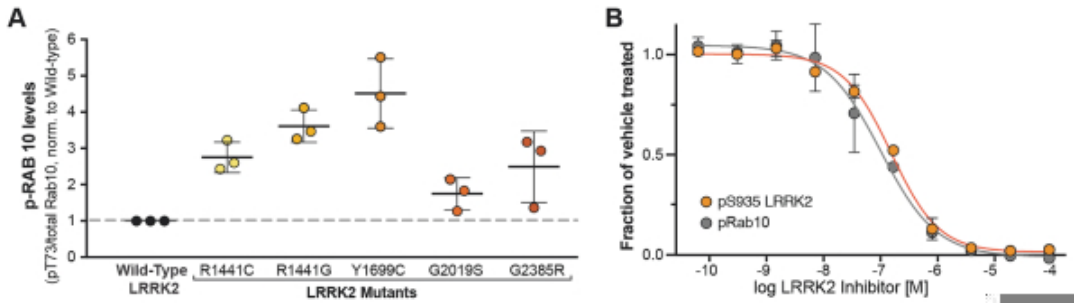


Figure 11. Phosphorylated Rabs are a novel marker of LRRK2 activity. Multiple distinct LRRK2 mutations result in elevated phosphorylation of the downstream marker Rab10 (A), while inhibition of LRRK2 results in a dose-dependent inhibition of Rab10 phosphorylation that is comparable to the inhibition of LRRK2 phosphorylation on Serine 935 (B).

Inhibition of LRRK2 kinase activity has been shown to be beneficial in several cellular and *in vivo* models. The most common LRRK2 mutation, G2019S, is a point mutation that results in increased kinase activity, abnormal lysosomal biology and an increased risk of Parkinson's disease. LRRK2 G2019S expression in cells from transgenic mice or other cell lines reduces the lysosomal capacity of the cell, leading to decreased lysosomal function. These defects are dependent on LRRK2 kinase activity, and treatment with DNL201 rescues the observed lysosomal phenotype (Figure 12). LRRK2 G2019S expression in neurons leads to a similar lysosomal phenotype and also results in reduced neurite outgrowth, an effect that can be rescued with LRRK2 kinase inhibition.

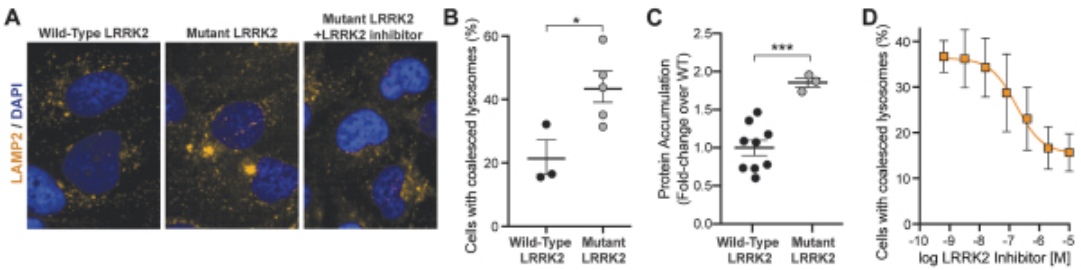


Figure 12: Effect of LRRK2 mutations on lysosomes. Cells expressing LRRK2 with the G2019S mutation display coalesced and dysfunctional lysosomes that are not present in cells expressing normal (WT) LRRK2. The presence of these abnormal lysosomes can be reversed through treatment with LRRK2 kinase inhibitors (A). Lysosomes can be visualized via LAMP2 (orange) while DAPI (blue) labels nuclei. This lysosomal defect is quantified in (B), and correlates with a loss of lysosomal function as measured by the amount of protein degradation (C). Inhibition of LRRK2 with our compounds results in a dose-dependent rescue of lysosomal abnormalities (D). * indicates p<0.05, * indicates p<0.001.**

Patients with Parkinson's disease often have high levels of activated immune cells and inflammatory markers in blood and CSF. LRRK2 is highly expressed in glia and other immune cells, and LRRK2 kinase inhibition or knockout of the LRRK2 gene protects animals in inflammatory disease models, including rhabdomyolysis kidney injury, exposure to the bacterial toxin lipopolysaccharide, and experimental autoimmune uveitis. These findings suggest that LRRK2 inhibition may reduce the deleterious inflammatory responses associated with Parkinson's disease.

Mutations in the aSyn gene and aSyn overexpression may cause certain forms of familial Parkinson's disease, and aSyn oligomers are thought to accelerate neurodegeneration. *In vitro* and *in vivo* models that employ aSyn oligomers to cause inflammation and cellular and lysosomal dysfunction are commonly used as preclinical models of Parkinson's disease. Microglia from mice that do not express LRRK2 absorb and degrade aSyn more effectively than wild-type mouse microglia. In most cell and mouse aSyn models, reducing LRRK2 kinase activity or expression protects animals from neurodegeneration and excessive inflammation. These findings provide further support for inhibition of LRRK2 activity as a therapeutic strategy to treat Parkinson's disease.

Patient Population

Mutations in the LRRK2 gene are the most frequent cause of familial Parkinson's disease and, in addition, are present in 1 to 2% of patients with sporadic Parkinson's disease in the United States. In total, we estimate that LRRK2 mutations account for approximately 2% to 3%, or 20,000 to 30,000, of one million total Parkinson's disease patients in the United States. The most common LRRK2 mutation, G2019S, is a point mutation that results in increased kinase activity and abnormal lysosomal biology. In addition to G2019S, six other pathogenic LRRK2 mutations resulting in increased LRRK2 expression or function have been strongly linked to Parkinson's disease.

While mutations that increase LRRK2 kinase activity provide the most direct link to the therapeutic rationale, other genetic drivers of Parkinson's disease, such as mutations in GBA and aSyn, are also associated with lysosomal dysfunction, which may be addressed through LRRK2 inhibition.

Furthermore, patients with idiopathic Parkinson's disease, i.e. patients with a clinical diagnosis of Parkinson's disease without a known genetic cause, typically also show signs of lysosomal dysfunction. Thus, as lysosomal dysfunction is a central pathology in patients with and without known

genetic drivers of disease, inhibition of LRRK2 may be a therapeutically beneficial approach for most patients with Parkinson's disease (Figure 13).

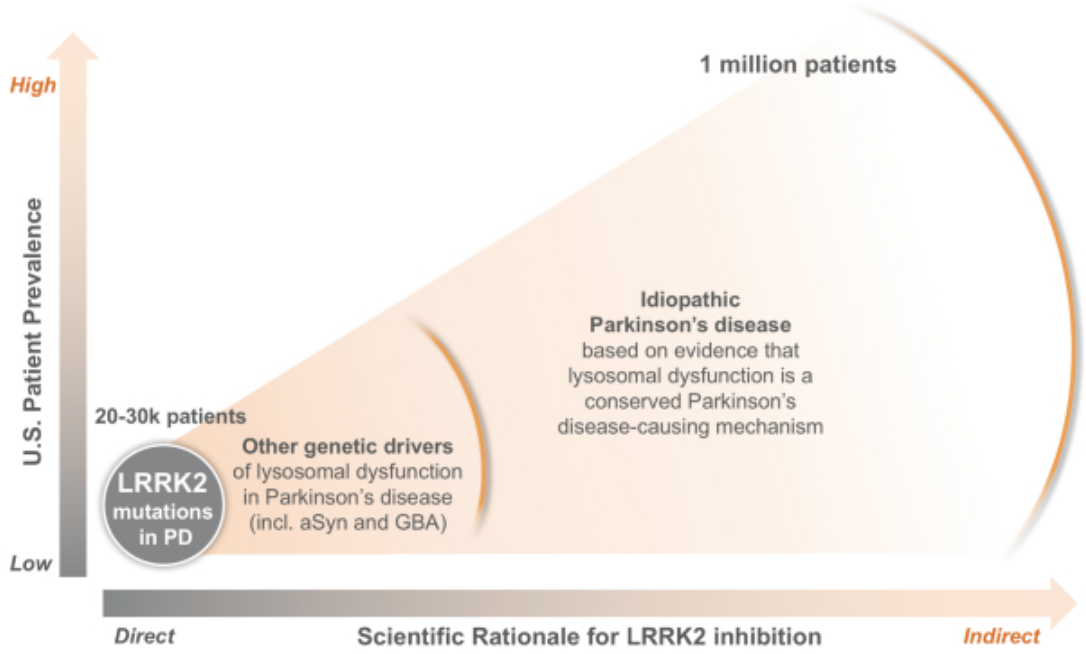


Figure 13: Target Parkinson's disease patient populations for LRRK2 inhibitor. (Figure not to scale)

Pharmacological Properties and Brain Exposure

We have a broad portfolio of potent, selective and brain penetrant LRRK2 inhibitors with attractive pharmacological properties. Our lead product candidates, DNL201 and DNL151, are selective, orally available, brain-penetrant, reversible small molecule inhibitors of LRRK2. The pharmacology of both product candidates has been investigated in a broad range of biochemical and cell-based *in vitro* assays, and both product candidates have been shown to inhibit LRRK2 activity with low nanomolar potency in human blood cells.

Both DNL201 and DNL151 displayed comparable potency of LRRK2 inhibition in both LRRK2 mutation carriers and non-carriers, with a trend to increased potency in G2019S mutation carriers (Figure 14).

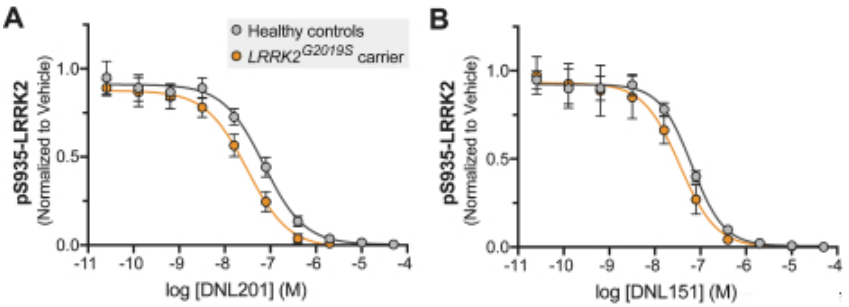


Figure 14. Treatment of peripheral blood mononuclear cells (PBMCs) derived from LRRK2 mutation and healthy non-carriers with our LRRK2 inhibitors. Both DNL201 (A) and DNL151 (B) demonstrated a small increase in potency in G2019S mutation carriers.

We have completed extensive preclinical PK and PK/PD evaluations of DNL201 and DNL151. Based on these data and preclinical modeling of clearance, the expected human half-life is compatible with BID (twice daily) dosing and QD (once daily) dosing for DNL201 and DNL151, respectively. Comparable unbound plasma and CSF exposures were observed in rodents and monkey, demonstrating that the compounds are brain penetrant and can achieve meaningful and sustained brain exposures as shown in a representative dataset for DNL201 (Figure 15). PD was characterized using a marker of LRRK2 kinase activity, pS935. Inhibition of pS935 in PBMCs is comparable to inhibition of pS935 in the brain after 28 days of dosing of DNL201 in monkey, demonstrating that peripheral blood inhibition of pS935 can be used to predict inhibition of pS935 in the brain. In toxicology studies in rodent and monkey, administration of DNL151 and DNL201 consistently resulted in dose-dependent inhibition of LRRK2 activity in peripheral tissues and in brain as measured by a reduction of pS935 LRRK2 levels.

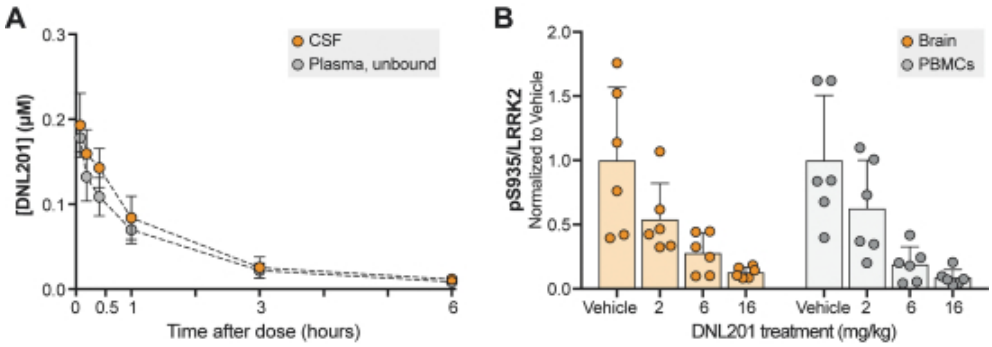


Figure 15. Exposure of DNL201 in monkey CSF and plasma (unbound) and activity of DNL201 in brain and PBMCs. Unbound DNL201 concentrations in plasma and CSF following intravenous administration of DNL201 are comparable (A). Similar pS935 inhibition is observed in PBMCs and brain 24 hours after the last dose is given (B).

The preclinical safety profiles of DNL201 and DNL151 have been characterized in a comprehensive battery of non-GLP and GLP safety pharmacology and single dose and repeat dose *in vivo* toxicology evaluations in rat and monkey. These PK, PK/PD and preclinical safety data indicate that both molecules can achieve significant levels of inhibition of LRRK2 kinase activity in the brain at dose levels that can be evaluated in clinical trials.

The definitive 28-day GLP toxicity studies for both DNL201 and DNL151 were conducted in monkey and rat. For these studies, the monkey was selected as the non-rodent species in order to fully

characterize previously reported data showing that multiple structurally distinct LRRK2 inhibitors cause pharmacologically-driven lung histology changes. A target-related kidney finding has also been previously reported in rodents dosed with LRRK2 inhibitors and in rodent transgenic models. These findings consist of accumulation of lipid membranes of lysosomal organelles (lamellar bodies) in cells in the lung and vacuolization (droplets) in the kidney, also a lysosomal phenotype. In summary, these histologic changes related to loss of function or inhibition of LRRK2 kinase did not impact life span in these animal models or have obvious functional effects. Mice that lack LRRK2 protein (LRRK2 knockout mice) live a normal life span with no obvious pulmonary or renal function abnormalities despite accumulation of lamellar bodies in the lung and droplets in the kidney. In a Michael J. Fox Foundation, or MJFF, sponsored study, three distinct LRRK2 kinase inhibitors produced a mild accumulation of the previously described lamellar bodies in the lung. After 15 days of dosing, there were no functionally significant alterations in any pulmonary function endpoint examined, including lung diffusion capacity, lung compliance, and forced vital capacity. In addition, after cessation of dosing, the findings were fully reversible. The conclusion of this MJFF sponsored study was that the morphological changes observed in the lungs of LRRK2 kinase inhibitor treated monkeys may not prevent the clinical evaluation of the therapeutic potential of LRRK2 kinase inhibitors in Parkinson's disease. We have further characterized the cellular effects of LRRK2 kinase inhibitors and believe that the histological changes seen with LRRK2 inhibition in kidney and lung are due to direct effects on lysosomal morphology that are related to the therapeutic potential of LRRK2 inhibition in treatment of Parkinson's disease. In a cellular model of Parkinson's disease, a LRRK2 G2019S cell line model, cellular abnormalities due to defects in lysosomal function are characterized by morphologic abnormalities including a reduced number of lysosomes and abnormally large lysosomes. With inhibition of LRRK2 in this cellular model, the altered lysosomal morphology can be corrected, and with full inhibition, increased lysosomal number and area is observed, similar to the changes seen in rodent models lacking LRRK2 function and in monkeys dosed with LRRK2 inhibitors.

In the 28-day GLP toxicity studies for DNL201 in rats and monkeys, no adverse findings were observed at doses with exposure multiples >9-fold higher than the predicted maximum concentration, or Cmax, at therapeutic dose levels. In both rats and monkeys, findings were determined to be reversible following a 28-day treatment free period. On-target histological changes of vacuolation in rat kidney and lamellar body accumulation in monkey lung with DNL201 dosing were observed as expected. In prior pilot toxicity studies for DNL201, which were designed to define the maximum tolerated dose of DNL201 in rat, severe clinical signs were observed at high doses where the observed exposure is well in excess of that required for therapeutic efficacy (e.g. Cmax is ^{3}20-fold higher than the predicted Cmax at therapeutic dose levels). These severe clinical signs included labored breathing and severe hypoactivity. Results from an investigative preclinical cardiovascular study performed by us in rats supports that these severe clinical signs are caused by a monitorable cardiovascular mechanism characterized by a mild drop in blood pressure and increased heart rate after the first and second dose in all animals studied, followed by more profound drops in blood pressure associated with severe clinical signs after the third dose in a subset of rats. In this study, the rats recovered from the clinical signs after cessation of dosing.

Based on these studies, the U.S. Food and Drug Administration, or FDA, approved the Phase 1 clinical trial for DNL201 but placed DNL201 on a partial clinical hold in order to impose an exposure cap. With the current exposure cap, we are able to dose to an exposure that we believe will be sufficient to inhibit LRRK2 50% on average over the dosing period and should effectively normalize LRRK2 kinase activity. The FDA may re-evaluate the exposure cap for this study, and may potentially raise it, based on the safety and tolerability data generated by the study as it progresses as well as the data supporting the monitorability of the effects of the study. If the exposure cap is not lifted in the Phase 1 clinical trial, we will not be able to evaluate doses and exposures that would potentially achieve higher degrees of LRRK2 kinase inhibition, which may negatively impact the development of DNL201.

For DNL151, in the 28-day GLP toxicity studies, no adverse findings were observed at doses with exposure multiples >11-fold higher than the predicted Cmax at therapeutic dose levels in both monkey and rat. All findings were determined to be non-adverse and reversible following a 28-day treatment free period. In pilot toxicity studies severe clinical signs were observed at Cmax ^{3} 18 fold and ^{3} 49 fold above the predicted Cmax at therapeutic dose levels in monkey and rat, respectively. These severe clinical signs include signs consistent with cardiovascular effects, and signs consistent with effects on the central nervous system, including tremors, pupillary changes, and decreased activity. Based on these studies, a CTA was submitted and accepted by the Netherlands Health Authority with proposed doses that enable exposures that inhibit LRRK2 up to 60% at trough in the Phase 1 clinical trial protocol and maintain margins at least 10-fold and 5-fold below the severe toxicities and the no-observed-adverse-effect-level, respectively. We believe that with the FDA mandated exposure cap for DNL201 and the protocol-defined doses for DNL151, we can achieve exposures that inhibit LRRK2 at least 50% on average over the dosing period.

Based on our robust biomarker assay capabilities to monitor target engagement and assess the exposures desired to reach our target engagement goals, the preclinical safety data support that both molecules can achieve significant levels of inhibition of LRRK2 kinase activity in the brain at dose levels that can be evaluated in clinical studies under the FDA mandated exposure cap and the protocol defined limits for DNL201 and DNL151, respectively.

Biomarker-Driven Development

We are using genetic, biochemical and imaging biomarkers to support evidence of target engagement, pathway engagement of biologic function relevant to Parkinson's disease (e.g., lysosomal biology) and effect on dopaminergic neurons as well as patient selection.

We have developed validated assays that measure pS935 and pRab10 phosphorylation as a marker of LRRK2 kinase activity to demonstrate target engagement. We are also developing techniques to further investigate the impact of LRRK2 inhibition on lysosomal function or inflammation in clinical studies, including methods to assess levels of phosphorylated Rab proteins.

Brain imaging techniques have been developed to measure deficits in dopaminergic transmission, which is closely associated with the decrease of dopaminergic neurons, a hallmark of Parkinson's disease. These techniques should allow us to monitor the potential beneficial effect of our LRRK2 product candidates on neurological function.

We are initiating efforts to recruit a targeted patient population with disease causing LRRK2 mutations including G2019S, R1441C, R1441G, I2020T and Y1699C. These mutations can be easily identified with a blood test.

Development Plan

In June 2017, we initiated a randomized, double-blind, placebo-controlled, single-center Phase 1 clinical trial in healthy young and healthy elderly subjects for DNL201 (Figure 16). The study aims to investigate the safety and tolerability of single and multiple oral doses of DNL201 and characterize the PK and PD of DNL201 in plasma and CSF. Target engagement is being assessed in blood (PBMCs) using the pS935 and pRab10 biomarkers and extrapolated to estimate target engagement in the brain. As an exploratory endpoint, candidate biomarkers in CSF are also being evaluated. The target engagement goal for the LRRK2 clinical development program is to achieve at least 50% average target inhibition over the dosing interval in order to normalize LRRK2 kinase activity. This target engagement goal is based on data indicating that LRRK2 activity in Parkinson's patients is estimated to be almost twice that of healthy individuals.

In the ongoing, blinded Phase 1 clinical trial in healthy volunteers, we have achieved dose escalation up to single doses of 60 mg and multiple doses of up to 40 mg BID. The mean CSF/unbound plasma concentration ratio was 0.99 demonstrating that DNL201 is distributed extensively into CSF, a measure of brain drug exposure. DNL201 exposures have reached the FDA mandated exposure limit. Based on clinical safety data to date, as well as investigative preclinical toxicology data supporting monitorability of these findings, we have submitted a complete response to the FDA mandated partial clinical hold in November 2017 to request lifting the exposure cap to permit additional dose escalation to achieve higher levels of target inhibition.

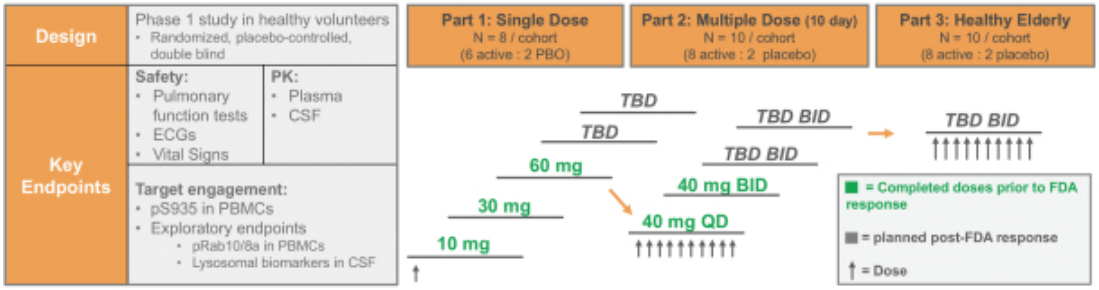


Figure 16. Overview of DNL201 Phase 1 clinical trial in healthy volunteers.

After completion of the ongoing Phase 1 clinical trial in healthy volunteers for DNL201 and the future Phase 1 clinical trial for DNL151, we plan to progress one of DNL201 or DNL151 into a 28-day Phase 1b double-blind, placebo-controlled safety, PK and biomarker study in LRRK2 mutation-carrying Parkinson's disease patients. The primary objectives of this trial will be to evaluate safety, PK and PD of such candidate in LRRK2 patients to identify the lead optimal dose(s) to study in potential future Phase 2 and Phase 3 clinical trials.

ATV:aSyn Program

Our ATV:aSyn program targets aSyn, a protein that has been identified as genetically linked to Parkinson's disease. We have developed high affinity antibodies for aSyn and are currently characterizing molecules in order to select a lead to couple with our proprietary ATV platform. We expect to file an IND or CTA for this program in 2020.

Therapeutic Rationale

aSyn is a protein in the brain linked to the development of Parkinson's disease. Lysosomal dysfunction in neurons can contribute to aSyn aggregation. This in turn leads to neuronal degeneration and results in the formation of Lewy bodies, the defining neuropathological characteristic of Parkinson's disease. Certain genetic mutations in aSyn and overexpression of the gene encoding aSyn have been identified as a cause of familial Parkinson's disease while a common polymorphism in this gene increases the risk for Parkinson's disease. Examination of human brains has revealed that aSyn pathology spreads spatially during the course of the disease, while animal model data demonstrate that this spread can be blocked with anti-aSyn antibodies (Figure 17).

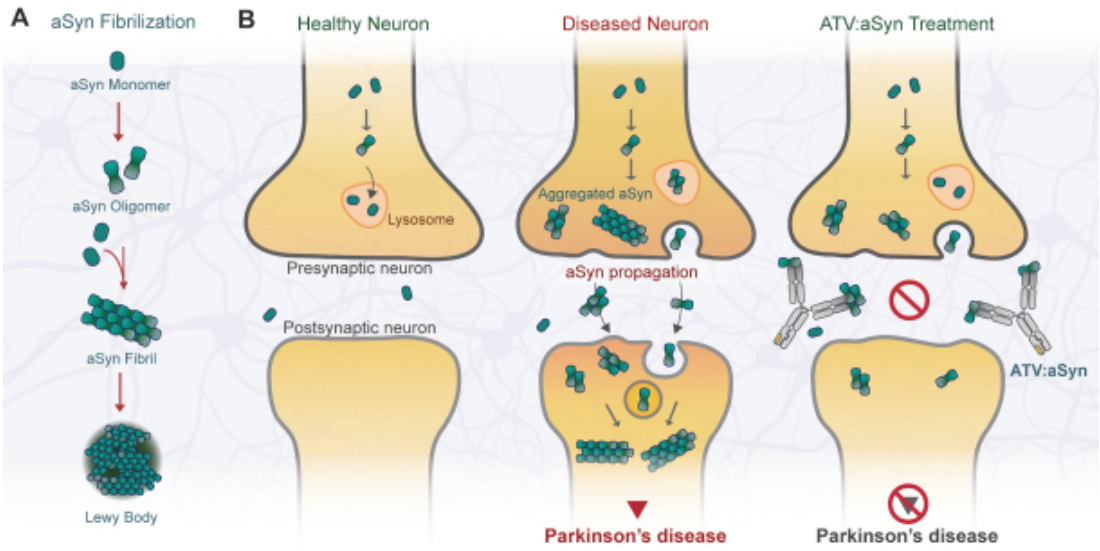


Figure 17: The aSyn protein is present in healthy neurons but can become misfolded and aggregated into oligomers, fibrils, and Lewy body pathology in Parkinson's disease (A). In diseased neurons, misfolded or oligomeric aSyn can be transmitted from one cell to another, resulting in spreading of aSyn pathology throughout the brain. ATV:aSyn antibodies are designed to block this spread through neutralizing extracellular aSyn (B).

We are developing ATV:aSyn for the treatment of Parkinson's disease. While at least one of our competitors has advanced an anti-aSyn antibody into early-stage clinical studies, we believe that ATV:aSyn will be differentiated from competitors by achieving higher brain concentrations through our ATV technology and higher affinity binding to the multiple forms of aSyn. We believe that this combination may result in superior target engagement leading to a higher probability of demonstrating efficacy in patients with Parkinson's disease.

Pharmacological Properties and Brain Exposure

We have identified a panel of anti-aSyn antibodies with different binding properties that may have best-in-class potential based on high affinity binding, distinct epitopes and excellent selectivity. We have designated three of these antibodies, anti-aSyn1, anti-aSyn2, and anti-aSyn3, as leads for further characterization. The aSyn present in the brains of Parkinson's disease patients can be found in monomer, soluble oligomer or insoluble fibril forms. Anti-aSyn1 and anti-aSyn2 display low nanomolar affinity to all forms of aSyn while anti-aSyn3 shows picomolar binding to aSyn oligomers, which have been hypothesized to represent a key toxic species in Parkinson's disease.

We determined that PK profiles for our lead anti-aSyn antibodies were comparable to a control antibody in mice. Target engagement for anti-aSyn1 and anti-aSyn2 was then demonstrated in brain using mice expressing the human form of aSyn. Both lead antibodies also demonstrated superior aSyn binding in CSF from Parkinson's disease patients as compared to benchmark anti-aSyn antibodies comparable to competitor antibodies currently in clinical development (Figure 18). This experiment establishes that both anti-aSyn1 and anti-aSyn2 bind to biologically relevant human aSyn in mice.

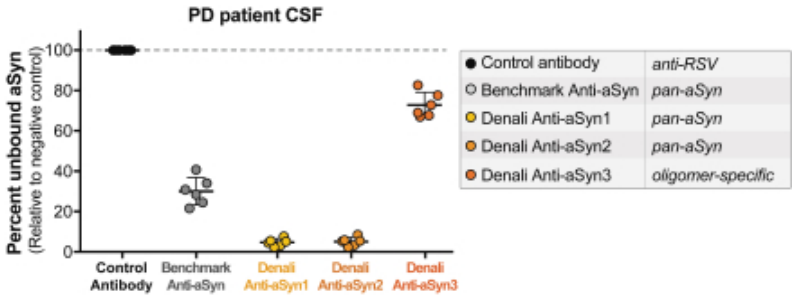


Figure 18: Our pan anti-aSyn antibodies, anti-aSyn1 and anti-aSyn2, recognize a greater proportion of extracellular aSyn present in CSF from six Parkinson's disease patients, as compared to a benchmark antibody while our oligomer-specific antibody anti-aSyn3 recognizes a smaller fraction of aSyn in CSF.

We plan to test our three lead anti-aSyn product candidates for their ability to block aSyn spreading in the brains of animal models. Our product candidate that demonstrates the most favorable profile of target engagement and efficacy will be selected for combination with our ATV platform as our first ATV:aSyn clinical candidate for IND-enabling studies. We plan to test the ability of our humanized ATV:aSyn to bind aSyn in the brain and prevent spreading of pathology using human TfR knock-in mice, as well as other experimental models.

Biomarker-Driven Development

We are focused on enabling our ATV:aSyn program via establishment of clinically translatable biomarkers of target engagement and pathway modulation. In preclinical models, we will measure levels of total aSyn and aSyn bound to antibody in the interstitial fluid of the brain, CSF and plasma to determine the level of target engagement required to block the spreading of aSyn. We plan to use these results to develop a model to identify target exposures in human required to achieve target goals for free and antibody bound aSyn in plasma and CSF that block the spread of aSyn in disease. In later stage trials, we plan to measure disease progression using imaging biomarkers (e.g. DAT imaging). We also plan to initiate work on an aSyn PET probe that would allow the extent of aSyn pathology in patient brains to be directly measured. If successful, PET imaging will be integrated into both preclinical and clinical studies to measure drug activity as well as to select patients for clinical trials.

Development Plan

Our ATV:aSyn program is currently in preclinical development, and we plan to file an IND or CTA application in 2020. Parkinson's disease will be the primary indication for this program. For our clinical studies, we plan to evaluate patients in the early stages of disease that have not yet been treated with dopaminergic replacement or dopamine agonist therapy in order to evaluate effects on function in Parkinson's disease patients. This stage of disease will also capture individuals prior to the broad spread of aSyn pathology and maximize our ability to modify the disease trajectory. Following proof of concept in Parkinson's disease, patients with other synucleinopathies, such as dementia with Lewy bodies, or DLB, and multiple system atrophy, or MSA, may also benefit and could be explored.

ETV:IDS Enzyme Replacement Therapy Program

We are developing ETV:IDS as a treatment for the lysosomal storage disorder MPS II. ETV:IDS is an IDS fusion protein that has been designed to have increased brain exposure. Lead ETV:IDS proteins are currently in preclinical development, and we plan to file an IND or CTA in the first half of 2019.

Therapeutic Rationale

MPS II, also known as Hunter Syndrome, is an X-linked recessive genetic LSD caused by a single gene defect leading to a deficiency in the enzyme IDS. IDS is essential for the breakdown of the glycosaminoglycans, or GAGs, heparan and dermatan sulfate, and its deficiency results in a toxic accumulation of these GAGs and perturbed lysosomal function (Figure 19). Clinical features of MPS II include an enlarged spleen and liver, hearing loss, respiratory tract and cardiac dysfunction, and skeletal abnormalities. Approximately two-thirds of patients suffer from the neuropathic form of the disease, which is characterized by intellectual disability and a progressive cognitive decline that emerges between three and five years of age.

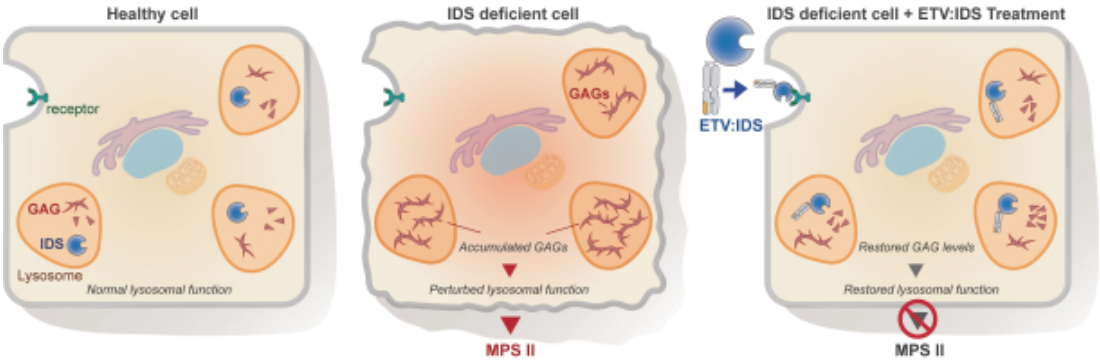


Figure 19: Lack of the lysosomal enzyme IDS results in GAG accumulation leading to lysosomal dysfunction and MPS II (Hunter Syndrome), which is characterized by a range of symptoms including neuronal degeneration. ETV:IDS is designed to promote GAG processing in the brain and reduce neuronal degeneration.

According to the MPS Society, MPS II affects between 1 in 100,000 to 1 in 150,000 males which would imply between 1,000 and 1,600 males in the United States are afflicted with MPS II based on current population estimates.

MPS II is currently treated with intravenous infusions of recombinant IDS protein. While these treatments can normalize spleen and liver size and improve walking ability, they do not efficiently distribute to the brain and, therefore, cannot address the neurological manifestations of the disease. There is a demonstrated need for therapies that effectively cross the BBB so as to treat both neurological and peripheral manifestations of MPS II and other LSDs.

Pharmacological Properties and Brain Exposure

We are developing therapeutic fusion proteins that effectively cross the BBB and diffuse to critical peripheral tissues. Our ETV platform fuses an engineered Fc, which includes a TfR binding site to improve brain uptake, with an enzyme. We have successfully generated active ETV:IDS fusion proteins that retain binding to TfR and reduce accumulation of GAGs in IDS knockout cells at sub-nanomolar concentrations, showing comparable activity to our IDS benchmark enzyme (Figure 20).

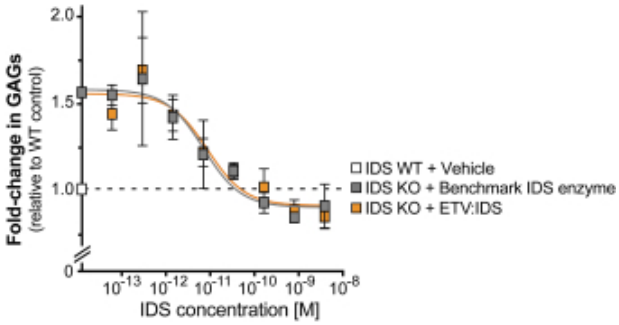


Figure 20: Measurement of ETV:IDS activity in cultured cells. Cells that do not produce the IDS enzyme (IDS KO cells) were treated with increasing doses of benchmark IDS enzyme or ETV:IDS, and the reduction in GAG accumulation was measured using LC-MS/MS. Treatment with ETV:IDS resulted in a dose-dependent reduction in GAG levels, lowering GAGs to levels seen in WT cells. ETV:IDS showed comparable cellular potency to the benchmark IDS enzyme.

We are currently analyzing the tissue distribution and efficacy of ETV:IDS fusion proteins *in vivo* using both IDS knockout mice and a proprietary human TfR knock-in mouse model. These studies are enabled by proprietary methodologies that we have developed to monitor the amount of GAG accumulation and the PK profile of intact ETV:IDS fusion proteins in these animals. Our initial studies in IDS knockout mice have shown that our lead ETV:IDS fusion protein is efficacious *in vivo*, significantly reducing GAGs in serum of mice lacking normal IDS function (Figure 21). Using our human TfR knock-in mouse model, we have also demonstrated a significant improvement in brain uptake with the ETV:IDS fusion protein, compared to an IDS-Fc control construct that does not bind TfR.

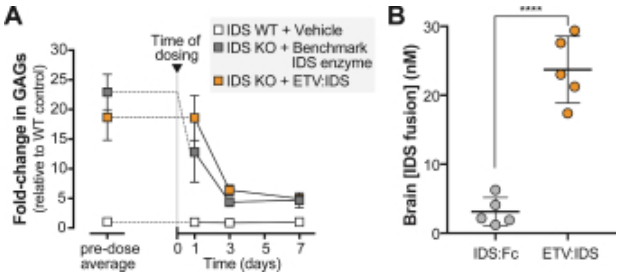


Figure 21. Measurement of the *in vivo* efficacy and brain uptake of ETV:IDS. GAG levels were measured in IDS KO mice dosed with 1mg/kg benchmark IDS enzyme, the equivalent dose of ETV:IDS (n=8), or vehicle. ETV:IDS administration reduced GAG levels in serum to levels comparable to that seen with the benchmark IDS enzyme (A). Human TfR knock-in mice were dosed with the ETV:IDS fusion or the IDS-Fc fusion control for four hours, and the concentration of IDS fusions in brain was measured using an ELISA-based assay. Significantly higher levels of the ETV:IDS fusion were detected in brain compared to the IDS-Fc control (B). ** indicates P<0.0001.**

Biomarker-Driven Development

Studies have demonstrated accumulation of GAGs in plasma and urine of MPS II patients as well as elevated levels of GAGs in CSF of both attenuated and neuronopathic MPS II patients. GAG levels have emerged as an accepted biomarker of therapeutic efficacy for treatment of MPS II and related LSDs based on positive correlations between the reduction of urine GAG levels and clinical endpoints following administration of approved therapy for MPS II. Because approved MPS II therapies are not able to cross the BBB, CSF GAG levels remain elevated in MPS II patients who are undergoing approved MPS II therapies.

We have developed a highly sensitive assay to assess levels of heparan and dermatan sulfate accumulation *in vivo* that will allow us to quantitatively investigate the PD effect of our product candidate in preclinical studies and clinical trials. This assay has shown that IDS deficiency leads to the accumulation of GAGs heparan and dermatan sulfate in tissues and fluids of IDS knock-out mice.

Development Plan

We plan to file an IND or CTA for our lead ETV:IDS product candidate in early 2019. We plan to study such product candidate in a Phase 1/2 12-week multiple-ascending dose study in MPS II patients, either in addition to IDS replacement therapy or in patients that have ceased administration of this therapy. We believe that the assessment of changes in CSF GAG levels in all patients, as well as the exploration of systemic effects such as reduction in urine and plasma GAG levels in patients not receiving IDS replacement therapy, will enable rapid confirmation of both distribution of ETV:IDS to the brain and the efficacy of our product candidates in brain and peripheral tissues.

Glial Biology Pathway Programs

RIPK1 Inhibitor Program

The most advanced product candidate in our RIPK1 inhibitor program, DNL747, is a potent, selective and brain penetrant small molecule RIPK1 inhibitor product candidate for Alzheimer's disease and ALS. DNL747 is in IND-enabling preclinical studies and we plan to submit a CTA in early 2018.

Therapeutic Rationale

Aberrant glial biology characterized by neuro-immune dysfunction is a cardinal feature of the pathology of many chronic neurodegenerative diseases including Alzheimer's disease and ALS. Recent GWAS have identified that a large proportion of the genetic risk for late-onset Alzheimer's disease can be explained by genes that are expressed in microglia, the resident immune cells of the brain, implicating microglia as an important effector of neurodegeneration. Mutations in Optineurin, or OPTN, that cause ALS result in increased levels of RIPK1 activity in microglia, while two additional genes with genetic links to ALS, Tank Binding Kinase, or TBK, and TNFAIP3-interacting protein 1, or TNIP1, have been shown to regulate RIPK1 signaling in cell-based experiments.

RIPK1 is highly expressed by microglia and levels of RIPK1 activity are increased in chronic neurodegenerative disease. RIPK1 activation in microglia results in production of a number of pro-inflammatory cytokines that can cause tissue damage. Stimulation of RIPK1 signaling in cultured microglia results in production of cytokines and other pro-inflammatory factors, including Ccl2 (MCP-1), IL-1b, and IL-6, while treatment with RIPK1 inhibitors attenuates the induction of these factors (Figure 22). In Alzheimer's disease patients carrying the APOE4 allele, which is a prevalent genetic risk factor for Alzheimer's disease, common polymorphisms in IL-6R result in earlier onset of disease, demonstrating the potential importance of RIPK1 dependent IL-6 signaling pathways. Together, these data suggest increased RIPK1 function in microglia contributes to Alzheimer's disease, ALS and potentially other neurodegenerative diseases.

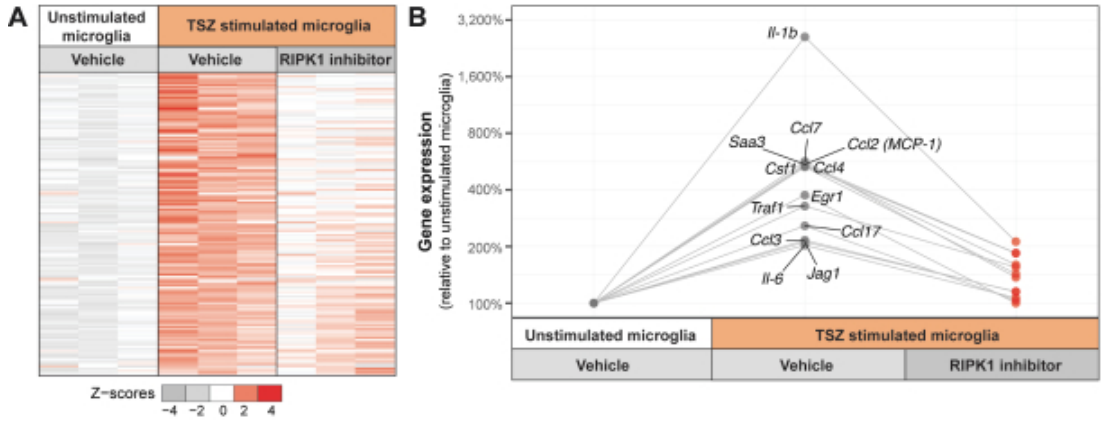


Figure 22: Production of pro-inflammatory cytokines in microglia is RIPK1 dependent. Stimulation of microglia with a TNF cocktail (TSZ) results in induction of many genes, and the majority of these changes are reversed after treatment with a RIPK1 inhibitor (A). Many of the top upregulated genes represent pro-inflammatory cytokines and chemokines such as IL-1b, IL-6 and Ccl2 (MCP-1). The up-regulation in all of these genes is reversed upon RIPK1 inhibitor treatment as shown in (B).

RIPK1 function is best characterized as being downstream of the receptor TNFR1. Specifically, the activation of RIPK1 downstream of TNFa signaling is likely a major component of the RIPK1-dependent neuro-immune phenotype observed in the context of chronic neurodegenerative disease (Figure 23). Brain penetrant inhibitors of RIPK1 therefore represent an attractive approach to targeting the TNF pathway, a highly validated biologic target in human disease, which we believe has not been adequately tested in the brain due to poor brain penetration of large molecule therapeutics, which are widely used for peripheral inflammatory disease. In addition, an oral, brain penetrant RIPK1 inhibitor could provide a more selective method to modulate TNF signaling through the pro-inflammatory TNFR1 receptor as compared to the non-selective anti-TNF antibodies that effect signaling through TNFR2, which is important for myelination of nerves, as well as TNFR1.

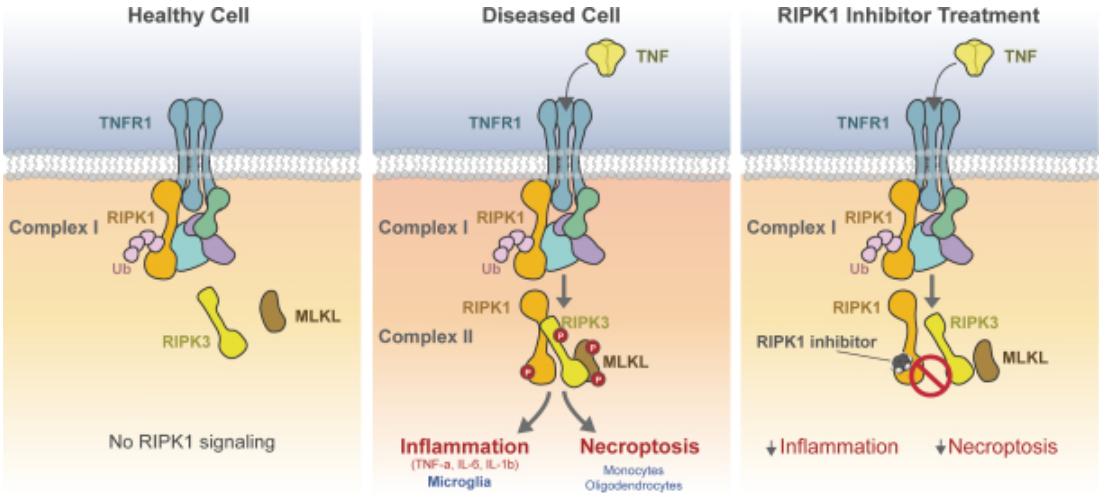


Figure 23: The RIPK1 signaling pathway displays minimal activity in healthy cells. Stimulation of TNFR1 in disease can lead to activation of RIPK1 kinase activity and generates a pro-inflammatory response in microglia and cell death via necroptosis in other cell types including monocytes and oligodendrocytes. Inhibition of RIPK1 activity with a small molecule is sufficient to block both the production of pro-inflammatory cytokines and necroptosis.

In addition to the role of RIPK1 in neuro-immune function, the RIPK1 pathway is also a central regulator of necroptosis, a form of programmed cell death. The role of RIPK1 in necroptosis of neurons has been implicated in Alzheimer's disease, providing another potential pathway where inhibition may be beneficial in disease.

We anticipate that an oral therapy targeting neuro-immune dysfunction could be used as either a monotherapy for treatment of Alzheimer's disease or in combination with therapeutics that target other mechanisms such as Tau and amyloid. Although delaying the progression of Alzheimer's disease may be most effective by targeting early stage disease (prodromal and mild Alzheimer's disease populations), we anticipate that a RIPK1 inhibitor would also have benefit in later stage Alzheimer's disease (mild to moderate Alzheimer's disease), where microglial pathology is pervasive.

Genetic risk factors identify subpopulations of the disease that may differentially respond to therapies. The neuro-immune cascade downstream of RIPK1 and the genetics of Alzheimer's disease provide candidate biomarkers for selection of a neuroinflammatory subpopulation of Alzheimer's disease that may be more responsive to a therapy targeting microglial dysfunction. These risk factors include biomarkers of neuro-immune dysfunction, such as soluble TREM2, RIPK1 dependent inflammatory cytokines in the CSF (e.g. MCP-1, IL-1b, and IL-6), and genetic risks identified by GWAS, such as the IL-6R polymorphism.

According to estimates from the Alzheimer's Association, 5.5 million people in the United States suffer from Alzheimer's disease. Approximately 4.9 million of these people have prodromal, mild and moderate Alzheimer's disease. We estimate that patients who represent a neuroinflammatory subpopulation as described above make up approximately 30% to 50% of the total patient population.

A similar approach to patient selection may be applied to ALS. According to estimates from the ALS Association, there are more than 20,000 ALS patients in the United States. Although OPTN mutations are found in only a small fraction of patients, postmortem analysis of CNS tissue reveals microglial activation and an inflammatory profile in nearly all ALS patients.

Pharmacological Properties and Brain Exposure

We have a broad portfolio of potent, selective and brain penetrant RIPK1 inhibitors with attractive pharmacological properties. The lead candidate, DNL747, is a potent, selective, orally available, brain penetrant small molecule inhibitor of RIPK1. The pharmacology of the lead has been investigated in a broad range of primary and secondary biochemical assays, cell-based *in vitro* assays, and in animals. *In vitro* studies demonstrate that DNL747 is highly selective against kinase and receptor panels. Treatment of cultured primary human microglia or macrophages with DNL747 results in a dose-dependent inhibition of RIPK1 kinase activity, as measured by reduction in pS166-RIPK1 (Figure 24A). Concentrations of DNL747 that only partially reduce pS166-RIPK1 are able to fully inhibit the production of RIPK1-dependent cytokines, such as IL-1b (Figure 24B).

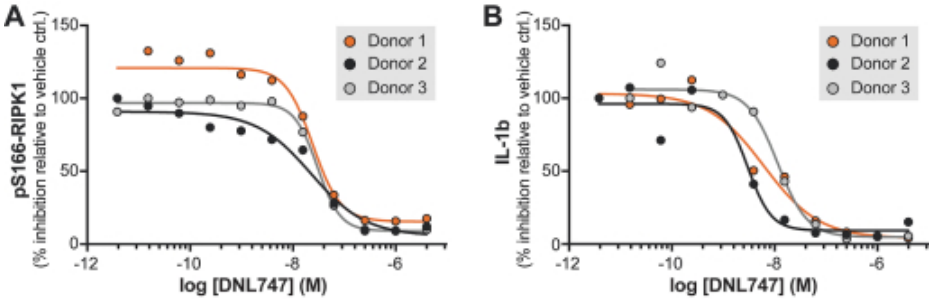


Figure 24: DNL747 demonstrates potent activity in human primary cells *in vitro*. Stimulation of primary human macrophage with a TNFa cocktail causes RIPK1 activation and production of IL-1b, while treatment with DNL747 results in a dose-dependent reduction in p-RIPK1 (A) and IL-1b production (B). Each circle represents the percent of p-RIPK1 or IL-1b relative to a control following treatment with the concentration of DNL747 denoted on the x-axis, while the lines represent curve-fits based on data from each donor throughout the range of concentrations tested. Doses evaluated in GLP toxicology studies have exposures that exceed *in vitro* concentrations showing >90% inhibition of p-RIPK1 and IL-1b.

Treatment with RIPK1 inhibitor tool compounds, including compounds we have generated, have neuro-immune modulatory effects in animal models. An increase in RIPK1 is observed both in animal models of chronic neurodegeneration and patients with Alzheimer's disease, which is correlated with microglial activation (Figure 25).

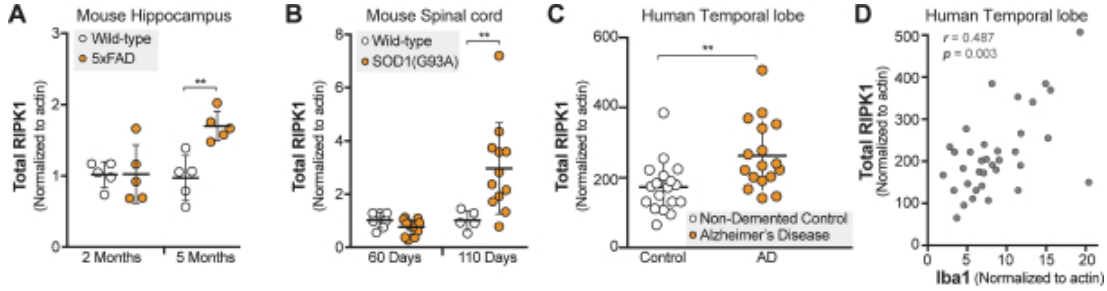


Figure 25: RIPK1 is elevated in models of chronic neurodegeneration and patients with Alzheimer's disease. An age dependent increase in RIPK1 that correlates with microglia activation can be seen in the 5XFAD model of Alzheimer's disease (A) and the SOD1 model of ALS (B). RIPK1 is also increased in the temporal lobe of patients with Alzheimer's disease (C), and this increase correlates with an elevation in the microglial marker Iba1 (D). ** indicates p<0.01.

Inhibition of RIPK1 kinase activity in animal models of neurodegeneration reduces key signatures of microglial activation and reduces levels of cytokines in the brain including soluble TREM2, IL-6 and total RIPK1 (Figure 26). Long-term treatment of Alzheimer's disease or ALS in animal models with

RIPK1 inhibitor tool compounds has been demonstrated to result in reduced neuro-immune dysfunction, attenuated neurodegeneration and improved function, as described in a recent publication in the journal *Science* by our collaborator Junying Yuan at Harvard University.

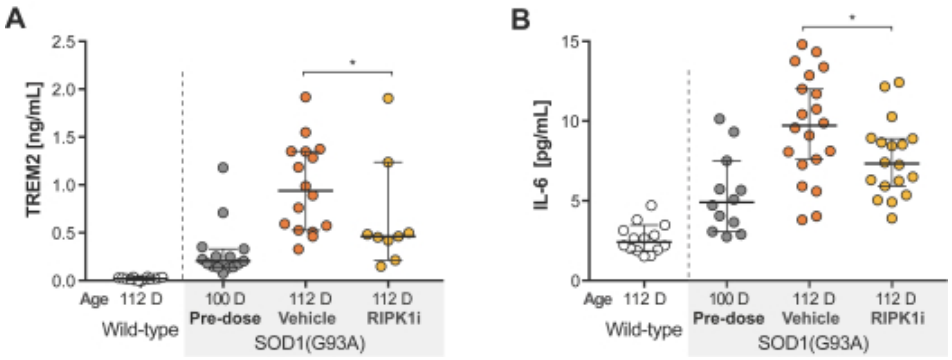


Figure 26: Short term treatment with a RIPK1 inhibitor reduces neuro-inflammatory microglial markers in neurodegenerative disease models. The SOD1 model of ALS displays elevated levels of sTREM2 and IL-6 as compared to wild type control mice at 100 days that further increases at 112 days as the disease progresses. Treatment of SOD1 mice with a RIPK1 inhibitor from 100 days of age to 112 days of age reduces levels of sTREM2 (A) and IL-6 (B) in the spinal cord to near the 100 day pre-dose levels. * indicates p<0.05.

We have completed extensive preclinical PK and PD studies with DNL747 in multiple species. Preclinical modeling of clearance predicts a human half-life compatible with twice daily dosing. PD has been characterized using a marker of RIPK1 activity, phosphorylation of RIPK1 at Serine 166, or pS166. This biomarker has been characterized in *in vitro* assays in human and monkey PBMCs and has been demonstrated to be robustly reduced by RIPK1 inhibitors.

DNL747 is currently being tested in comprehensive GLP toxicity studies, including 28-day repeat-dose studies in rat and monkey and safety pharmacology studies. DNL747 was well tolerated in pilot 7-day repeat-dose toxicity studies up to high doses and exposures. Exposures were 10- to 87-fold higher than the exposures at predicted therapeutic dose levels to achieve IC90 coverage at trough. No concerns were identified in *in vitro* safety screening for genotoxicity, cardiovascular ion channel inhibition, and hepatotoxicity assessments. We recently completed 28-day GLP safety studies in cynomolgus monkeys and rats and have reviewed preliminary data, and we expect to complete analysis of the data by the end of 2017.

Based on preliminary data from the 28-day GLP study in rat, testing at dose levels of 20 mg/kg BID to 500 mg/kg BID, it appears that DNL747 was well tolerated to the highest dose tested of 500 mg/kg BID; only minimal, non-adverse changes associated with metabolic induction were noted. Based on preliminary data from the 28-day GLP study in cynomolgus monkey, testing at dose levels of 20 mg/kg BID to 500 mg/kg BID, it appears that DNL747 was well tolerated to the mid dose of 100 mg/kg BID, with immune-mediated histopathology findings noted at the high dose of 500 mg/kg BID. Histopathology findings included lymphocytic infiltrates in the skin and/or lymphoid hyperplasia in the spleen and lymph nodes in all high dose (500 mg/kg BID) animals at terminal necropsy after the 28-day dosing phase. Clinical findings were only observed in the recovery period, two days after the last dose. One high dose animal administered 500 mg/kg BID was euthanized on Recovery Day 8 due to extensive skin lesions and histopathology findings that were more severe than, but consistent with, the other animals. One other high dose animal, which was also administered 500 mg/kg BID, had mild skin lesions and completed the recovery period. At the high dose of 500 mg/kg BID, the projected safety margins were 14- to 35-fold relative to the exposures at the predicted therapeutic dose levels to achieve IC90 coverage at trough; whereas at the mid dose of 100 mg/kg BID the projected safety

margins were 6.5- to 16-fold relative to the exposures at the predicted therapeutic dose levels to achieve IC90 coverage at trough. Because IC90 coverage at trough is expected to allow for robust inhibition of RIPK1 activity and cytokine production, we believe that these margins provide an adequate safety window to explore a robust pharmacodynamic range in humans. We believe that the preliminary data support advancing DNL747 to clinical testing with a clinical monitoring plan based on adequate safety margins in GLP toxicity studies, since we believe the projected safety margins should allow us to achieve DNL747 exposures that inhibit RIPK1 up to 90% target inhibition at trough concentrations. However, the adverse findings in the 28-day GLP study in cynomolgus monkey could result in the FDA or other regulatory authorities imposing, or us proactively proposing, an exposure cap in our planned Phase 1 clinical trial for DNL747. We intend to file a CTA with a protocol-defined maximum exposure not to exceed two fold over that which enables 90% inhibition at trough.

Biomarker-Driven Development

We have generated a number of assays to measure target engagement and pathway modulation for our RIPK1 program in order to facilitate and increase the probability of success of clinical development. To directly measure the level of RIPK1 activity, we have developed an assay to measure autophosphorylation of RIPK1 at pS166. This assay will enable quantitative measurement of target engagement in the blood of patients following a single dose or multiple doses of our RIPK1 inhibitor in Phase 1 clinical trials. Based on this information, we expect to be able to select the appropriate dose levels for later stage trials.

To measure the effect of RIPK1 on the production of pro-inflammatory cytokines by microglia, we have identified candidate pathway biomarkers of RIPK1 activity, including RIPK1 dependent cytokines, such as TNFa, IL-1b and IL-6, which are elevated in brains of patients with Alzheimer's disease. We will first use these assays to directly measure these cytokines in the CSF of subjects in a Phase 1 healthy volunteer trial to begin to determine a relationship between drug exposure and reduction of basal levels of inflammation in the brain. We then plan to use the same assays to determine the effect of RIPK1 inhibition on reduction of inflammatory cytokines in Alzheimer's disease patients and ALS patients in a small Phase 2a clinical trial. In addition to development of fluid biomarker assays, we have also invested in the development of a novel PET tracer related to a mitochondrial protein that is a biomarker of glial biology dysfunction. We are currently running a translocator protein, or TSPO, imaging study, which is a PET study in ALS patients to determine the test-retest reliability of this imaging biomarker and its utility as a direct and non-invasive measure of neuro-immune dysfunction.

In order to examine the effect of RIPK1 inhibition on the progression of neurodegeneration, we are also assessing the effect of RIPK1 inhibition in preclinical models for the effect on neurofilament (axon support) levels in blood plasma and CSF. It has recently been reported that the loss of neurons in many neurodegenerative conditions increases the levels of the protein neurofilament in both the CSF and plasma of patients. We believe that a relatively small, short clinical trial focusing on a biomarker-like neurofilament could demonstrate that a product candidate can reduce neurodegenerative processes and, therefore, build confidence in the clinical benefit of the product candidate in a larger pivotal trial.

GWAS genetic data have identified a polymorphism in the IL-6 receptor in a subset of Alzheimer's disease patients that may be a useful biomarker for selection of patients expected to benefit from RIPK1 inhibition. This common genetic variant is associated with a more prevalent neuroinflammatory phenotype in an APOE4 carrier subpopulation of Alzheimer's disease patients. As increased levels of IL-6 results from increased activity of the RIPK1 signaling pathway, patients with this IL-6 receptor mutation are expected to be more likely to respond to treatment with a RIPK1 inhibitor.

Development Plan

Pending the results from our IND-enabling preclinical studies, we plan to submit a CTA for DNL747 in early 2018 and initiate a Phase 1 clinical trial in healthy volunteers in the first half of 2018. The Phase 1 study is expected to be randomized, double-blind, placebo-controlled, single-center Phase 1 clinical trial in healthy young and elderly subjects to investigate the safety and tolerability of single and multiple oral doses of DNL747 and characterize the PK and PD of DNL747 in plasma and CSF. Target engagement will be assessed in PBMCs using the pS166 biomarker and extrapolated to estimate target engagement in brain. As an exploratory endpoint, candidate inflammatory biomarkers in the CSF are also being evaluated. We anticipate the target engagement goal for the RIPK1 clinical development program will be to achieve 70% to 90% target inhibition at trough concentrations in order to maximize inhibition of the RIPK1 pathway to enable testing of a broad range of doses in future clinical studies in patients. As an extension to our Phase 1 clinical trial design, we also plan to enroll a cohort of Alzheimer's disease patients to assess PK, safety and target engagement in this population. This will provide key insight to guide dose selection for subsequent patient trials and the identification of potential biomarker and clinical endpoints.

After completion of the Phase 1 trial in healthy volunteers, we plan to proceed to two Phase 2a studies evaluating biomarker endpoints in ALS and Alzheimer's disease. The primary objectives of these patient studies is expected to be to evaluate safety, PK and PD of DNL747 in Alzheimer's disease and ALS patients and identify evidence of central pathway engagement. We are currently evaluating endpoints to be used in these studies including CSF cytokines and TSPO imaging to demonstrate relevant effects on inflammatory cytokines and microglial function.

Back-up and Other Compounds

As part of our parallel development strategy, we have also developed a number of structurally diverse backup RIPK1 inhibitor molecules that are currently being characterized. Upon completion, we expect to be able to advance these candidates to the IND or CTA filing stage in 2019.

In August 2016, we filed a CTA for an earlier RIPK1 inhibitor compound, DNL104, and initiated a single center, randomized, double blind, placebo-controlled, dose escalating Phase 1 study in the Netherlands. Thirty-six subjects received a single dose of DNL104 and 16 subjects received multiple doses of DNL104. This study provided evidence of peripheral and CSF drug exposure and pathway inhibition by measurement of pRIPK1 in blood, and identified candidate RIPK1 dependent cytokines that change in human CSF. DNL104 was well tolerated during the dosing interval and there were no CNS related safety signals. However, three out of 16 active-treated subjects who received multiple dose developed liver test abnormalities of 2.5x to 5x above normal levels of liver enzyme activity. Based on both preclinical and clinical data, we believe that these findings are off-target liabilities that are molecule specific to the DNL104 molecule and not a result of RIPK1 inhibition. This conclusion resulted in a decision to discontinue DNL104 and advance the structurally distinct molecule DNL747, which we predict to have a superior PK profile and low risk for liver toxicity.

ATV:TREM2 Program

ATV: TREM2 is a therapeutic candidate designed to rescue microglial function in Alzheimer's disease through modulating the activity of a genetically validated target. We have developed high affinity antibodies for TREM2 and are currently characterizing molecules in order to select a lead to couple with our proprietary ATV platform. We plan to file an IND or CTA for this program in 2020.

Therapeutic Rationale

A major component of Alzheimer's disease pathology is the presence of neuro-immune dysfunction. Microglia, the resident immune cells of the brain, show signs of activation and release of

toxic cytokines in patients with Alzheimer's disease. Recent human genetic studies have identified single nucleotide polymorphism in a number of microglia specific genes that contribute to Alzheimer's disease, which strongly implicates glial function as a contributor to disease risk. TREM2 is a cell surface receptor expressed exclusively by microglia in the brain which regulates multiple processes including survival, migration, phagocytosis, and cytokine release (Figure 27). In 2013, a rare variant of TREM2 was found to be associated with a three-fold higher risk of Alzheimer's disease onset, which strongly implicates TREM2 as a functional contributor to disease progression.

The TREM2 mutations identified in patients with Alzheimer's disease results in loss of normal TREM2 function. Mouse models of Alzheimer's disease display more severe phenotypes in the absence of TREM2, including more diffuse amyloid plaques and increased synaptic loss. Conversely, data from our TREM2 expressing myeloid cell-based assays demonstrate that increasing TREM2 signaling can improve cellular survival and function, indicating that activating TREM2 has a beneficial effect on this cell type (Figure 29). Based on this combination of genetic and functional data, we hypothesize that positive modulation of TREM2 activity will improve microglia function and slow the progression of Alzheimer's disease.

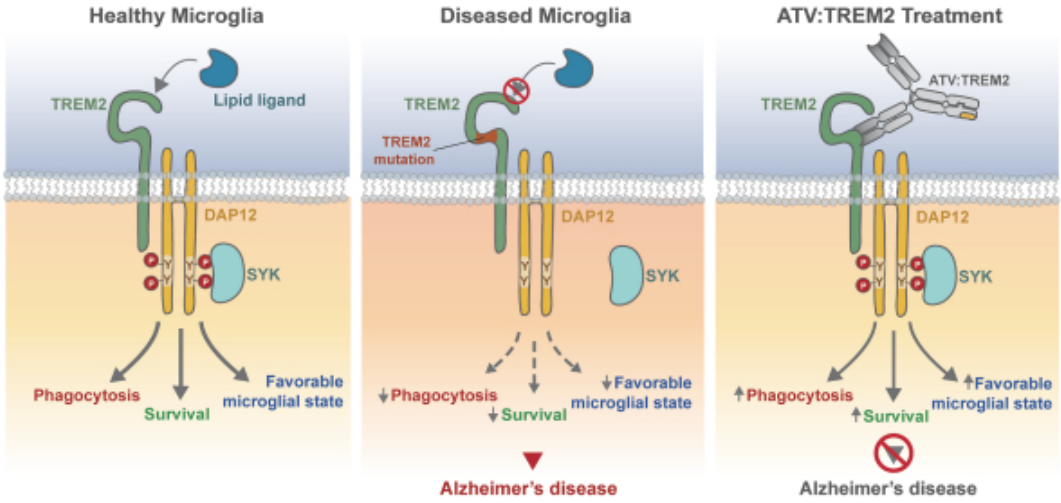


Figure 27: TREM2 is a cell surface receptor expressed on microglia. Activation of the TREM2 signaling pathway in healthy microglia leads to improved survival and promotes a favorable microglial state. TREM2 mutations result in reduced signaling and attenuated microglia function, while treatment with ATV:TREM2 is designed to improve survival and boost microglial function.

We believe that patients with a specific neuroinflammatory signature as a result of glial dysfunction may particularly benefit from therapeutics targeting positive modulation of TREM2. These patients could be identified through a combination of genetic, CSF and imaging biomarkers. This population could be expanded to encompass all prodromal to mild and moderate Alzheimer's disease patients based on a demonstration of pathway modulation in the clinic.

Pharmacological Properties and Brain Exposure

We have generated multiple classes of anti-TREM2 antibodies with affinities less than 10nM. By using an array of functional assays, we have demonstrated that these antibodies have diverse functional effects, including several that show agonism, antagonism and positive allosteric modulation (Figure 28).

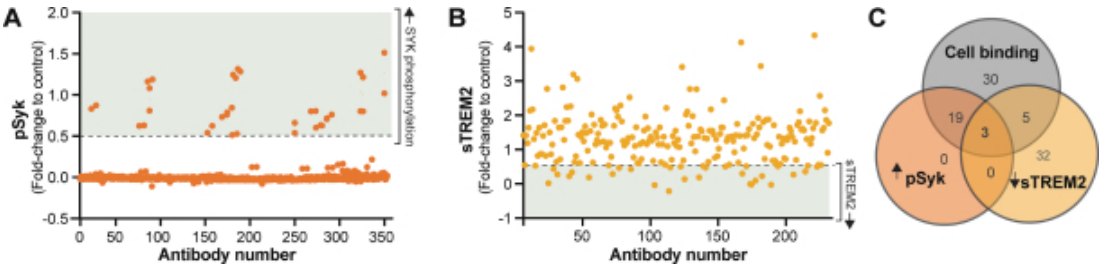


Figure 28: Profiling of our anti-TREM2 antibodies. Antibodies were profiled for their ability to induce TREM2 signaling and measured by pSyk (A) and for their effect on shedding of soluble TREM2 (sTREM2) from the cell surface (B). Anti-TREM2 antibodies were identified with various combinations of activities. This includes 57 antibodies that bound TREM2 on the surface of cells (Cell binding), of which 19 increased Syk phosphorylation (pSyk), 5 lowered soluble TREM2 levels (sTREM2), and 3 antibodies displayed both of these activities (C).

We have demonstrated that select antibodies with TREM2 agonist activity are able to improve the survival of cultured human macrophage (Figure 29). These data indicate that increasing TREM2 function can have a beneficial effect on myeloid linage cells. We are currently testing these and other anti-TREM2 antibodies in additional assays to determine which mechanism of action results in the desired effect on TREM2-mediated microglial function. We intend to then progress a lead antibody with a favorable affinity and activity profile to *in vivo* studies.

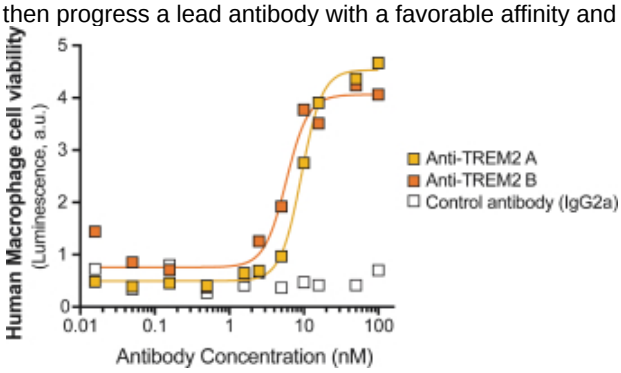


Figure 29: Our anti-TREM2 antibodies improve survival of cultured human macrophage. Treatment of primary human macrophage with anti-TREM2A and anti-TREM2B is sufficient to increase survival in a dose-dependent fashion.

We will evaluate the lead TREM2 antibodies *in vivo* for target engagement and disease-relevant efficacy in animal models of Alzheimer's disease. We will then progress the most promising of the lead TREM2 antibodies as a potential clinical candidate to be humanized and coupled with our ATV platform, ATV:TREM2, in order to improve brain uptake and enable target engagement in clinical studies.

Biomarker-Driven Development

The development of ATV:TREM2 is expected to be facilitated by a number of biomarkers to measure target engagement, pathway modulation and impact on disease progression. Upon cleavage of the extracellular domain of TREM2, a soluble form of TREM2, sTREM2, is released from the cell surface. sTREM2 is detectable in CSF. We have focused on anti-TREM2 antibodies that modulate the levels of sTREM2, enabling sTREM2 to be used as a biomarker of target engagement both in preclinical models and Phase 1 clinical trials. We intend to correlate TREM2 levels with downstream functional endpoints using preclinical models, allowing measurement of sTREM2 levels in a Phase 1 clinical trial to confirm target engagement and increase the probability of success.

The ability of ATV:TREM2 to modulate microglial function in preclinical models will be measured through histology and examination of microglial gene expression. These endpoints will be correlated to readouts that can be measured in clinical studies such TSPO-PET imaging and cytokine levels in CSF. As part of clinical trials, we plan to examine these endpoints both pre-dose and following treatment to assess microglia activation state.

Development Plan

The primary indication for ATV:TREM2 is Alzheimer's disease. The development of ATV:TREM2 will be facilitated by a number of biomarkers to measure target engagement, pathway modulation and an impact on disease progression. Our focus on anti-TREM2 antibodies that modulate levels of sTREM2, a soluble form of TREM2, will enable sTREM2 to be used as a biomarker of target engagement both in preclinical models and Phase 1 clinical trials. sTREM2 is released from the cell surface upon cleavage of the extracellular domain of TREM2 and is detectable in CSF. In preclinical models dosed with ATV: TREM2, sTREM2 levels will be correlated with the ability of ATV:TREM2 to modulate microglial function as assessed through histology and examination of microglial gene expression. Understanding the relationship between changes in sTREM2 and microglial function, will enable assessment of both target engagement and a biologically relevant effect of ATV:TREM2 dosing in Phase 1 clinical trials. Early stage clinical studies will also assess candidate biomarkers to identify patients that are most likely to benefit from a TREM2 mediated approach. Examples of these candidate biomarkers include CSF sTREM2 and TSPO-PET, two biomarkers that are elevated in patients with Alzheimer's disease. These examples may be used as both a patient selection biomarker to identify patients with pathologic neuro-immune function and as a measure of TREM2 pathway modulation.

These endpoints will be correlated to readouts that can be measured in clinical studies such TSPO-PET imaging and cytokine levels in CSF. As part of clinical trials, we plan to examine these endpoints both pre-dose and following treatment to assess microglia activation state. We plan to file an IND or CTA for this program in 2020.

Cellular Homeostasis Pathway Program

ATV: BACE1/Tau Program

ATV: BACE1/Tau is a bispecific program targeting the production of amyloid beta, or Abeta, and the spreading of Tau, the two key pathological processes of Alzheimer's disease. We have developed high affinity antibodies for BACE1 and Tau and are currently optimizing them before combining them into a single therapeutic agent using our proprietary ATV platform. We plan to file an IND or CTA in 2020.

Therapeutic Rationale

Alzheimer's disease pathology is characterized by the presence of amyloid plaques and neurofibrillary tangles. The pathologies arise as a consequence of protein aggregation, a form of disrupted cellular homeostasis, eventually leading to neuronal degeneration. Amyloid plaques are comprised of Abeta, an extracellular fragment of amyloid precursor protein, or APP, which is generated by cleavage of APP by BACE1 and gamma secretase. Mutations in APP processing components that increase Abeta levels are sufficient to cause early onset Alzheimer's disease. Conversely, mutations in APP that reduce BACE1 cleavage may protect individuals from Alzheimer's disease. These genetic links demonstrate the central role of the amyloid pathway in Alzheimer's disease, and are particularly supportive of BACE1 inhibition as a therapeutic approach (Figure 30).

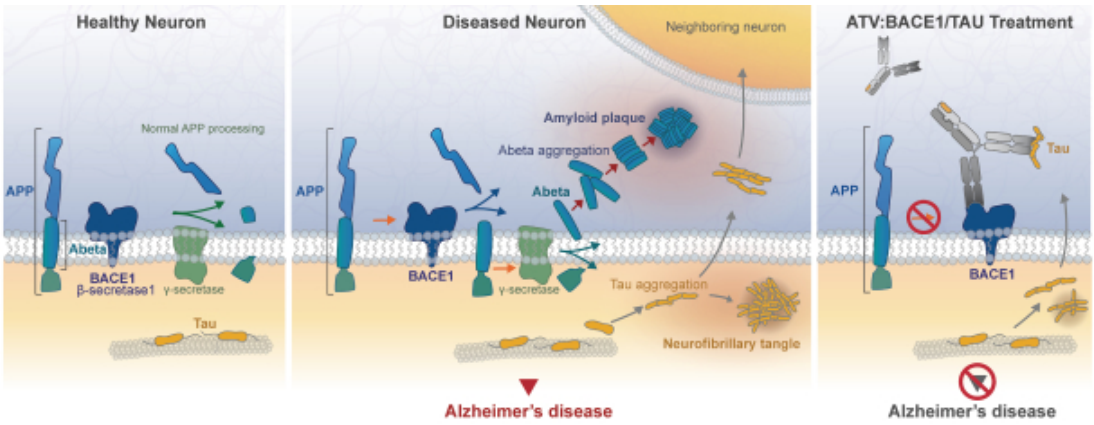


Figure 30: Abeta is generated through sequential cleavage of APP by beta-secretase 1 (BACE1) and gamma secretase to generate Abeta. In Alzheimer's disease, Abeta aggregates to form oligomers and amyloid plaques. Tau is present in healthy neurons but can misfold and aggregate in disease to form either neurofibrillary tangles or Tau oligomers that can spread from one cell to another in disease. ATV:BACE1/Tau is designed to block both of these Alzheimer's disease pathologies through inhibiting cleavage of APP by BACE1 and sequestering extracellular Tau to prevent its spread.

Tau is believed to regulate microtubule stability in neurons, but it can also aggregate to form neurofibrillary tangles present in many neurodegenerative diseases, including Alzheimer's disease. Detailed examination of Alzheimer's disease patients' brains has revealed that Tau pathology spreads spatially during the course of the disease. This spreading of Tau pathology is correlated with cognitive decline. Tau antibodies are currently in clinical development based on animal model data demonstrating that they are capable of blocking the spread of Tau pathology.

Preclinical data also show amyloid pathology accelerates Tau pathological spreading, which is consistent with findings in Alzheimer's disease patients that show Tau pathology progresses later as compared to amyloid plaques. Therefore, our approach of targeting both pathologies with a bispecific antibody may also have synergistic activity. The target patient population for our ATV:BACE1/Tau clinical studies is patients with early-stage Alzheimer's disease and confirmed Abeta pathology as measured by amyloid PET imaging.

Pharmacological Properties and Brain Exposure

We have discovered lead anti-BACE1 and anti-Tau antibodies that have been humanized and are now undergoing optimization processes designed to further improve affinity and cellular potency. Our anti-BACE1 lead displays less than 10nM cellular potency for inhibition of Abeta production (Figure 31). We have also identified a backup anti-BACE1 antibody with improved inhibition of BACE1 that is currently undergoing affinity maturation. Anti-BACE1 antibodies have demonstrated improved selectivity as compared to small molecule approaches currently in clinical development by sparing inhibition of BACE2, which has the potential to lead to a superior safety profile following chronic dosing. When coupled to our ATV platform, anti-BACE1 antibodies have been shown to reduce Abeta levels in the brain by approximately 55% in a human TfR mouse model.

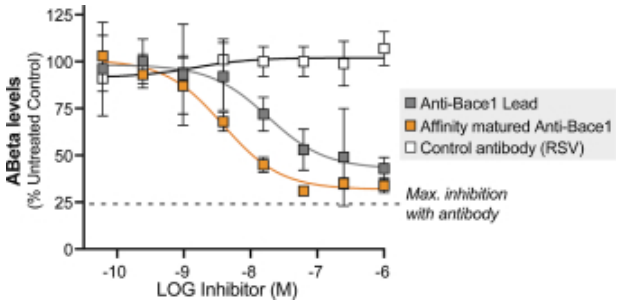


Figure 31: Activity of our anti-BACE1 antibodies. Our lead anti-BACE1 antibody and an affinity matured humanized version of anti-BACE1, are each able to inhibit Abeta production by cells. The affinity-matured humanized anti-BACE1 antibody demonstrates improved potency as compared to the parent anti-BACE1 antibody.

Our lead anti-Tau antibody recognizes all forms of Tau present in the brains of Alzheimer's disease patients and has high affinity. It demonstrates superior target engagement in animal models as compared to our benchmark antibodies which are similar to certain antibodies that third parties currently have in clinical development, even without being coupled to our ATV platform (Figure 32). We believe the epitope recognized by our Tau antibody is advantageous relative to binding sites of benchmark antibodies as it would recognize truncated forms of Tau not recognized by antibodies directed against N-terminal or C-terminal epitopes.

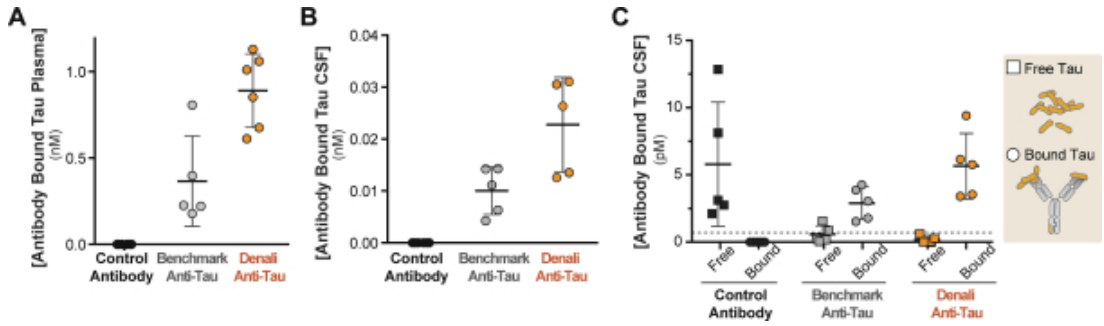


Figure 32. Our lead anti-Tau antibody displays target engagement that is superior to benchmark antibodies. The amount of antibody bound Tau in either plasma (A) or CSF (B) following a single dose of our lead anti-Tau antibody, a benchmark anti-Tau antibody or a control anti-Tau antibody. Our lead anti-Tau also recognizes a significant portion of the extracellular Tau present in Alzheimer's patient CSF (C).

We have conducted proof of concept studies with anti-BACE1/Tau bispecific antibodies that demonstrate both arms retain full functionality when combined into a single molecule as measured by a reduction of Abeta in cellular assays and blocking of Tau seeding in cells.

We believe our ATV:BACE1/Tau program may be the first therapeutic to target both hallmark Alzheimer's disease pathologies as a single therapeutic agent and has the potential for synergistic activity, restoring protein homeostasis with regards to the two most common Alzheimer's disease pathologies. To directly demonstrate the efficacy of the ATV:BACE1/Tau molecule, we are developing a proprietary mouse model by crossing our human TfR knock-in mouse with an established genetic model of Tau pathology. These preclinical efficacy studies are planned for 2018, and are expected to enable the examination of brain exposure and Abeta levels in the brain, and assess the effect on spreading of Tau pathology.

Biomarker-Driven Development

We plan to use validated genetic, biochemical and imaging biomarkers to support patient selection, evidence of target engagement and functional efficacy for our ATV:BACE1/Tau program. These include assays for measurement of CSF Abeta and Tau, as well as Abeta and Tau PET imaging tracers. The acute measurement of Abeta after BACE1 inhibition can be utilized to confirm ATV:BACE1/Tau uptake and target engagement, thus validating our ATV platform for BBB uptake in humans in Phase 1 clinical testing.

In preclinical models, brain levels of Abeta are reduced following a single dose of a BACE1 antibody coupled to the ATV platform (Figure 5), while dosing Tau antibodies led to increased levels of Tau bound to antibody in plasma and CSF. These two readouts can be translated to human testing by measuring CSF levels as a direct measure of target engagement for an ATV:BACE1/Tau molecule. Preclinical studies will be conducted to measure CSF levels of Abeta and Tau in animal models and correlated to effects on amyloid and Tau pathology following chronic dosing. These data and established CSF biomarkers are expected to enable effective testing of ATV:BACE1/Tau in humans.

Development Plan

Our Phase 1 clinical trials will be designed to evaluate the safety and pharmacology of ATV:BACE1/Tau and evaluate target engagement in both healthy volunteers and Alzheimer's disease patients. In this study and in later stage clinical trials, we plan to measure the activity of ATV:BACE1/Tau through CSF Abeta measurement, confirming BACE1 inhibition. In later stage clinical studies we plan to use Tau PET imaging to ascertain whether ATV:BACE1/Tau is able to prevent the spread of Tau pathology. Our target patient population is patients with prodromal and mild Alzheimer's disease and confirmed Abeta pathology as measured by amyloid PET imaging. We estimate this patient population to be approximately 3.4 million in the United States.

The results from this Phase 1 study with ATV:BACE1/Tau will provide information on the overall safety and pharmacologic profile of our ATV platform.

Back-up and Other Compounds

We are also pursuing ATV:Tau bivalent as an alternative approach to ATV:BACE1/Tau. This molecule will have the added advantage of two antibody arms engaging Tau, resulting in potentially higher affinity target engagement, combined with ATV to improve brain exposure. This approach is attractive as local target concentrations of Tau in the synapse may be high. A decision to advance ATV:Tau will be based on establishing superior target engagement biomarker data in animal model CSF and human CSF as compared to known competitor molecules. We plan to file an IND or CTA in 2020.

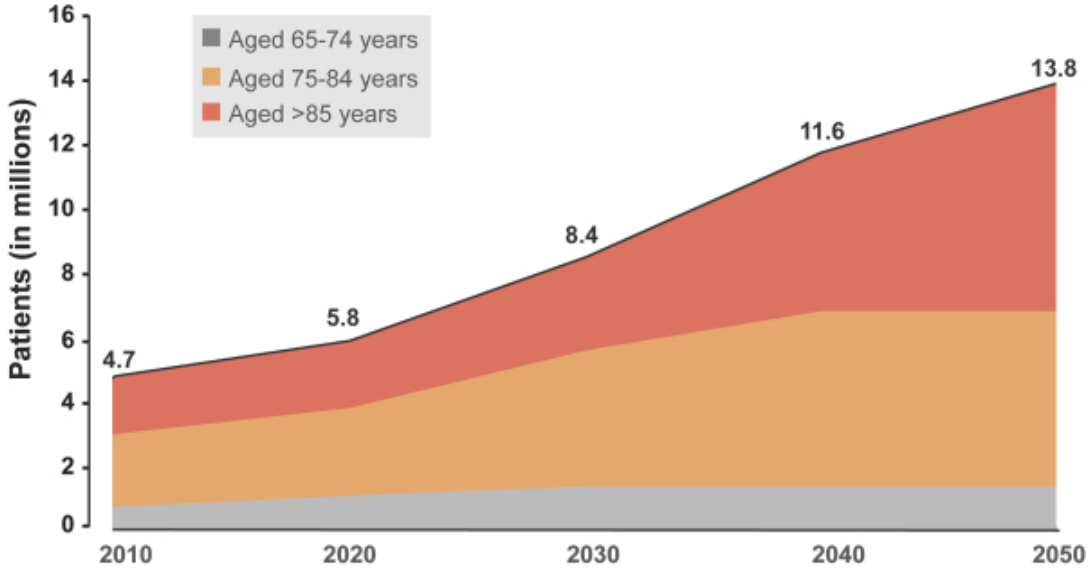
Neurodegeneration: A Significant Unmet Medical Need

Neurodegeneration is one of the largest unmet medical needs of our time, with a rapidly growing patient population. The risk of most neurodegenerative diseases increases with age, but people of all ages can also be affected due to genetic and/or environmental factors. Neurodegenerative diseases are generally progressive in nature and result in the degeneration and/or death of neurons in the brain that result in cognitive decline, functional impairment and eventually death. Alzheimer's and Parkinson's diseases represent the largest among the neurodegenerative diseases.

There are few effective therapeutic options available for patients with Alzheimer's disease, Parkinson's disease, ALS and other neurodegenerative diseases.

Alzheimer's Disease

Alzheimer's disease is a progressive form of dementia that impacts cognitive and motor function in those with the disease. Alzheimer's disease is likely a heterogenous disease driven by genetic risk and environmental factors with common pathology of amyloid deposition in the brain. It is estimated by the World Health Organization to represent between 60% to 70% of all cases of dementia. Alzheimer's disease is the sixth leading cause of death in the United States. As the disease progresses, patients lose the ability to carry out basic daily tasks and eventually to respond to their environment. According to estimates from the Alzheimer's Association, 5.5 million people in the United States suffer from Alzheimer's disease, and patient prevalence is expected to increase to 13.8 million people by 2050.



Source: Alzheimer's Association
Figure 33: Projected number of people in the United States with Alzheimer's disease.

The cost of care to society is massive. The direct costs of caring for individuals with Alzheimer's disease and other dementias in the United States will total an estimated $259 billion in 2017, and is projected to increase to $1.1 trillion by 2050, according to the Alzheimer's Association.

The two classes of drugs approved for the treatment of Alzheimer's disease dementia are cholinesterase inhibitors (donepezil, galantamine, rivastigmine and tacrine) and NMDA receptor antagonists (memantine). These therapeutic products do not modify or alter the progression of the underlying disease and provide only modest efficacy in treating the symptoms of Alzheimer's disease. Namenda (memantine), the most recent FDA-approved new therapeutic product for Alzheimer's disease, was approved in the United States in 2003.

Parkinson's Disease

Parkinson's disease is the second most common neurodegenerative disease of adult onset, behind only Alzheimer's disease. Parkinson's disease is a chronic and progressive movement disorder. According to the Parkinson's Disease Foundation, as many as one million people in the United States today suffer from Parkinson's disease, with approximately 60,000 Americans diagnosed with Parkinson's disease each year.

Lysosomal dysfunction is a central pathology of Parkinson's disease. Certain genetic mutations affecting lysosomal dysfunction, such as LRRK2, aSyn and GBA mutations, are linked to Parkinson's disease. In addition, clinical diagnosis of Parkinson's disease without a known cause is called idiopathic Parkinson's disease and represents the majority of known cases.

For Parkinson's disease, most therapeutic products approved for treatment of the motor symptoms of the disease are related to levodopa and other dopamine agonists. While some existing products provide meaningful symptomatic relief, they have significant side effect risks, fail to address the progression of the disease, and over time gradually lose their effectiveness in treating the symptoms of the disease.

Other Rare Neurodegenerative Diseases

There are many types of rare neurodegenerative diseases, including ALS and LSDs, among others. ALS is a severe and fast progressing neurodegenerative disease. The incidence rate of ALS in the United States is approximately 2 in 100,000 people, with more than 20,000 people in the United States currently suffering from ALS, according to estimates from the ALS Association. The life expectancy of a patient with ALS averages two to five years after diagnosis. By 2040, the projected number of ALS cases in the United States is expected to increase to approximately 30,000.

LSDs are a group of approximately 50 inherited metabolic diseases that are characterized by an abnormal build-up of various toxic materials in the body's cells. LSDs are usually triggered when a particular enzyme is missing or exists in too small an amount to enable the complete breakdown of macromolecules. Each LSD is characterized by the nature of the substances that accumulate and their effects on the body. As a group, LSDs have an estimated frequency of about one in every 5,000 live births. Some of the most common LSDs are Gaucher disease, Fabry disease, and MPS II (Hunter Syndrome). Other rare neurodegenerative indications include Huntington's disease, frontotemporal dementia and spinal muscular atrophy, among others.

Manufacturing

We believe it is important to our business and success to have a reliable, high-quality preclinical and clinical drug supply. As we mature as a company and approach commercial stage operations, securing reliable high-quality commercial drug supply will be critical.

We do not currently own or operate facilities for product manufacturing, storage, distribution or testing.

We rely on third-party contract manufacturers, or CMOs, to manufacture and supply our preclinical and clinical materials to be used during the development of our product candidates. We have established relationships with several CMOs, including Lonza Sales AG, or Lonza, as described below.

We currently do not need commercial manufacturing capacity. When and if this becomes relevant, we intend to evaluate both third-party manufacturers as well as building out internal capabilities and capacity. We may choose one or both options, or a combination of the two.

Effective September 2017, we entered into a development and manufacturing services agreement with Lonza, which agreement we amended in October 2017 to add the initial scope of work under this agreement. We refer to this agreement, as amended, as the DMSA or the Lonza agreement. Pursuant to the Lonza agreement, Lonza agreed to provide clinical development and manufacturing services with respect to certain of our biologic products on a fee-for-service basis. In addition, as long as we are not in breach of the Lonza agreement and Lonza has not terminated the Lonza agreement for our

material breach or insolvency, we have the right to transfer the manufacturing process for our products to ourselves or a third party designated by us and approved by Lonza, subject to payment of a reasonable royalty or licensing fee and terms to be negotiated.

Under the Lonza agreement, Lonza has a right of first refusal to exclusively manufacture a certain number of our biologic products produced in mammalian expression systems that we progress into clinical development for neurodegenerative indications. We refer to these products as pipeline products. If Lonza does not exercise its right of first refusal to manufacture a particular pipeline product, we will be free to utilize a third party manufacturer for such product. Lonza's right of first refusal will not apply with respect to any pipeline product if we enter into a bona fide partnership with a third party (other than a CMO) with respect to such product and such partner will perform development or manufacturing services with respect to such product. We retain the right to conduct any in-house development and manufacturing activities with respect to pipeline products.

If we elect to use Lonza's proprietary expression system in the manufacture of a product, we are required to negotiate a license with Lonza to use such system prior to *in vivo* clinical studies or commercial use or sale of such product. Pursuant to such license, we will be required to pay annual license fees on a product-by-product basis if (i) we (or our strategic partner) and Lonza both manufacture a particular product using such system and we do not guarantee Lonza a certain high double digit percentage of our production requirements of such product, or (ii) if we utilize a third party CMO to manufacture a product using such system. However, we will not be required to pay any annual license fee for any product produced using such system if (i) Lonza is the sole manufacturer of such product or if (ii) we and Lonza both manufacture such product and we guarantee Lonza a certain high double-digit percentage of our production requirements of such product.

Except for products for which Lonza is the sole manufacturer, we will also be required under this license to pay royalties in a range up to a maximum in the low single-digit percentages on net sales of each product produced using such system. Our royalty payment obligations will expire on a country-by-country and product-by-product basis upon the later of (i) the expiration of the last valid licensed patent claim covering such product in such country or (ii) ten years after the first commercial sale of such product in such country.

Unless earlier terminated, the Lonza agreement will expire on September 6, 2022. Lonza may terminate the Lonza agreement for convenience with 24 months' notice and Lonza may terminate the Lonza agreement if we assign the Lonza agreement to one of our affiliates or a third party or undergo certain change of control transactions and the assignee or acquirer is (i) a competing contract manufacturing organization, (ii) located outside of the European Union or United States, or (iii) an entity about which Lonza has bona fide concerns. We may terminate the Lonza agreement for convenience with 12 months' notice. Finally, either we or Lonza may terminate a particular project in the event the services required to complete such project cannot be completed following a specified notice and resolution period.

Except in the event we terminate the Lonza agreement for Lonza's material breach, in addition to other termination-related fees, we will be obligated to pay Lonza all or a portion of the amounts payable for any cancelled services, depending on how far in advance of the start of such services we terminate the agreement.

Commercialization Plan

We do not currently have any approved drugs and we do not expect to have any approved drugs in the near term. Therefore, we have no sales, marketing or commercial product distribution capabilities and have no experience as a company in marketing drugs.

When and if any of our product candidates are approved for commercialization, we intend to develop a commercialization infrastructure for those products in the United States and potentially in certain other key markets. We may also rely on partnerships to provide commercialization infrastructure, including sales and marketing and commercial distribution.

Competition

The biotechnology and pharmaceutical industries, including in the neurodegenerative disease field, are characterized by rapidly advancing technologies, strong competition and an emphasis on intellectual property. We face substantial competition from many different sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions, governmental agencies and public and private research institutions. We believe that the key competitive factors affecting the success of any of our product candidates will include efficacy, safety profile, method of administration, cost, level of promotional activity and intellectual property protection.

Our product candidates will compete with current therapies approved for the treatment of neurodegenerative diseases, which to date have been primarily targeted at treating the symptoms of such diseases rather than halting or slowing the progression of the disease. However, in addition to such currently approved therapies, we believe that our product candidates, if approved, may also compete with other potential therapies intended to halt or slow the progression of neurodegenerative disease that are being developed by a number of companies and institutions, including but not limited to:

- *Alzheimer's Disease*: Potentially disease modifying therapeutics are being developed by several large and specialty pharmaceutical and biotechnology companies, including Biogen, Eli Lilly, Eisai, GlaxoSmithKline, Merck and Roche (including Genentech, its wholly owned subsidiary), and are in various stages of clinical trials.
- *Parkinson's Disease*: Potentially disease modifying therapeutics are being developed by several large and specialty pharmaceutical and biotechnology companies, including Prothena, Roche, Sage Therapeutics and Sanofi, and are in various stages of clinical trials.
- *ALS:* Potentially disease modifying therapeutics are being developed by several large and specialty pharmaceutical and biotechnology companies and academic institutions, including Cytokinetics and Mallinckrodt, and are in various stages of clinical trials.
- *Lysosomal Storage Diseases*: The currently approved treatments for LSDs are enzyme based therapies. Potentially disease modifying therapeutics are being developed by several large and specialty pharmaceutical and biotechnology companies, including ArmaGen, BioMarin, JCR Pharmaceuticals, Sanofi, Shire and Ultragenyx, and are in various stages of clinical trials.

In addition, there are companies that are developing technologies that would compete directly with our technologies, including:

- *Blood-Brain Barrier Technology*: There are several large and specialty pharmaceutical and biotechnology companies developing BBB delivery technologies that utilize RMT, including AbbVie, biOasis Technologies, ArmaGen, JCR Pharmaceuticals and Roche (including Genentech, its wholly owned subsidiary), among others.

Intellectual Property

Our intellectual property is critical to our business and we strive to protect it, including by obtaining and maintaining patent protection in the United States and internationally for our product candidates,

novel biological discoveries and BBB platform technology, including new targets and applications, and other inventions that are important to our business. We also rely on trademarks, trade secrets, know-how, continuing technological innovation and licensing opportunities to develop and maintain our proprietary position.

For our product candidates, we generally pursue patent protection covering compositions of matter, methods of use and manufacture. For example, our most advanced product candidate in the LRRK2 program, DNL201, is covered by an issued composition of matter patent in the United States and several other countries. Furthermore, we own and have filed patent applications in the United States that are directed to the composition of matter of certain antibodies and small molecule product candidates that we intend to develop, as well as the Fc domain portion of our BBB platform technology that binds to TfR. However, given that the development of our technology and product candidates is at an early stage, our intellectual property portfolio with respect to certain aspects of our technology and product candidates is also at an early stage. We do not own or in-license any issued patents in the United States directed to the composition of matter of any of the antibodies or enzymes that we have thus far developed using our BBB platform technology, or issued patents in the United States directed to the composition of the Fc domain portion of our BBB platform technology that binds to TfR, or issued patents in the United States directed to the composition of the specific product candidates being developed in our TREM2, aSyn or IDS core programs. As further described below, we have filed or intend to file patent applications on these and other aspects of our technology and product candidates, and as we continue the development of our product candidates, we intend to identify additional means of obtaining patent protection that would potentially enhance commercial success, including protection for additional methods of use, formulation or manufacture.

ATV/ETV Programs

For our ATV programs, we license multiple patent families from F-star directed to, among other things, modifying immunoglobulin non-CDR loops to create antigen binding sites. These licensed patent families include approximately four issued U.S. patents and five pending U.S. non-provisional patent applications, and over 180 issued foreign patents and over 10 pending foreign patent applications, with pending or issued claims related to the modification process for, and in one issued European patent, the composition of, the modified immunoglobulin non-CDR loops. The issued patents in the earliest of these families are expected to expire in 2026, not including any patent term adjustments and any patent term extensions.

Furthermore, we own three pending U.S. provisional applications directed to the composition and sequences of our TfR-binding ATVs. Any future U.S. and foreign patents that may issue from these patent families (assuming the necessary non-provisional patent applications are timely filed and all other applicable requirements are satisfied) would be expected to expire in 2038, excluding any patent term adjustments and any patent term extensions. We do not own or in-license any issued U.S. patents that are directed to the composition of matter of our ATV programs.

ATV: BACE1/Tau

In addition, we license one patent family from VIB that is directed to, among other things, our anti-BACE1 antibody to be used with our BBB platform technology licensed from F-star. This licensed family includes one issued U.S. patent and one pending U.S. non-provisional patent application; and approximately 16 issued foreign patents and three pending foreign patent applications, with pending or issued claims related to composition of hybridomas, their active fragments and key epitopes. The issued patents in this family are expected to expire in 2030, excluding any patent term adjustments and any patent term extensions. Furthermore, we own one pending U.S. provisional application directed to additional anti-BACE1 antibodies of ours for use with our BBB platform technology licensed from F-star. Any future U.S. and foreign patents that may issue from this patent family (assuming the

necessary non-provisional patent applications are timely filed and all other applicable requirements are satisfied) would be expected to expire in 2038, excluding any patent term adjustments and any patent term extensions. We own two pending U.S. provisional applications directed to, among other things, our anti-Tau antibody to be used with our BBB platform technology licensed from F-star. Any future U.S. and foreign patents that may issue from this patent family (assuming the necessary non-provisional patent applications are timely filed and all other applicable requirements are satisfied) would be expected to expire in 2038, excluding any patent term adjustments and any patent term extensions. We also own one pending U.S. provisional application directed to, among other things, anti-BACE1/anti-Tau bispecific antibodies for use with our BBB platform technology licensed from F-star. Any future U.S. and foreign patents that may issue from this patent family (assuming the necessary non-provisional patent applications are timely filed and all other applicable requirements are satisfied) would be expected to expire in 2038, excluding any patent term adjustments and any patent term extensions.

ATV: aSyn

We own two pending U.S. provisional applications directed to, among other things, our anti-aSyn antibodies to be used with our BBB platform technology licensed from F-star. Any future U.S. and foreign patents that may issue from this patent family (assuming the necessary non-provisional patent applications are timely filed and all other applicable requirements are satisfied) would be expected to expire in 2038, excluding any patent term adjustments and any patent term extensions.

ATV: TREM2

We own two pending U.S. provisional applications directed to, among other things, our anti-TREM2 antibodies to be used with our BBB platform technology licensed from F-star. Any future U.S. and foreign patents that may issue from this patent family (assuming the necessary non-provisional patent applications are timely filed and all other applicable requirements are satisfied) would be expected to expire in 2038, excluding any patent term adjustments and any patent term extensions.

ETV: IDS

We own two pending U.S. provisional applications directed to, among other things, our ETV:IDS constructs that incorporate our BBB platform technology licensed from F-star. Any future U.S. and foreign patents that may issue from this patent family (assuming the necessary non-provisional patent applications are timely filed and all other applicable requirements are satisfied) would be expected to expire in 2038, excluding any patent term adjustments and any patent term extensions.

LRRK2

We license multiple patent families from Genentech directed to, among other things, our LRRK2 program, including DNL201, DNL151 and other related compounds. These licensed patent families include approximately 10 granted U.S. patents, and approximately 155 granted foreign patents and 55 pending foreign patent applications. The issued patents in these licensed families are expected to expire in 2031, excluding any patent term adjustments and any patent term extensions.

DNL201

We license a patent family from Genentech directed to, among other things, DNL201, which includes one issued U.S. patent, and approximately 38 granted foreign patents and five pending foreign patent applications. The issued U.S. patent claims the composition of matter of DNL201 and is expected to expire in 2031, excluding any patent term adjustments and any patent term extensions.

DNL151

We own one patent family directed to DNL151, which includes one pending U.S. non-provisional patent application, one pending patent cooperation treaty, or PCT, application and two pending foreign patent applications, with pending claims covering the composition and use of DNL151. Future U.S. and foreign patents issued from this patent family are expected to expire in 2037, excluding any patent term adjustments and any patent term extensions. In addition, we license approximately 38 foreign patents from Genentech, with issued claims related to the DNL151 compound class. We do not own or in-license any issued U.S. patents covering the composition of matter of DNL151 specifically.

RIPK1

For our most advanced RIPK1 product candidate, DNL747, we own a patent family directed to the composition of matter of DNL747, which includes one issued U.S. patent, one pending U.S. non-provisional patent application, one PCT application and two pending foreign patent applications. Future U.S. and foreign patents issued from this patent family are expected to expire in 2037, excluding any patent term adjustments and any patent term extensions.

We cannot guarantee that our owned and licensed pending patent applications, or any patent applications that we may in the future file or license from third parties, will result in the issuance of patents. We also cannot predict the scope of claims that may be allowed or enforced in our patents. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Consequently, we may not obtain or maintain adequate patent protection for any of our programs and product candidates. For more information regarding the risks related to our intellectual property, see “Risk Factors—Risks Related to Our Intellectual Property.”

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the United States, the patent term of a patent that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. Patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to an approved drug may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our products receive FDA approval, we expect to apply for patent term extensions on patents covering those products. We plan to seek patent term extensions to any of our issued patents in any jurisdiction where these are available, however there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment of whether such extensions should be granted, and if granted, the length of such extensions. For more information regarding the risks related to our intellectual property, see “Risk Factors—Risks Related to Our Intellectual Property.”

In addition to patent protection, we also rely on trademark registration, trade secrets, know how, other proprietary information and continuing technological innovation to develop and maintain our competitive position. We seek to protect and maintain the confidentiality of proprietary information to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third parties may

independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. Thus, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. Our agreements with employees also provide that all inventions conceived by the employee in the course of employment with us or from the employee's use of our confidential information are our exclusive property. However, such confidentiality agreements and invention assignment agreements can be breached and we may not have adequate remedies for any such breach. For more information regarding the risks related to our intellectual property, see "Risk Factors—Risks Related to Our Intellectual Property."

The patent positions of biotechnology companies like ours are generally uncertain and involve complex legal, scientific and factual questions. Our commercial success will also depend in part on not infringing upon the proprietary rights of third parties. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies, or our drugs or processes, obtain licenses or cease certain activities. Our breach of any license agreements or our failure to obtain a license to proprietary rights required to develop or commercialize our future products may have a material adverse impact on us. If third parties prepare and file patent applications in the United States that also claim technology to which we have rights, we may have to participate in interference or derivation proceedings in the USPTO to determine priority of invention. For more information, see "Risk Factors—Risks Related to Our Intellectual Property."

Government Regulation

Government authorities in the United States at the federal, state and local level and in other countries regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of drug and biological products. Generally, before a new drug or biologic can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific for each regulatory authority, submitted for review and approved by the regulatory authority.

U.S. Drug Development

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations, and biologics under the FDCA, the Public Health Service Act, or PHSA, and their implementing regulations. Both drugs and biologics also are subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or post-market may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, untitled or warning letters, product recalls or market withdrawals, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement and civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Any future product candidates must be approved by the FDA through either a new drug application, or NDA, or a biologics license application, or BLA, process before they may be legally marketed in the United States. The process generally involves the following:

- Completion of extensive preclinical studies in accordance with applicable regulations, including studies conducted in accordance with good laboratory practice, or GLP, requirements;
- Submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- Approval by an independent institutional review board, or IRB, or ethics committee at each clinical trial site before each trial may be initiated;
- Performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, good clinical practice, or GCP, requirements and other clinical trial-related regulations to establish the safety and efficacy of the investigational product for each proposed indication;
- Submission to the FDA of an NDA or BLA;
- A determination by the FDA within 60 days of its receipt of an NDA or BLA to accept the filing for review;
- Satisfactory completion of a FDA pre-approval inspection of the manufacturing facility or facilities where the drug or biologic will be produced to assess compliance with current good manufacturing practices, or cGMP, requirements to assure that the facilities, methods and controls are adequate to preserve the drug or biologic's identity, strength, quality and purity;
- Potential FDA audit of the preclinical and/or clinical trial sites that generated the data in support of the NDA or BLA;
- FDA review and approval of the NDA or BLA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the drug or biologic in the United States; and
- Compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

The data required to support an NDA or BLA are generated in two distinct developmental stages: preclinical and clinical. The preclinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for any future product candidates will be granted on a timely basis, or at all.

Preclinical Studies and IND

The preclinical developmental stage generally involves laboratory evaluations of drug chemistry, formulation and stability, as well as studies to evaluate toxicity in animals, which support subsequent clinical testing. The sponsor must submit the results of the preclinical studies, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational product to humans, and must become effective before human clinical trials may begin.

Preclinical studies include laboratory evaluation of product chemistry and formulation, as well as *in vitro* and animal studies to assess the potential for adverse events and in some cases to establish a

rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations for safety/toxicology studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time, the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical Trials

The clinical stage of development involves the administration of the investigational product to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Furthermore, each clinical trial must be reviewed and approved by an IRB for each institution at which the clinical trial will be conducted to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative, and must monitor the clinical trial until completed. There also are requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

A sponsor who wishes to conduct a clinical trial outside of the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of an NDA or BLA. The FDA will accept a well-designed and well-conducted foreign clinical study not conducted under an IND if the study was conducted in accordance with GCP requirements and the FDA is able to validate the data through an onsite inspection if deemed necessary.

Clinical trials in the United States generally are conducted in three sequential phases, known as Phase 1, Phase 2 and Phase 3, and may overlap.

- Phase I clinical trials generally involve a small number of healthy volunteers or disease-affected patients who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, side effect tolerability and safety of the drug.
- Phase II clinical trials involve studies in disease-affected patients to determine the dose required to produce the desired benefits. At the same time, safety and further PK and PD information is collected, possible adverse effects and safety risks are identified and a preliminary evaluation of efficacy is conducted.
- Phase III clinical trials generally involve a large number of patients at multiple sites and are designed to provide the data necessary to demonstrate the effectiveness of the product for its intended use, its safety in use and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product approval. These trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA or BLA.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the drug, findings from animal or *in vitro* testing that suggest a significant risk for human subjects and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure.

Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug or biologic has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether a trial may move forward at designated check points based on access to certain data from the trial. Concurrent with clinical trials, companies usually complete additional animal studies and also must develop additional information about the chemistry and physical characteristics of the drug or biologic as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product and, among other things, companies must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that our product candidates do not undergo unacceptable deterioration over their shelf life.

NDA/BLA Review Process

Following completion of the clinical trials, data are analyzed to assess whether the investigational product is safe and effective for the proposed indicated use or uses. The results of preclinical studies and clinical trials are then submitted to the FDA as part of an NDA or BLA, along with proposed labeling, chemistry and manufacturing information to ensure product quality and other relevant data. In short, the NDA or BLA is a request for approval to market the drug or biologic for one or more specified indications and must contain proof of safety and efficacy for a drug or safety, purity and potency for a biologic. The application may include both negative and ambiguous results of preclinical studies and clinical trials, as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational product to the satisfaction of FDA. FDA approval of an NDA or BLA must be obtained before a drug or biologic may be marketed in the United States.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each NDA or BLA must be accompanied by a user fee. FDA adjusts the PDUFA user fees on an annual basis. According to the FDA's fee schedule, effective through September 30, 2016, the user fee for an application requiring clinical data, such as an NDA or BLA, is $2,380,100. PDUFA also imposes an annual product fee for human drugs and biologics (approximately $97,750) and an annual establishment fee (approximately $580,000) on facilities used to manufacture prescription drugs and biologics. Fee waivers or reductions

are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on NDAs or BLAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA reviews all submitted NDAs and BLAs before it accepts them for filing, and may request additional information rather than accepting the NDA or BLA for filing. The FDA must make a decision on accepting an NDA or BLA for filing within 60 days of receipt. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA or BLA. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has ten months, from the filing date, in which to complete its initial review of a new molecular-entity NDA or original BLA and respond to the applicant, and six months from the filing date of a new molecular-entity NDA or original BLA designated for priority review. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs or BLAs, and the review process is often extended by FDA requests for additional information or clarification.

Before approving an NDA or BLA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with cGMP requirements. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The FDA also may audit data from clinical trials to ensure compliance with GCP requirements. Additionally, the FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions, if any. The FDA is not bound by recommendations of an advisory committee, but it considers such recommendations when making decisions on approval. The FDA likely will reanalyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process. After the FDA evaluates an NDA or BLA, it will issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes all of the specific deficiencies in the NDA or BLA identified by the FDA. The Complete Response Letter may require additional clinical data, additional pivotal Phase 3 clinical trial(s) and/or other significant and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the NDA or BLA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the NDA or BLA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data.

Orphan Drugs

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making the product available in the United States for this type of disease or condition will be recovered from sales of the product.

Orphan drug designation must be requested before submitting an NDA or BLA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years from the date of such approval, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity by means of greater effectiveness, greater safety or providing a major contribution to patient care or in instances of drug supply issues. Competitors, however, may receive approval of either a different product for the same indication or the same product for a different indication but that could be used off-label in the orphan indication. Orphan drug exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval before we do for the same product, as defined by the FDA, for the same indication we are seeking approval, or if a product candidate is determined to be contained within the scope of the competitor's product for the same indication or disease. If one of our products designated as an orphan drug receives marketing approval for an indication broader than that which is designated, it may not be entitled to orphan drug exclusivity. Orphan drug status in the European Union has similar, but not identical, requirements and benefits.

Expedited Development and Review Programs

The FDA has a fast track program that is intended to expedite or facilitate the process for reviewing new drugs and biologics that meet certain criteria. Specifically, new drugs and biologics are eligible for fast track designation if they are intended to treat a serious or life threatening condition and preclinical or clinical data demonstrate the potential to address unmet medical needs for the condition. Fast track designation applies to both the product and the specific indication for which it is being studied. The sponsor can request the FDA to designate the product for fast track status any time before receiving NDA or BLA approval, but ideally no later than the pre-NDA or pre-BLA meeting.

Any product submitted to the FDA for marketing, including under a fast track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review if it treats a serious or life-threatening condition and, if approved, would provide a significant improvement in safety and effectiveness compared to available therapies.

A product may also be eligible for accelerated approval, if it treats a serious or life-threatening condition and generally provides a meaningful advantage over available therapies. In addition, it must demonstrate an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of approval, the FDA may require that a sponsor of a drug or biologic receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. If the FDA concludes that a drug or biologic shown to be effective can be safely used only if distribution or use is restricted, it may require such post-marketing restrictions, as it deems necessary to assure safe use of the product.

Additionally, a drug or biologic may be eligible for designation as a breakthrough therapy if the product is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints. The benefits of breakthrough therapy designation include the same benefits as fast track designation, plus intensive guidance from the FDA to ensure an efficient drug development program. Fast track designation, priority review, accelerated approval and breakthrough therapy designation do not change the standards for approval, but may expedite the development or approval process.

Abbreviated Licensure Pathway of Biological Products as Biosimilar or Interchangeable

The Patient Protection and Affordable Care Act, or PPACA, or Affordable Care Act, or ACA, signed into law in 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA, created an abbreviated approval pathway for biological products shown to be highly similar to an FDA-licensed reference biological product. The BPCIA attempts to minimize duplicative testing, and thereby lower development costs and increase patient access to affordable treatments. An application for licensure of a biosimilar product must include information demonstrating biosimilarity based upon the following, unless the FDA determines otherwise:

- analytical studies demonstrating that the proposed biosimilar product is highly similar to the approved product notwithstanding minor differences in clinically inactive components;
- animal studies (including the assessment of toxicity); and
- a clinical study or studies (including the assessment of immunogenicity and PK or PD) sufficient to demonstrate safety, purity and potency in one or more conditions for which the reference product is licensed and intended to be used.

In addition, an application must include information demonstrating that:

- the proposed biosimilar product and reference product utilize the same mechanism of action for the condition(s) of use prescribed, recommended, or suggested in the proposed labeling, but only to the extent the mechanism(s) of action are known for the reference product;
- the condition or conditions of use prescribed, recommended, or suggested in the labeling for the proposed biosimilar product have been previously approved for the reference product;
- the route of administration, the dosage form, and the strength of the proposed biosimilar product are the same as those for the reference product; and
- the facility in which the biological product is manufactured, processed, packed or held meets standards designed to assure that the biological product continues to be safe, pure, and potent.

Biosimilarity means that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components; and that there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product. In addition, the law provides for a designation of “interchangeability” between the reference and biosimilar products, whereby the biosimilar may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product. The higher standard of interchangeability must be demonstrated by information sufficient to show that:

- the proposed product is biosimilar to the reference product;
- the proposed product is expected to produce the same clinical result as the reference product in any given patient; and
- for a product that is administered more than once to an individual, the risk to the patient in terms of safety or diminished efficacy of alternating or switching between the biosimilar and the reference product is no greater than the risk of using the reference product without such alternation or switch.

FDA approval is required before a biosimilar may be marketed in the United States. However, complexities associated with the large and intricate structures of biological products and the process by which such products are manufactured pose significant hurdles to the FDA’s implementation of the law

that are still being worked out by the FDA. For example, the FDA has discretion over the kind and amount of scientific evidence—laboratory, preclinical and/or clinical—required to demonstrate biosimilarity to a licensed biological product.

The FDA intends to consider the totality of the evidence, provided by a sponsor to support a demonstration of biosimilarity, and recommends that sponsors use a stepwise approach in the development of their biosimilar products. Biosimilar product applications thus may not be required to duplicate the entirety of preclinical and clinical testing used to establish the underlying safety and effectiveness of the reference product. However, the FDA may refuse to approve a biosimilar application if there is insufficient information to show that the active ingredients are the same or to demonstrate that any impurities or differences in active ingredients do not affect the safety, purity or potency of the biosimilar product. In addition, as with BLAs, biosimilar product applications will not be approved unless the product is manufactured in facilities designed to assure and preserve the biological product's safety, purity and potency.

The submission of a biosimilar application does not guarantee that the FDA will accept the application for filing and review, as the FDA may refuse to accept applications that it finds are insufficiently complete. The FDA will treat a biosimilar application or supplement as incomplete if, among other reasons, any applicable user fees assessed under the Biosimilar User Fee Act of 2012 have not been paid. In addition, the FDA may accept an application for filing but deny approval on the basis that the sponsor has not demonstrated biosimilarity, in which case the sponsor may choose to conduct further analytical, preclinical or clinical studies and submit a BLA for licensure as a new biological product.

The timing of final FDA approval of a biosimilar for commercial distribution depends on a variety of factors, including whether the manufacturer of the branded product is entitled to one or more statutory exclusivity periods, during which time the FDA is prohibited from approving any products that are biosimilar to the branded product. The FDA cannot approve a biosimilar application for twelve years from the date of first licensure of the reference product. Additionally, a biosimilar product sponsor may not submit an application for four years from the date of first licensure of the reference product. A reference product may also be entitled to exclusivity under other statutory provisions. For example, a reference product designated for a rare disease or condition (an "orphan drug") may be entitled to seven years of exclusivity, in which case no product that is biosimilar to the reference product may be approved until either the end of the twelve-year period provided under the biosimilarity statute or the end of the seven-year orphan drug exclusivity period, whichever occurs later. In certain circumstances, a regulatory exclusivity period can extend beyond the life of a patent, and thus block biosimilarity applications from being approved on or after the patent expiration date. In addition, the FDA may under certain circumstances extend the exclusivity period for the reference product by an additional six months if the FDA requests, and the manufacturer undertakes, studies on the effect of its product in children, a so-called pediatric extension.

The first biological product determined to be interchangeable with a branded product for any condition of use is also entitled to a period of exclusivity, during which time the FDA may not determine that another product is interchangeable with the reference product for any condition of use. This exclusivity period extends until the earlier of: (1) one year after the first commercial marketing of the first interchangeable product; (2) 18 months after resolution of a patent infringement against the applicant that submitted the application for the first interchangeable product, based on a final court decision regarding all of the patents in the litigation or dismissal of the litigation with or without prejudice; (3) 42 months after approval of the first interchangeable product, if a patent infringement suit against the applicant that submitted the application for the first interchangeable product is still ongoing; or (4) 18 months after approval of the first interchangeable product if the applicant that submitted the application for the first interchangeable product has not been sued.

Post-Approval Requirements

Following approval of a new product, the manufacturer and the approved product are subject to continuing regulation by the FDA, including, among other things, monitoring and record-keeping requirements, requirements to report adverse experiences, and comply with promotion and advertising requirements, which include restrictions on promoting drugs for unapproved uses or patient populations (known as "off-label use") and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such uses. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use. Further, if there are any modifications to the drug or biologic, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA/BLA or NDA/BLA supplement, which may require the development of additional data or preclinical studies and clinical trials.

The FDA may also place other conditions on approvals including the requirement for a Risk Evaluation and Mitigation Strategy, or REMS, to assure the safe use of the product. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Product approvals may be withdrawn for non-compliance with regulatory standards or if problems occur following initial marketing.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications;
- applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the market. Drugs and biologics may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Other U.S. Regulatory Matters

Manufacturing, sales, promotion and other activities following product approval are also subject to regulation by numerous regulatory authorities in the United States in addition to the FDA, including the Centers for Medicare & Medicaid Services, other divisions of the Department of Health and Human Services, the Department of Justice, the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments.

For example, in the United States, sales, marketing and scientific and educational programs also must comply with state and federal fraud and abuse laws. These laws include the federal Anti-Kickback Statute, which makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf), to knowingly and willfully solicit, receive, offer or pay any remuneration that is intended to induce or reward referrals, including the purchase, recommendation, order or prescription of a particular drug, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. Violations of this law are punishable by up to five years in prison, criminal fines, administrative civil money penalties and exclusion from participation in federal healthcare programs. Moreover, the ACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

Pricing and rebate programs must comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990 and more recent requirements in the ACA. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, sales, promotion and other activities also are potentially subject to federal and state consumer protection and unfair competition laws.

The distribution of biologic and pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The failure to comply with any of these laws or regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, requests for recall, seizure of products, total or partial suspension of production, denial or withdrawal of product approvals or refusal to allow a firm to enter into supply contracts, including government contracts. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

U.S. Patent-Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of any future product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits restoration of the patent term of up to five years as compensation for patent term lost during product development and FDA regulatory review process. Patent-term restoration, however, cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent-term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA or BLA plus the time between the submission date of an NDA or BLA and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only

one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The U.S. PTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent term for our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA or BLA.

Market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of a NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for a NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

A reference biological product is granted twelve years of data exclusivity from the time of first licensure of the product, and the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product. “First licensure” typically means the initial date the particular product at issue was licensed in the United States. Date of first licensure does not include the date of licensure of (and a new period of exclusivity is not available for) a biological product if the licensure is for a supplement for the biological product or for a subsequent application by the same sponsor or manufacturer of the biological product (or licensor, predecessor in interest, or other related entity) for a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength, or for a modification to the structure of the biological product that does not result in a change in safety, purity, or potency. Therefore, one must determine whether a new product includes a modification to the structure of a previously licensed product that results in a change in safety, purity, or potency to assess whether the licensure of the new product is a first licensure that triggers its own period of exclusivity. Whether a subsequent application, if approved, warrants exclusivity as the “first licensure” of a biological product is determined on a case-by-case basis with data submitted by the sponsor.

European Union Drug Development

As in the United States, medicinal products can be marketed only if a marketing authorization from the competent regulatory agencies has been obtained.

Similar to the United States, the various phases of preclinical and clinical research in the European Union are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the EU clinical trials regulatory framework, setting out common

rules for the control and authorization of clinical trials in the EU, the EU Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the member state regimes. Under the current regime, before a clinical trial can be initiated it must be approved in each of the EU countries where the trial is to be conducted by two distinct bodies: the National Competent Authority, or NCA, and one or more Ethics Committees, or ECs. Under the current regime all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred.

The EU clinical trials legislation currently is undergoing a transition process mainly aimed at harmonizing and streamlining clinical-trial authorization, simplifying adverse-event reporting procedures, improving the supervision of clinical trials and increasing their transparency. Recently enacted Clinical Trials Regulation EU No 536/2014 ensures that the rules for conducting clinical trials in the EU will be identical. In the meantime, Clinical Trials Directive 2001/20/EC continues to govern all clinical trials performed in the EU.

European Union Drug Review and Approval

In the European Economic Area, or EEA, which is comprised of the 27 Member States of the European Union (including Norway and excluding Croatia), Iceland and Liechtenstein, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations.

- The Community MA is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the European Medicines Agency, or EMA, and is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, advanced-therapy medicines such as gene-therapy, somatic cell-therapy or tissue-engineered medicines and medicinal products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.
- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State, or RMS. The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics, or SPC, and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Member States Concerned) for their approval. If the Member States Concerned raise no objections, based on a potential serious risk to public health, to the assessment, SPC, labeling, or packaging proposed by the RMS, the product is subsequently granted a national MA in all the Member States (i.e., in the RMS and the Member States Concerned).

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Coverage and Reimbursement

Sales of our products will depend, in part, on the extent to which our products will be covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. In the United States no uniform policy of coverage and reimbursement for drug or biological products exists. Accordingly, decisions regarding the extent of coverage and amount of reimbursement to be provided for any of our products will be made on a payor-by-payor basis. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

The United States government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price-controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. For example, the ACA contains provisions that may reduce the profitability of drug products through increased rebates for drugs reimbursed by Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Adoption of general controls and measures, coupled with the tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceutical drugs.

The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. The ACA made several changes to the Medicaid Drug Rebate Program, including increasing pharmaceutical manufacturers' rebate liability by raising the minimum basic Medicaid rebate on most branded prescription drugs from 15.1% of average manufacturer price, or AMP, to 23.1% of AMP and adding a new rebate calculation for "line extensions" (i.e., new formulations, such as extended release formulations) of solid oral dosage forms of branded products, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP. The ACA also expanded the universe of Medicaid utilization subject to drug rebates by requiring pharmaceutical manufacturers to pay rebates on Medicaid managed care utilization and by enlarging the population potentially eligible for Medicaid drug benefits. The Centers for Medicare & Medicaid Services, or CMS, have proposed to expand Medicaid rebate liability to the territories of the United States as well.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. Unlike Medicare Part A and B, Part D coverage is not standardized. While all Medicare drug plans must give at least a standard level of coverage set by Medicare, Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of

the costs of prescription drugs may increase demand for products for which we receive marketing approval. However, any negotiated prices for our products covered by a Part D prescription drug plan likely will be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

For a drug product to receive federal reimbursement under the Medicaid or Medicare Part B programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. The required 340B discount on a given product is calculated based on the AMP and Medicaid rebate amounts reported by the manufacturer. As of 2010, the ACA expanded the types of entities eligible to receive discounted 340B pricing, although, under the current state of the law, with the exception of children's hospitals, these newly eligible entities will not be eligible to receive discounted 340B pricing on orphan drugs. In addition, as 340B drug prices are determined based on AMP and Medicaid rebate data, the revisions to the Medicaid rebate formula and AMP definition described above could cause the required 340B discount to increase.

As noted above, the marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. An increasing emphasis on cost containment measures in the United States has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

In addition, in most foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union do not follow price structures of the United States and generally prices tend to be significantly lower.

Licenses and Collaborations

F-star License and Collaboration Agreement

Overview

In August 2016, we entered into a license and collaboration agreement with F-star Gamma Limited, f-star Biotechnologische Forschungs- und Entwicklungsges m.b.H and F-star Biotechnology Limited, or, collectively, F-star. The goal of the collaboration is the development of certain constant Fc domains of an antibody with non-native antigen binding activity, or Fcabs, to enhance delivery of therapeutics across the BBB into the brain. The collaboration leverages F-star's modular antibody technology and our expertise in the development of therapies for neurodegenerative diseases.

Under the terms of the F-star collaboration agreement, we can nominate up to three Fcab targets, or Accepted Fcab Targets, within the first three years of the date of the collaboration agreement; and

we have selected TfR as the first Accepted Fcab Target. With respect to each Accepted Fcab Target, we can nominate up to eight Fab targets, or Accepted Fab Targets, which are targets bound by the variable domains of an antibody or other therapeutic modalities, or Fabs. Under the F-star collaboration agreement, F-star is prohibited from developing, commercializing and manufacturing any antibody or other molecule that incorporates any Fcab directed to an Accepted Fcab Target, which we refer to as a Selected Fcab, or any Selected Fcab as a standalone product, and from authorizing any third party to take any such action until the expiration of our buy-out option, as described below. In addition, we are obligated to use commercially reasonable efforts during the research term to perform development activities in accordance with certain specified development plans.

Financial Obligations

We paid F-star Gamma an upfront fee of $5.5 million, which includes the selection of the first Accepted Fcab Target, TfR, under the collaboration. We are obligated to pay a one-time fixed fee in the low single-digit millions for each additional Accepted Fcab Target we select, technical milestone payments for each Accepted Fcab Target, up to a maximum of $15.0 million in the aggregate for all Accepted Fcab Targets, and, at specified times, monthly exclusivity fees for Accepted Fcab Targets and Accepted Fab Targets, which may be eliminated in certain circumstances. We are also responsible for certain research costs incurred by F-star in conducting activities under each agreed development plan, for up to 24 months. These research costs for the agreed TfR development plan will be up to $2.1 million.

Buy-Out Option

In connection with the entry into the F-star collaboration agreement, we also purchased an option for an upfront option fee of $0.5 million, which we refer to as the buy-out-option, to acquire all of the outstanding shares of F-star Gamma pursuant to a pre-negotiated buy-out option agreement. We must elect whether to exercise our buy-out option before the earlier of (i) dosing of the fifth patient dosed in the first Phase 1 trial of an antibody that binds to an Accepted Fab Target and an Accepted Fcab Target, (ii) the fourth anniversary of the first delivery by F-star of an Fcab meeting certain delivery criteria, and (iii) five and one half years after the delivery by us of a notice that we are progressing an Fcab identified from our library that binds to an Accepted Fcab Target. In addition, if we exercise the buy-out option, we will become an owner of certain intellectual property owned by F-star Gamma (by way of our ownership of F-star Gamma) and we will become a direct licensee of certain intellectual property of F-star Biotechnology (by way of our assumption of F-star Gamma's license agreement with F-star Biotechnology). If we exercise the buy-out option we will be obligated to make initial exercise payments under the buy-out option agreement and F-star Gamma's license agreement with F-star Biotechnology ranging from, in the aggregate, approximately $18.0 million to $50.0 million, plus a payment under the buy-out option agreement of the estimated net cash of F-star Gamma at the time of such exercise. In addition, we will be required under the buy-out option agreement and F-star Gamma's license agreement with F-star Biotechnology to make certain contingent payments upon the achievement of certain preclinical, clinical, regulatory and commercial milestones, up to a maximum amount of $447.0 million in the aggregate. The amount of the initial exercise and contingent payments varies based on whether F-star delivers an Fcab that meets pre-defined criteria, whether the Fcab has been identified solely by us or solely by F-star or jointly by us and F-star and the timing of our exercise of the buy-out option. Following exercise of the buy-out option, we will not be required to make any further milestone or royalty payments under the F-star collaboration agreement.

If we exercise the buy-out option, then f-star Biotechnologische Forschungs-und Entwicklungsges m.b.H and F-star Biotechnology will continue to be prohibited from developing, commercializing and manufacturing any antibody or other molecule that incorporates any Selected Fcab, or any Selected Fcab as a standalone product, and from authorizing any third party to take any such action.

If we do not exercise the buy-out option prior to the expiration of the buy-out option period, then, from the lapse of the buy-out option period until our rights with respect to an Accepted Fab Target expire or terminate, F-star is prohibited from developing, commercializing and manufacturing any antibody or other molecule that contains both a Selected Fcab and a Fab that specifically binds to the relevant Accepted Fab Target. In addition, in the event that we do not exercise the buy-out option prior to expiration of the buy-out option period, we have granted F-star Gamma a non-exclusive, royalty-free, irrevocable, perpetual, sublicensable license under our background and program intellectual property and any joint program intellectual property, to exploit any Fcab (other than one identified solely by us) against an Accepted Fcab Target and/or any antibody to the extent containing such Fcab (other than an Fcab identified solely by us or jointly with F-star), but excluding any rights to any Fabs and Accepted Fab Targets. If we elect not to exercise the buy-out option, we continue to have the option to obtain certain exclusive licenses as we describe further below.

License Option

With respect to each Accepted Fab Target, we have the right to obtain from F-star an exclusive, worldwide license to certain intellectual property to develop and commercialize licensed products that contain (i) a Fab that specifically binds to such Accepted Fab Target and (ii) an Fcab that we or F-star identify, either solely or jointly, and that specifically binds to an Accepted Fcab Target, for up to eight Accepted Fab Targets per each Accepted Fcab Target, as described above. Under each such license, we will be obligated to use commercially reasonable efforts to develop and commercialize the applicable licensed product in certain major market countries. If we do not exercise such a license option or otherwise elect to terminate it, such license option will generally expire upon the dosing of the fifth patient dosed in the first Phase 1 trial of the relevant antibody that binds to the applicable Accepted Fab Target.

Each time we exercise the license option described above, we will be obligated to pay F-star Gamma (i) a one-time fixed fee in the low single-digit millions, (ii) milestone payments upon the achievement of certain clinical development and commercial milestones, up to a maximum of $362.5 million in the aggregate; (iii) additional sales-based milestones if net sales of licensed products achieve certain specified levels, up to a maximum amount payable to F-star of $650.0 million in the aggregate and (iv) low-to-mid single-digit percentage royalties on net sales of licensed products. Our royalty payment obligations will expire on a country-by-country and licensed product-by-licensed product basis upon the later of (a) the expiration of the last valid claim of a licensed patent covering such licensed product in such country, (b) the expiration of regulatory exclusivity for such licensed product in such country, and (c) the twelfth anniversary of the first commercial sale of such licensed product in such country. Such amounts may be reduced by a specified percentage depending on the origin of the Fcab incorporated in the applicable licensed product and whether F-star delivers to us an Fcab that meets pre-defined criteria. We have the right to credit a certain amount of royalty payments that we pay to third parties with respect to certain licensed products against our royalty obligation to F-star Gamma but such credit cannot reduce our royalty obligation to F-star Gamma by more than fifty percent.

Other Rights

In addition to the buy-out option and option to obtain certain exclusive licenses described above, F-star Gamma and F-star Biotechnology granted us non-exclusive licenses under certain intellectual property to conduct technology development to discover and develop Fcabs. We also received a non-exclusive license under certain of F-star Biotechnology's platform patents and know-how to develop and commercialize products in connection with the delivery of therapeutics across the blood brain barrier, subject to certain specified restrictions.

F-star retains the right to use its intellectual property, including any intellectual property that we and F-star jointly own pursuant to the terms of the collaboration agreement, outside the scope of the

licenses granted to us. In addition, we granted F-star Biotechnology a non-exclusive, irrevocable, perpetual, sublicensable license under certain of our intellectual property to develop and commercialize certain of F-star's platform technology, subject to certain exclusivity obligations and the licenses granted to us under the collaboration agreement. Further, we are obligated to assign to F-star certain patents and know-how that we generate under the collaboration agreement related to F-star's platform technology or certain Fcabs identified solely by F-star.

Termination

Unless earlier terminated, the F-star collaboration agreement will remain in effect until all of our royalty and milestone payment obligations to F-star Gamma expire. Either party may terminate the F-star collaboration agreement if the other party materially breaches the collaboration agreement, subject to specified notice and cure provisions, or for the other party's bankruptcy or insolvency. In addition, F-star Gamma may terminate the F-star collaboration agreement if we challenge any of the patent rights licensed to us by F-star. We are able to terminate the F-star collaboration agreement for convenience, either in its entirety or on an Accepted Fcab Target-by-Accepted Fcab Target basis or an Accepted Fab Target-by-Accepted Fab Target basis, on 90 days' prior written notice to F-star.

Upon any termination by us for convenience or by F-star Gamma for our material uncured breach or insolvency, in each case either in whole or on an Accepted Fcab Target-by-Accepted Fcab Target or an Accepted Fab Target-by-Accepted Fab Target basis, among other things, the rights granted to us under the F-star collaboration agreement will terminate. Further, upon any such termination, if we have not exercised the buy-out option, (i) we must grant F-star Gamma certain non-exclusive, irrevocable and perpetual licenses under certain intellectual property owned by us arising out of the collaboration agreement to exploit certain antibodies that do not contain our proprietary Fabs or Fcabs identified solely by us, and (ii) F-star will no longer be restricted from developing and commercializing licensed products with respect to any terminated Accepted Fcab Target and/or Accepted Fab Target, as applicable.

Genentech Exclusive License Agreement

In June 2016, we entered into an exclusive license agreement with Genentech. The agreement gives us access to Genentech's preclinical stage LRRK2 small molecule program, which can be used to enhance and further progress our in-house LRRK2 program for Parkinson's disease. Under the agreement, Genentech granted us (i) an exclusive, worldwide, sublicenseable license under Genentech's rights to certain patents and patent applications directed to small molecule compounds which bind to and inhibit LRRK2 and (ii) a non-exclusive, worldwide, sublicenseable license to certain related know-how, in each case, to develop and commercialize certain compounds and licensed products incorporating any such compound. We are obligated to use commercially reasonable efforts during the first three years of the agreement to research, develop and commercialize at least one licensed product.

Our financial obligations under the agreement with Genentech included an upfront payment of $8.5 million and a technology transfer fee of $1.5 million. In addition, we may owe Genentech milestone payments upon the achievement of certain development, regulatory and commercial milestones, up to a maximum of $315.0 million in the aggregate. In addition, we are obligated to pay royalties on net sales of licensed products ranging from low to high single-digit percentages, with the exact royalty rate dependent on various factors, including (i) whether the compound incorporated in the relevant licensed product is a Genentech-provided compound or a compound acquired or developed by us, (ii) the date a compound was first discovered, derived or optimized by us, (iii) the existence of patent rights covering the relevant licensed product in the relevant country, (iv) the existence of orphan drug exclusivity covering a licensed product that is a Genentech-provided compound and (v) the level

of annual net sales of the relevant licensed product. We also have the right to credit a certain amount of third-party royalty and milestone payments against royalty and milestone payments owed to Genentech, but such credit cannot reduce our royalty obligation to Genentech by more than fifty percent. Our royalty payment obligations will expire on a country-by-country and licensed product-by-licensed product basis upon the later of (a) ten years after the first commercial sale of such licensed product in such country or (b) the expiration of the last valid claim of a licensed patent covering such licensed product in such country. If one of our licensed products incorporates a compound provided to us by Genentech, has orphan drug exclusivity, and is not covered by a valid claim of a licensed patent, we must pay royalties on net sales of such licensed products on a country-by-country and licensed product-by-licensed product basis until such orphan drug exclusivity in such country expires, but our obligation to pay these royalties may be eliminated or reduced if there is a clinically superior product marketed in such country.

Unless earlier terminated, our agreement with Genentech will continue in effect until all of our royalty and milestone payment obligations to Genentech expire. Following expiration of the agreement, we will retain our licenses under the intellectual property Genentech licensed to us on a non-exclusive, royalty-free basis. Genentech may terminate the agreement if we challenge any of the patent rights licensed to us by Genentech, or if we materially breach the agreement, subject to specified notice and cure provisions, or enter into bankruptcy or insolvency proceedings. If Genentech terminates the agreement for our material breach, bankruptcy or insolvency after we have made a milestone payment to Genentech, then we are obligated to grant to Genentech an exclusive right of first negotiation with respect to certain of our patents, know-how and regulatory filings directed to Genentech-provided compounds. We do not have the right to terminate the agreement without cause, but may terminate the agreement for Genentech's material breach, subject to specified notice and cure provisions.

Scientific Advisory Board

We have assembled a highly qualified scientific advisory board comprised of advisors who have, collectively, deep expertise in neurodegenerative diseases, genomics, protein engineering, drug development and drug discovery as well as translational medicine. Our scientists work in collaboration with these advisors to identify new disease targets, develop a biomarker strategy, enhance our BBB platform technology and accelerate discovery and development.

Name	Affiliated Entity
Marc Tessier-Lavigne, Ph.D. (Chair)	Stanford University
Scott Biller, Ph.D.	Agios Pharmaceuticals
Alison Goate, DPhil	Mount Sinai
David Holtzman, M.D.	Washington University in St. Louis
Leonard Petrucelli, Ph.D.	Mayo Clinic
Eric Reiman, M.D.	Banner Alzheimer's Institute
Lee Rubin, Ph.D.	Harvard University
Kevan Shokat, Ph.D.	University of California San Francisco
Scott Small, M.D.	Columbia University
Huda Zoghbi, M.D.	Baylor University

Employees

As of September 30, 2017, we had approximately 125 employees, all of whom were full-time and around 100 of whom were engaged in research and development activities. Approximately two-thirds of our employees hold Ph.D. or M.D. degrees. Substantially all of our employees are located in South San Francisco, California. None of our employees are represented by a labor union or covered under a collective bargaining agreement.

Facilities

Our corporate headquarters are located in South San Francisco, California, where we lease approximately 38,000 square feet of office, research and development, engineering and laboratory space pursuant to a lease agreement which commenced on August 1, 2016 and expires on July 31, 2024, with an option to extend for 5 years. This facility houses all our personnel. We believe that our existing facilities are adequate for our near-term needs, but expect to need additional space as we grow. We believe that suitable additional or alternative space would be available as required in the future on commercially reasonable terms.

Legal Proceedings

From time to time, we may become involved in litigation or other legal proceedings. We are not currently a party to any litigation or legal proceedings that, in the opinion of our management, are likely to have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

MANAGEMENT

Executive Officers and Directors

The following table sets forth the names, ages and positions of our executive officers and directors as of November 24, 2017:

Name	Age	Position
Executive Officers:		
Ryan J. Watts, Ph.D.	41	President, Chief Executive Officer and Director
Alexander O. Schuth, M.D.	44	Chief Operating Officer and Secretary
Steve E. Krognes	49	Chief Financial Officer and Treasurer
Carole Ho, M.D.	44	Chief Medical Officer
Non-Employee Directors:		
Vicki Sato, Ph.D.(3)	69	Chairperson of our Board of Directors
Douglas Cole, M.D.(1)	57	Director
Jay Flatley(1)(2)	65	Director
Robert Nelsen(2)	54	Director
David Schenkein, M.D.(3)	60	Director
Marc Tessier-Lavigne, Ph.D.(2)	57	Director

(1) Member of the audit committee
(2) Member of the compensation committee
(3) Member of the corporate governance and nominating committee

Executive Officers

Ryan J. Watts, Ph.D. is one of our Co-Founders and has served as a member of our board of directors since March 2015 and as our President and Chief Executive Officer since August 2015. From March 2015 to August 2015, Dr. Watts acted as our interim President, Chief Scientific Officer and Head of Research and Development. Dr. Watts co-founded and joined Denali from Genentech, a biotechnology company, where he held various research and leadership roles of increasing responsibility between 2004 and 2015; from 2013 to February 2015, Dr. Watts served as Director of the Department of Neuroscience; from 2010 to 2013, Dr. Watts served as Associate Director of the Department of Neuroscience; and from 2004 to 2010, Dr. Watts led or served on numerous research and early development teams. In addition, Dr. Watts led Genentech's BBB team between 2009 and 2015, and he served as Chair of the Joint Research Committee with AC Immune between 2006 and 2010 (program currently in Phase 3) and between 2012 and 2014 (program currently in Phase 1). Dr. Watts received his Ph.D. in Biological Sciences from Stanford University and his B.S. in Biology from the University of Utah. Dr. Watts has authored and co-authored more than 60 scientific papers and has been an invited peer reviewer in numerous publications including *Cell, Nature Biotechnology, Nature Medicine, Neuron, Science* and *Science Translational Medicine*.

We believe Dr. Watts is qualified to serve on our board of directors because of the perspective and experience he provides as one of our founders and as our President and Chief Executive Officer, as well as his broad experience within the pharmaceutical industry, particularly in the area of neuroscience and drug discovery and development.

Alexander O. Schuth, M.D. is one of our Co-Founders and has served as our Chief Operating Officer since March 2015 and as Secretary since June 2015. Dr. Schuth co-founded and joined Denali from Genentech, where he held various roles of increasing responsibility between 2005 and 2015; from September 2014 to March 2015, Dr. Schuth served as Head of Technology Innovation and Diagnostics

Partnering; from March 2010 to September 2014, Dr. Schuth served as Head of Neuroscience Partnering; from January 2007 to March 2010, Dr. Schuth worked in the business development team; and from August 2005 to January 2007, Dr. Schuth worked as an R&D finance manager. From January 2001 to May 2003, he served as Investment Banking Associate in the equity capital markets group at Merrill Lynch in London. He currently serves on the board of directors of Molecular Health, a privately held biopharmaceutical company. Dr. Schuth received his M.B.A. from The Wharton School of the University of Pennsylvania and his M.D. from the Charite Medical School at the Humboldt University in Berlin, Germany.

Steve E. Krognes has served as our Chief Financial Officer since October 2015 and Treasurer since November 2015. Mr. Krognes joined Denali from Genentech, where he served as Chief Financial Officer and a member of the Executive Committee from April 2009 to September 2015. Mr. Krognes also oversaw Genentech's Site Services organization between 2011 and 2015, and Genentech's IT organization between 2009 and 2011. He chaired the Genentech Access to Care Foundation between 2009 and 2015. From January 2004 to April 2009, Mr. Krognes served as Head of Mergers & Acquisitions and a member of the Finance Executive Committee at Roche, a Swiss biotechnology company. From July 2002 to December 2003, Mr. Krognes served as Director of M&A at Danske Bank based in Norway. From April 2000 to June 2002, he served as a Venture Capitalist with Pylonia Ventures, a Swedish venture investments company. Prior to that, Mr. Krognes worked as a consultant at McKinsey and an investment banker at Goldman Sachs, based in London and Boston. Mr. Krognes currently serves as a member of the boards of directors of Corvus Pharmaceuticals, a biopharmaceutical company, RLS Global, a Swedish life science company, and the California Academy of Sciences, a private scientific and educational institution. Mr. Krognes served as a board member of the California Life Science Association between 2010 and 2015. He received his M.B.A. from Harvard Business School and his B.S. in Economics from The Wharton School of the University of Pennsylvania.

Carole Ho, M.D. has served as our Chief Medical Officer and Head of Development since June 2015. Dr. Ho joined Denali from Genentech, where she held various roles of increasing responsibility between 2007 and 2015; from October 2014 to June 2015, Dr. Ho served as Vice President, Non-Oncology Early Clinical Development; from November 2013 to October 2014, Dr. Ho served as Senior Group Medical Director, Early Clinical Development; from April 2011 to November 2013, Dr. Ho served as Group Medical Director, Early Clinical Development; from June 2009 to April 2011, Dr. Ho served as Group Medical Director Global Product Development (Inflammation); and from October 2007 to June 2009, Dr. Ho served as Medical Director, Early Clinical Development. From November 2006 to October 2007, Dr. Ho served as Associate Medical Director at Johnson & Johnson, a health care products company. From June 2002 to November 2006, she was an instructor in the Department of Neurology and Neurological Sciences at Stanford University. Dr. Ho completed a residency in neurology at Partners Neurology Residency of the Massachusetts General and Brigham and Women's Hospital and was board certified in neurology and psychiatry between 2004 and 2014. Dr. Ho received her M.D. from Cornell University and her B.S. in Biochemical Sciences from Harvard College.

Non-Employee Directors

Vicki Sato, *Ph.D.* has served as a member of our board of directors since April 2015 and as Chairperson of our board of directors since August 2016. From September 2006 until July 2017, Dr. Sato served as a professor of management practice at Harvard Business School. From July 2005 until October 2015, she also had an appointment as Professor of the Practice in the Department of Molecular and Cell Biology at Harvard University. From September 2000 to May 2005, Dr. Sato served as the President of Vertex Pharmaceuticals, a pharmaceutical company, with general management responsibility for business and corporate development, commercial operations, legal and finance, in addition to research and development. From 1992 until 2000, she served as the Chief Scientific Officer

and Senior Vice President of Research and Development of Vertex Pharmaceuticals. Dr. Sato joined Vertex Pharmaceuticals in 1992, after serving as Vice President of Research at Biogen, a biotechnology company, where she also served as a member of the Scientific Board. Dr. Sato serves on the boards of directors of Bristol Myers Squibb, Syros Pharmaceuticals and BorgWarner. She previously served on the board of directors of PerkinElmer until April 2017. Dr. Sato received her A.M. and Ph.D. degrees from Harvard University and her A.B. in Biology from Radcliffe College.

We believe Dr. Sato is qualified to serve on our board of directors because of her extensive industry experience and leadership experience as a senior executive and director of several life sciences companies.

Douglas Cole, *M.D.* has served as a member of our board of directors since May 2015. Dr. Cole joined Flagship Pioneering, which conceives, creates, resources and develops first-in-category life sciences companies, in 2001, and is currently Managing Partner, where he has focused on life science investments. He currently serves on the board of directors of Editas Medicine, a public biotechnology company, and serves on the board of directors of a number of private companies. Previously, Dr. Cole served on the boards of directors of Agios Pharmaceuticals, Receptos, AVEO Pharmaceuticals, Tetraphase Pharmaceuticals and Concert Pharmaceuticals. Dr. Cole received his M.D. from the University of Pennsylvania School of Medicine and his B.A. in English from Dartmouth College.

We believe Dr. Cole is qualified to serve on our board of directors because of his substantial experience as a venture capital investor in emerging life sciences companies, as well as his experience serving on the boards of directors for several life sciences companies.

Jay Flatley has served as a member of our board of directors since April 2015. Since July 2016, Mr. Flatley has served as the Executive Chairman of the board of directors of Illumina, a public company focused on sequencing- and array-based solutions for genetic analysis. From January 2016 to July 2016, he served as Illumina's Chairman and has served as a member of its board of directors since October 1999. From December 2013 to July 2016, Mr. Flatley served as the Chief Executive Officer of Illumina and as the President and Chief Executive Officer from October 1999 to December 2013. Prior to joining Illumina, Mr. Flatley was Co-founder, President, Chief Executive Officer, and a director of Molecular Dynamics, a life sciences company focused on genetic discovery and analysis, from July 1994 until its sale to Amersham Pharmacia Biotech in September 1998. Mr. Flatley is an advisory board member for U.C. San Diego's Moore Cancer Center and serves on the board of directors at Coherent, a photonics manufacturing company. Mr. Flatley received his B.S. and M.S. in Industrial Engineering from Stanford University and his B.A. in Economics from Claremont McKenna College.

We believe Mr. Flatley is qualified to serve on our board of directors because of his extensive leadership experience and industry knowledge.

Robert Nelsen has served as a member of our board of directors since May 2015. Mr. Nelsen has served as a Co-founder and Managing Director of ARCH Venture Partners, a venture capital firm focused on early-stage technology companies, or its affiliated entities, since 1986. Mr. Nelsen is a director of Juno Therapeutics, Sienna Biopharmaceuticals and Syros Pharmaceuticals, along with certain private companies. Previously, Mr. Nelsen served on the boards of directors of Agios Pharmaceuticals, KYTHERA Biopharmaceuticals, Adolor Corporation, Illumina, Fate Therapeutics, deCODE genetics, NeurogesX, Bellerophon Therapeutics, Sage Therapeutics and Caliper Life Sciences. He also previously served as trustee of Fred Hutchinson Cancer Research Center. Mr. Nelsen received his M.B.A. from the University of Chicago and his B.S. degrees in Economics and Biology from the University of Puget Sound.

We believe Mr. Nelsen is qualified to serve on our board of directors because of his experience as a venture capitalist building and serving on the boards of directors of many public and private emerging companies, including biotechnology companies.

David Schenkein, *M.D.* has served as a member of our board of directors since April 2015. Since August 2009, Dr. Schenkein has served as President and Chief Executive Officer of Agios Pharmaceuticals, a pharmaceuticals company. From April 2006 to July 2009, Dr. Schenkein served as a Senior Vice President of Oncology Development at Genentech. Dr. Schenkein currently serves on the boards of directors of Agios Pharmaceuticals and bluebird bio. Previously, Dr. Schenkein served on the board of directors of Foundation Medicine. He also currently serves as an adjunct attending physician in hematology at Tufts Medical Center. Dr. Schenkein received his M.D. from the State University of New York Upstate Medical School and his B.A. in Chemistry from Wesleyan University.

We believe that Dr. Schenkein is qualified to serve on our board of directors because of his extensive background in the biotechnology industry and leadership experience as a senior executive and director of biotechnology companies.

Marc Tessier-Lavigne, *Ph.D.* is one of our Co-Founders and has served as a member of our board of directors since March 2015. From March 2015 to August 2016, Dr. Tessier-Lavigne served as the Chairman of our board of directors. Since September 2016, Dr. Tessier-Lavigne has served as President of Stanford University. From March 2011 to September 2016, he served as President of the Rockefeller University, as well as professor and head of the Laboratory of Brain Development and Repair. From September 2003 to March 2011, Dr. Tessier-Lavigne served in positions of increasing responsibility at Genentech, where in 2009 he was named Executive Vice President for Research and Chief Scientific Officer. He currently serves on the board of directors of Regeneron Pharmaceuticals. Previously, he served on the boards of directors of Pfizer, Juno Therapeutics and Agios Pharmaceuticals. Dr. Tessier-Lavigne received his Ph.D. in Neurophysiology from University College London, his B.A. in Philosophy and Physiology from Oxford University and his B.Sc. in Physics from McGill University. He conducted postdoctoral work at the MRC Developmental Neurobiology Unit in London and at Columbia University.

We believe Dr. Tessier-Lavigne is qualified to serve on our board of directors because of his pioneering research, scientific knowledge, service on boards of directors of public companies in the life sciences industry and leadership in the biotechnology industry.

Board of Directors Composition

Our board of directors currently consists of seven members. After the completion of this offering, the number of directors will be fixed by our board of directors, subject to the terms of our amended and restated certificate of incorporation and amended and restated bylaws. Each of our current directors will continue to serve as a director until the election and qualification of his or her successor, or until his or her earlier death, resignation or removal.

Our amended and restated certificate of incorporation will provide that our board of directors will be divided into three classes with staggered three-year terms. Only one class of directors will be elected at each annual meeting of stockholders, with the other classes continuing for the remainder of their respective three-year terms. Our current directors will be divided among the three classes as follows:

- the Class I directors will be Drs. Cole and Tessier-Lavigne and Mr. Flatley, and their terms will expire at the annual meeting of stockholders to be held in 2018;
- the Class II directors will be Mr. Nelson and Dr. Sato, and their terms will expire at the annual meeting of stockholders to be held in 2019; and

- the Class III directors will be Drs. Schenkein and Watts, and their terms will expire at the annual meeting of stockholders to be held in 2020.

At each annual meeting of stockholders, upon the expiration of the term of a class of directors, the successor to each such director in the class will be elected to serve from the time of election and qualification until the third annual meeting following his or her election and until his or her successor is duly elected and qualified, in accordance with our amended and restated certificate of incorporation. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of our directors.

This classification of our board of directors may have the effect of delaying or preventing changes in control of our company.

Director Independence

Upon the completion of this offering, we anticipate that our common stock will be listed on the NASDAQ Global Select Market, or NASDAQ. Under the rules of NASDAQ, independent directors must comprise a majority of a listed company's board of directors within one year of the completion of its initial public offering. In addition, the rules of NASDAQ require that, subject to specified exceptions, each member of a listed company's audit, compensation and corporate governance and nominating committees be independent. Audit committee members and compensation committee members must also satisfy the independence criteria set forth in Rule 10A-3 and Rule 10C-1, respectively, under the Exchange Act. Under the rules of NASDAQ, a director will only qualify as an "independent director" if, in the opinion of that company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director.

To be considered to be independent for purposes of Rule 10A-3 and under the rules of NASDAQ, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board of directors committee: (1) accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries; or (2) be an affiliated person of the listed company or any of its subsidiaries.

To be considered independent for purposes of Rule 10C-1 and under the rules of NASDAQ, the board of directors must affirmatively determine that the member of the compensation committee is independent, including a consideration of all factors specifically relevant to determining whether the director has a relationship to the company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: (i) the source of compensation of such director, including any consulting, advisory or other compensatory fee paid by the company to such director; and (ii) whether such director is affiliated with the company, a subsidiary of the company or an affiliate of a subsidiary of the company.

Our board of directors undertook a review of its composition, the composition of its committees and the independence of our directors and considered whether any director has a material relationship with us that could compromise his or her ability to exercise independent judgment in carrying out his or her responsibilities. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that Drs. Cole, Sato and Schenkein and Messrs. Flatley and Nelsen, representing five of our seven directors, do not have relationships that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is "independent" as that term is defined under the rules of NASDAQ. Drs. Tessier-Lavigne

and Watts are not independent under NASDAQ's independence standards. We intend to rely on the phase-in rules of NASDAQ with respect to the independence of our compensation committee.

In making these determinations, our board of directors considered the current and prior relationships that each non-employee director has with our company and all other facts and circumstances our board of directors deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director, and the transactions involving them described in the section titled "Certain Relationships and Related Party Transactions." There are no family relationships among any of our directors or executive officers.

Board of Directors Leadership Structure

Our board of directors is currently chaired by Dr. Sato. As a general policy, our board of directors believes that separation of the positions of Chairperson and Chief Executive Officer reinforces the independence of our board of directors from management, creates an environment that encourages objective oversight of management's performance and enhances the effectiveness of our board of directors as a whole. As such, Dr. Watts serves as our President and Chief Executive Officer while Dr. Sato serves as the Chairperson of our board of directors but is not an officer. We expect and intend the positions of Chairperson of our board of directors and Chief Executive Officer to continue to be held by two separate individuals in the future.

Board of Directors Committees

Our board of directors has an audit committee, a compensation committee and a corporate governance and nominating committee, each of which has the composition and the responsibilities described below.

Audit Committee

The members of our audit committee are Dr. Cole and Mr. Flatley. Mr. Flatley is the chair of our audit committee, and is our audit committee financial expert, as that term is defined under the SEC rules implementing SOX Section 407, and possesses financial sophistication, as defined under the rules of NASDAQ. Following the completion of this offering, we will appoint a third independent director to serve on our audit committee in accordance with the rules of NASDAQ. Our audit committee oversees our corporate accounting and financial reporting process and assists our board of directors in monitoring our financial systems. Our audit committee will also:

- select and hire the independent registered public accounting firm to audit our financial statements;
- help to ensure the independence and performance of the independent registered public accounting firm;
- approve audit and non-audit services and fees;
- review financial statements and discuss with management and the independent registered public accounting firm our annual audited and quarterly financial statements, the results of the independent audit and the quarterly reviews and the reports and certifications regarding internal controls over financial reporting and disclosure controls;
- prepare the audit committee report that the SEC requires to be included in our annual proxy statement;
- review reports and communications from the independent registered public accounting firm;

- review the adequacy and effectiveness of our internal controls and disclosure controls and procedure;
- review our policies on risk assessment and risk management;
- review related party transactions; and
- establish and oversee procedures for the receipt, retention and treatment of accounting related complaints and the confidential submission by our employees of concerns regarding questionable accounting or auditing matters.

Our audit committee will operate under a written charter, to be effective prior to the completion of this offering, which will satisfy the applicable rules of the SEC and the listing standards of NASDAQ.

Compensation Committee

The members of our compensation committee are Mr. Flatley, Mr. Nelsen and Dr. Tessier-Lavigne. Dr. Tessier-Lavigne is the chair of our compensation committee. Dr. Tessier-Lavigne is not independent under NASDAQ's independence standards. We intend to rely upon the phase-in rules of NASDAQ with respect to the independence of our compensation committee. Our compensation committee oversees our compensation policies, plans and benefits programs. The compensation committee will also:

- oversee our overall compensation philosophy and compensation policies, plans and benefit programs;
- review and approve or recommend to our board of directors for approval compensation for our executive officers and directors;
- prepare the compensation committee report that the SEC will require to be included in our annual proxy statement; and
- administer our equity compensation plans.

Our compensation committee will operate under a written charter, to be effective prior to the completion of this offering, which will satisfy the applicable rules of the SEC and the listing standards of NASDAQ.

Corporate Governance and Nominating Committee

The members of our corporate governance and nominating committee are Dr. Sato and Dr. Schenkein. Dr. Sato is the chair of our corporate governance and nominating committee. Our corporate governance and nominating committee oversees and assists our board of directors in reviewing and recommending nominees for election as directors. Specifically, the corporate governance and nominating committee will:

- identify, evaluate and make recommendations to our board of directors regarding nominees for election to our board of directors and its committees;
- consider and make recommendations to our board of directors regarding the composition of our board of directors and its committees;
- review developments in corporate governance practices;
- evaluate the adequacy of our corporate governance practices and reporting; and
- evaluate the performance of our board of directors and of individual directors.

Our corporate governance and nominating committee will operate under a written charter, to be effective prior to the completion of this offering, which will satisfy the applicable rules of the SEC and the listing standards of NASDAQ.

Director Compensation

To date, none of our non-employee directors has received any cash compensation for serving on our board of directors, other than Mr. Flatley and Drs. Sato, Schenkein and Tessier-Lavigne, who each earn $30,000 annually, paid on a quarterly basis, for service as a member of our board of directors. From time to time, we have granted stock options or issued restricted stock to those non-employee directors who are also not affiliated with our venture fund investors for their service on our board of directors, and such grants were made in April 2015 to Mr. Flatley and Drs. Sato and Schenkein. An additional grant was made to Dr. Sato for her service as the Chairperson of our board of directors in August 2016. We also reimburse our directors for expenses associated with attending meetings of our board of directors and its committees.

The following table presents the total compensation each of our non-employee directors received during the year ended December 31, 2016. Other than as set forth in the table, we did not pay any compensation, make any equity awards or non-equity awards to or pay any other compensation to any of our non-employee directors in 2016.

	Fees Earned or Paid in Cash ($)	Option Awards ($) (1)	Total ($)
Vicki Sato, Ph.D.(2)	15,000	148,095	163,095
Douglas Cole, M.D.	—	—	—
Jay Flatley(3)	15,000	—	15,000
Stephen Knight, M.D.(4)	—	—	—
Robert Nelsen	—	—	—
David Schenkein, M.D.(5)	15,000	—	15,000
Marc Tessier-Lavigne, Ph.D.(6)	15,000	—	15,000
Stacie Weninger, Ph.D.(7)	—	—	—

(1) The amounts disclosed represent the aggregate grant date fair value of the award as calculated in accordance with FASB Accounting Standards Codification Topic 718, or ASC 718. The assumptions used in calculating the grant date fair value of the award disclosed in this column are set forth in the notes to our audited consolidated financial statements included elsewhere in this prospectus. These amounts do not correspond to the actual value that may be recognized by the directors upon vesting of the applicable awards.

(2) Dr. Sato is paid a quarterly cash retainer of $7,500 for her service on our board of directors. As of December 31, 2016, Dr. Sato held an option to purchase 37,500 shares of our common stock. One-third of the shares subject to the option vested on August 23, 2017, and two-thirds of the remaining shares vest annually thereafter, subject to continued service through each such vesting date. As of December 31, 2016, Dr. Sato held 75,000 restricted shares of our common stock. One-fourth of the shares subject to the restricted stock award vested on April 17, 2016, and one thirty-sixth of the remaining shares vest monthly thereafter, subject to continued service through each such vesting date.

(3) Mr. Flatley is paid a quarterly cash retainer of $7,500 for his service on our board of directors. As of December 31, 2016, Mr. Flatley held 75,000 restricted shares of our common stock. One-fourth of the shares subject to the restricted stock award vested on April 17, 2016, and one thirty-sixth of the remaining shares vest monthly thereafter, subject to continued service through each such vesting date.

(4) Dr. Knight resigned as a member of our board of directors on August 11, 2017.

(5) Dr. Schenkein is paid a quarterly cash retainer of $7,500 for his service on our board of directors. As of December 31, 2016, Dr. Schenkein held 75,000 restricted shares of our common stock. One-fourth of the shares subject to the restricted stock award vested on April 17, 2016, and one thirty-sixth of the remaining shares vest monthly thereafter, subject to continued service through each such vesting date.

(6) Dr. Tessier-Lavigne is paid a quarterly cash retainer of $7,500 for his service on our board of directors. As of December 31, 2016, Dr. Tessier-Lavigne held an aggregate of 3,114,043 restricted shares of our common stock. Of the total number of shares, 2,734,375 shares are subject to a restricted stock agreement whereby one-fourth of the shares vested on March 12, 2016, and one thirty-sixth of the remaining shares vest monthly thereafter, subject to continued service through each such vesting date. Of the total number of shares, 379,668 shares are subject to a restricted stock agreement whereby one-fourth of the shares vested on March 24, 2016, and one thirty-sixth of the remaining shares vest monthly thereafter, subject to continued service through each such vesting date.

(7) Dr. Weninger resigned as a member of our board of directors on August 11, 2017.

Directors who are also our employees receive no additional compensation for their service as directors. During 2016, Dr. Watts was our only employee director. See the section titled “Executive Compensation” for additional information about Dr. Watts’ compensation.

In November 2017, our board of directors adopted our outside director compensation policy. Members of our board of directors who are not employees are eligible for compensation under our outside director compensation policy. Our outside director compensation policy will be effective as of the effective date of the registration statement of which this prospectus forms a part. Under our outside director compensation policy, after the effective date of the registration statement of which this prospectus forms a part, each non-employee director will be eligible to receive compensation for his or her service consisting of annual cash retainers and equity awards as described below. Our board of directors may revise outside director compensation as it deems necessary or appropriate.

Cash Compensation

Under our outside director compensation policy, all non-employee directors will be entitled to receive the following cash compensation for their services following the effective date of the registration statement of which this prospectus forms a part:

- $40,000 per year for service as a board member;
- $30,000 per year additionally for service as non-executive chair of the board;
- $15,000 per year additionally for service as chair of the audit committee;
- $7,500 per year additionally for service as member of the audit committee (excluding committee chair);
- $10,000 per year additionally for service as chair of the compensation committee;
- $5,000 per year additionally for service as member of the compensation committee (excluding committee chair);
- $8,000 per year additionally for service as chair of the corporate governance and nominating committee;
- $4,000 per year additionally for service as member of the corporate governance and nominating committee (excluding committee chair);
- $10,000 per year additionally for service as chair of the science and technology committee; and

- $5,000 per year additionally for service as member of the science and technology committee (excluding committee chair).

All cash payments to non-employee directors who served in the relevant capacity at any point during the immediately preceding prior fiscal quarter will be paid quarterly in arrears on a prorated basis. A non-employee director who served in the relevant capacity during only a portion of the prior fiscal quarter will receive a pro-rated payment of the quarterly payment of the applicable cash retainer.

Equity Compensation

Beginning with the effective date of the registration statement of which this prospectus forms a part, nondiscretionary, automatic grants of stock options will be made to our non-employee directors under our outside director compensation policy. Under our 2017 Equity Incentive Plan, or 2017 Plan, no non-employee directors may be granted, in any fiscal year, awards with a grant date fair value (determined in accordance with U.S. generally accepted accounting principles) of more than $1 million, increased to $1.6 million in connection with his or her initial service. Any awards granted to an individual while he or she was an employee, or while he or she was a consultant but not a non-employee director, will not count for purposes of these limitations. Subject to these limitations:

- *Initial Award*. Each person who first becomes a non-employee director on or following the effective date of the registration statement of which this prospectus forms a part will be granted a nonstatutory stock option with a grant date value of $600,000 (with the shares covered by the award rounded down to the nearest whole share), or the Initial Award. The Initial Award will be granted on the date on which such person first becomes a non-employee director on or following the effective date of this offering. Subject to the terms of the policy, the Initial Award will vest and become exercisable as to 25% of the shares subject to the Initial Award on the one-year anniversary of the date of grant and as to 1/48th of the shares subject to the Initial Award on each monthly anniversary of the date of grant thereafter (and if there is no corresponding day, on the last day of the month), in each case, provided that the non-employee director continues to serve as a non-employee director through the applicable vesting date. A director who is an employee who ceases to be an employee director but who remains a director will not receive an Initial Award.
- *Continuing Director IPO Award.* Each person who serves as a non-employee director as of immediately prior to the effective date of the registration statement of which this prospectus forms a part and continues to serve as a non-employee director as of such effective date automatically will be granted a nonstatutory stock option with a grant date value of $600,000 (with the shares covered by the award rounded down to the nearest whole share), or the Continuing Director IPO Award. The Continuing Director IPO Award will be granted on the effective date of the registration statement of which this prospectus forms a part. Subject to the terms of the policy, the Continuing Director IPO Award will vest and become exercisable as to 25% of the shares subject to the Continuing Director IPO Award on the one-year anniversary of the date of grant and as to 1/48th of the shares subject to the Continuing Director IPO Award on each monthly anniversary of the date of grant thereafter (and if there is no corresponding day, on the last day of the month), in each case, provided that the non-employee director continues to serve as a non-employee director through the applicable vesting date.
- *Annual Award*. On the date of each annual meeting of stockholders beginning with the first annual meeting following the effective date of the registration statement of which this prospectus forms a part, each non-employee director who, as of such annual meeting date, has served on the board as a director for at least the preceding six months, automatically will be granted a nonstatutory stock option having a grant date value equal to $350,000 (with the shares covered by the award rounded down to the nearest whole share), or the Annual

Award. Any non-employee director who is not continuing as a director following the applicable annual meeting will not receive an Annual Award with respect to such annual meeting. Subject to the terms of the policy, the Annual Award will vest and become exercisable as to 100% of the shares subject to the Annual Award upon the earlier of the one year anniversary of the grant date or the day prior to our next annual meeting of stockholders occurring after the grant date, in each case, provided that the non-employee director continues to serve as a non-employee director through the applicable vesting date.

The grant date value of all the Initial Awards, Continuing Director IPO Awards and Annual Awards granted under our outside director compensation policy will be calculated in accordance with the Black-Scholes option valuation methodology or such other methodology as our board or the compensation committee of our board may determine prior to the grant of such award.

Non-employee directors are also eligible to receive all types of equity awards (except incentive stock options) under our 2017 Plan, including discretionary awards not covered under our outside director compensation policy.

Our 2017 Plan, as described below under the section titled “Executive Compensation-Employee Benefit and Stock Plans,” provides that in the event of a change in control, as defined in our 2017 Plan, where awards granted to non-employee directors are assumed or substituted for, if on the date of or following such assumption or substitution, the non-employee director’s status as a director or director of the successor corporation, as applicable, is terminated other than upon a voluntary resignation by the non-employee director (unless such resignation is at the request of the acquirer), then each outstanding equity award granted under our 2017 Plan to a non-employee director will fully vest, all restrictions on the shares subject to such award will lapse, and with respect to awards with performance-based vesting, all performance goals or other vesting criteria will be deemed achieved at 100% of target levels, and all of the shares subject to such award will become fully exercisable, if applicable, unless specifically provided otherwise under the applicable award agreement or other written agreement with the director.

Scientific Advisory Board Compensation

Each member of our scientific advisory board earns $10,000 annually for service as a member of our scientific advisory board. We also reimburse each member of our scientific advisory board for all reasonable and necessary expenses in connection with the performance of his or her services. In addition, we grant each new member an option to purchase 15,000 shares of our common stock, of which one-third of the shares vest on each anniversary of the date of commencement of service on the scientific advisory board. Members of the scientific advisory board who are also our employees or directors receive no additional compensation for their service on the scientific advisory board.

Compensation Committee Interlocks and Inside Participation

None of the members of our compensation committee is or has been an officer or employee of our company. None of our executive officers currently serves, or in the past fiscal year has served, as a member of the board of directors or compensation committee (or other board of directors committee performing equivalent functions or, in the absence of any such committee, the entire board of directors) of any entity that has one or more executive officers serving on our board of directors or compensation committee.

Code of Business Conduct and Ethics

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal

accounting officer or controller, or persons performing similar functions. Following the completion of this offering, the code of business conduct and ethics will be available on our website at www.denalitherapeutics.com. We intend to disclose future amendments to such code, or any waivers of its requirements, applicable to any principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions or our directors on our website identified above. The inclusion of our website address in this prospectus does not include or incorporate by reference the information on our website into this prospectus.

Limitation of Liability and Indemnification

Our amended and restated certificate of incorporation and amended and restated bylaws, each to be effective upon the completion of this offering, will provide that we will indemnify our directors and officers, and may indemnify our employees and other agents, to the fullest extent permitted by Delaware law. Delaware law prohibits our amended and restated certificate of incorporation from limiting the liability of our directors for the following:

- any breach of the director's duty of loyalty to us or to our stockholders;
- acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- unlawful payment of dividends or unlawful stock repurchases or redemptions; and
- any transaction from which the director derived an improper personal benefit.

If Delaware law is amended to authorize corporate action further eliminating or limiting the personal liability of a director, then the liability of our directors will be eliminated or limited to the fullest extent permitted by Delaware law, as so amended. Our amended and restated certificate of incorporation does not eliminate a director's duty of care and, in appropriate circumstances, equitable remedies, such as injunctive or other forms of non-monetary relief, remain available under Delaware law. This provision also does not affect a director's responsibilities under any other laws, such as the federal securities laws or other state or federal laws. Under our amended and restated bylaws, we will also be empowered to purchase insurance on behalf of any person whom we are required or permitted to indemnify.

In addition to the indemnification required in our amended and restated certificate of incorporation and amended and restated bylaws, we have entered into an indemnification agreement with each member of our board of directors and each of our officers. These agreements provide for the indemnification of our directors and officers for certain expenses and liabilities incurred in connection with any action, suit, proceeding or alternative dispute resolution mechanism, or hearing, inquiry or investigation that may lead to the foregoing, to which they are a party or other participant, or are threatened to be made a party or other participant, by reason of the fact that they are or were a director, officer, employee, agent or fiduciary of our company, by reason of any action or inaction by them while serving as an officer, director, agent or fiduciary, or by reason of the fact that they were serving at our request as a director, officer, employee, agent or fiduciary of another entity. In the case of an action or proceeding by or in the right of our company or any of our subsidiaries, no indemnification will be provided for any claim where a court determines that the indemnified party is prohibited from receiving indemnification. We believe that these charter and bylaw provisions and indemnification agreements are necessary to attract and retain qualified persons as directors and officers.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against directors for breach of their fiduciary duties. They may also reduce the likelihood of derivative

litigation against directors and officers, even though an action, if successful, might benefit us and our stockholders. Moreover, a stockholder's investment may be harmed to the extent we pay the costs of settlement and damage awards against directors and officers pursuant to these indemnification provisions. Insofar as indemnification for liabilities arising under the Securities Act may be permitted to our directors, officers and controlling persons pursuant to the foregoing provisions, or otherwise, we have been advised that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act, and is, therefore, unenforceable. There is no pending litigation or proceeding naming any of our directors or officers as to which indemnification is being sought, nor are we aware of any pending or threatened litigation that may result in claims for indemnification by any director or officer.

EXECUTIVE COMPENSATION

Our named executive officers for 2016, which consist of our principal executive officer and the next three most highly compensated executive officers, are:

- Ryan J. Watts, Ph.D., our President and Chief Executive Officer;
- Alexander O. Schuth, M.D., our Chief Operating Officer and Secretary;
- Steve E. Krognes, our Chief Financial Officer and Treasurer; and
- Carole Ho, M.D., our Chief Medical Officer.

Summary Compensation Table

The following table sets forth information regarding the compensation of our named executive officers for the year ended December 31, 2016.

Name and Principal Position	Year	Salary ($)	Bonus ($)	Option Awards ($)(1)	Total ($)
Ryan J. Watts, Ph.D. *President and Chief Executive Officer*	2016	$450,000	$157,500(2)	$ —	$ 607,500
Alexander O. Schuth, M.D. *Chief Operating Officer and Secretary*	2016	$350,000	$122,500(2)	$ —	$ 472,500
Steve E. Krognes *Chief Financial Officer and Treasurer*	2016	$425,000	$398,750(3)	$ —	$ 823,750
Carole Ho, M.D. *Chief Medical Officer*	2016	$395,000	$138,250(2)	$495,600	$1,028,850

(1) The amounts disclosed represent the aggregate grant date fair value of the award as calculated in accordance with ASC 718. The assumptions used in calculating the grant date fair value of the award disclosed in this column are set forth in the notes to our audited consolidated financial statements included elsewhere in this prospectus. These amounts do not correspond to the actual value that may be recognized by the named executive officers upon vesting of the applicable awards.

(2) The amount reported represents a bonus based upon the achievement of company objectives for the year ended December 31, 2016, which was paid in January 2017.

(3) The amount reported represents (i) the portion of the sign-on bonus from 2015 of $250,000, which was earned in October 2016 pursuant to the terms of Mr. Krognes' employment agreement and (ii) a bonus of $148,750 based upon the achievement of company objectives for the year ended December 31, 2016, which was paid in January 2017. Had Mr. Krognes' employment been terminated by us for cause or by Mr. Krognes other than for good reason, in each case before October 1, 2016, he would have been required to repay the signing bonuses paid to him, including the $250,000 that was paid to him upon the commencement of his employment with us on October 1, 2015.

Outstanding Equity Awards at Fiscal Year-End

The following table sets forth information concerning outstanding equity awards held by each of our named executive officers as of December 31, 2016:

		Option Awards					Stock Awards	
Name	Grant Date [1]	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Equity incentive awards: number of securities underlying unexercised unearned options (#)	Option Exercise Price ($) [2]	Option Expiration Date	Number of Shares of Stock That Have Not Vested (#)	Market Value of Shares of Stock That Have Not Vested ($) [3]
Ryan J. Watts, Ph.D.	03/13/2015	—	—	—	—	—	1,333,008[4]	7,038,282
	08/21/2015	—	—	1,245,617[5]	0.68	8/20/2025	—	—
	08/21/2015	—	—	—	—	—	185,088[4]	977,265
Alexander O. Schuth, M.D.	03/13/2015	—	—	—	—	—	457,996[6]	2,418,219
	08/21/2015	—	—	249,123[5]	0.68	8/20/2025	—	—
	08/21/2015	—	—	—	—	—	63,596[6]	335,787
Steve E. Krognes	11/20/2015	—	—	125,000[5]	0.68	11/19/2025	—	—
	11/20/2015	—	—	—	—	—	354,166[7]	1,869,996
Carole Ho, M.D.	08/21/2015	—	—	125,000[5]	0.68	8/20/2025	—	—
	08/21/2015	—	—	—	—	—	156,250[8]	825,000
	07/02/2016	—	125,000[9]	—	5.28	7/01/2026	—	—

(1) Each of the outstanding options to purchase shares of our common stock was granted pursuant to our 2015 Plan.

(2) This column represents the fair market value of a share of our common stock on the date of grant, as determined by our board of directors or its authorized committee.

(3) Because our common stock was not traded on a public market on December 31, 2016, the market value has been calculated based on an estimated per-share common stock value of $5.28 per share as of December 31, 2016.

(4) One-fourth of the total number of shares subject to each restricted stock grant vested on February 23, 2016, and one thirty-sixth of the remaining shares subject to each restricted stock grant is scheduled to vest monthly thereafter, subject to continued service to us through each such vesting date. In the event of a change of control, the vesting of the shares subject to the restricted stock grants shall be accelerated in part so that the number of shares, if any, that would otherwise have first become vested in the period between the date of change of control and the date on which all but the unvested shares that would have vested in the final 12 months of the vesting period shall have first become vested shall immediately become vested. The remaining number of shares representing the last 12 months of vesting shall continue to vest in accordance with the original vesting schedule within the next 12 months set forth in the award agreement, provided, however, that each such award shall be immediately vested in full if on or within 12 months following the consummation of the change of control, Dr. Watts' employment with us is terminated without cause by us or by Dr. Watts for good reason, subject to Dr. Watts' execution of a release of claims in our favor and the terms and conditions of the Severance Plan, as described below.

(5) The shares subject to the option will vest upon certain performance goals being met as follows, in each case subject to the named executive officer's continued service to us: (a) 50% of the shares subject to the option vest upon (i) the date on which the reported closing price of our common stock on NASDAQ or the New York Stock Exchange (or other national securities exchange) has, for 90 consecutive trading days, equaled or exceeded $40.00 per share (subject to adjustments for any stock split, reverse stock split or certain other changes in capitalization), with the first day of the 90-day measurement period no earlier than the date that is 180 days after our initial public offering for our common stock, or (ii) the date on which we close a change of control (as defined in the applicable award agreement) transaction in which the stockholders receive consideration equal to no less than $40.00 per share (subject to adjustments for any stock split, reverse stock split or certain other changes in capitalization) in exchange for the sale of their capital stock and (b) 50% of the shares subject to the option vest upon (i) the date on which the reported closing price of our common

stock on NASDAQ or the New York Stock Exchange (or other national securities exchange) has, for 90 consecutive trading days, equaled or exceeded $80.00 per share (subject to adjustments for any stock split, reverse stock split or certain other changes in capitalization), with the first day of the 90-day measurement period no earlier than the date that is 180 days after our initial public offering for our common stock, or (ii) the date on which we close a change of control transaction in which the stockholders receive consideration equal to no less than $80.00 per share (subject to adjustments for any stock split, reverse stock split or certain other changes in capitalization) in exchange for the sale of their capital stock.

(6) The shares subject to each restricted stock grant will vest as follows, in each case subject to Dr. Schuth's continued service to us: (a) 54.54% of the total number of shares subject to each restricted stock grant, or Tranche 1, vested as to one-fourth of the original number of Tranche 1 shares on March 17, 2016, and then as to 1/36 of the remaining number of shares of Tranche 1 each month thereafter and (b) 45.46% of the total number of shares subject to each restricted stock grant, or Tranche 2, shall vest on March 17, 2018. In the event of a change of control, the vesting of the shares subject to each restricted stock grant shall be accelerated in part so that the number of shares, if any, that would otherwise have first become vested in the period between the date of change of control and the date on which all but the unvested shares that would have vested in the final 12 months of the vesting period shall have first become vested shall immediately become vested. The remaining number of shares representing the last 12 months of vesting shall continue to vest in accordance with the original vesting schedule within the next 12 months set forth in the award agreement, provided, however, that each such award shall be immediately vested in full if on or within 12 months following the consummation of the change of control, Dr. Schuth's employment with us is terminated without cause by us or by Dr. Schuth for good reason, subject to Dr. Schuth's execution of a release of claims in our favor and the terms and conditions of the Severance Plan, as described below.

(7) The shares were acquired pursuant to an early exercise provision and remain subject to our repurchase right in accordance with the vesting schedule of the options. One-fourth of the total number of shares subject to the option vested on October 1, 2016, and one thirty-sixth of the remaining shares vest monthly thereafter, subject to continued service to us through each such vesting date. In the event of a change of control, the vesting of these shares shall be accelerated in part so that the number of shares, if any, that would otherwise have first become vested in the period between the date of change of control and the date on which all but the unvested shares that would have vested in the final 12 months of the vesting period shall have first become vested shall immediately become vested. The remaining number of shares representing the last 12 months of vesting shall continue to vest in accordance with the original vesting schedule within the next 12 months set forth in the equity award agreement, provided however that the shares shall be immediately vested in full if on or within 12 months following the consummation of the change of control, Mr. Krognes' employment with us is terminated without cause by us or by Mr. Krognes for good reason, subject to Mr. Krognes' execution of a release of claims in our favor and the terms and conditions of the Severance Plan, as described below.

(8) The shares were acquired pursuant to an early exercise provision and remain subject to our repurchase right in accordance with the vesting schedule of the options. One-fourth of the total number of shares subject to the option vested on June 19, 2016, and one thirty-sixth of the remaining shares vest monthly thereafter, subject to continued service to us through each such vesting date. In the event of a change of control, the vesting of these shares shall be accelerated in part so that the number of shares, if any, that would otherwise have first become vested in the period between the date of change of control and the date on which all but the unvested shares that would have vested in the final 12 months of the vesting period shall have first become vested shall immediately become vested and exercisable. The remaining number of shares representing the last 12 months of vesting shall continue to vest in accordance with the original vesting schedule within the next 12 months set forth in the equity award agreement, provided however that the shares shall be immediately vested in full if on or within 12 months following the consummation of the change of control, Dr. Ho's employment with us is terminated without cause by us or by Dr. Ho for good reason, subject to Dr. Ho's execution of a release of claims in our favor and the terms and conditions of the Severance Plan, as described below.

(9) One-fourth of the total number of shares subject to the option vested on July 2, 2017, and one thirty-sixth of the remaining shares vest monthly thereafter, subject to continued service to us through each such vesting date. In the event of a change of control, the vesting of these shares shall be accelerated in part so that the number of shares, if any, that would otherwise have first become vested in the period between the date of change of control and the date on which all but the unvested shares that would have vested in the final 12 months of the vesting period shall have first become vested shall immediately become vested and exercisable. The remaining number of shares representing the last 12 months of vesting shall continue to vest

in accordance with the original vesting schedule within the next 12 months set forth in the equity award agreement, provided however that the shares shall be immediately vested in full if on or within 12 months following the consummation of the change of control, Dr. Ho's employment with us is terminated without cause by us or by Dr. Ho for good reason, subject to Dr. Ho's execution of a release of claims in our favor and the terms and conditions of the Severance Plan, as described below.

Non-Equity Incentive Plan Compensation

Each of our named executive officers was awarded a discretionary annual cash bonus for 2016 based on attainment of corporate objectives for 2016. The 2016 target bonus amounts for each named executive officer (35% of base salary for each named executive officer), along with a target bonus pool equal to 100% of all employees' target bonuses, and the related 2016 corporate objectives, were recommended by the compensation committee of our board of directors to our board of directors in mid-2015 and approved by our board of directors in November 2015. The corporate objectives were comprised of key short-term and long-term goals of one or more facets of our business relating to research and development, hiring goals, finance, corporate development and operations. At the same time, our board of directors determined that if at least 70% of the corporate objectives were achieved by the end of the 2016 calendar year, the bonus pool would be funded at 100%.

In November 2016, the compensation committee of our board of directors reviewed the progress against the applicable 2016 corporate objectives, determined that 73% of the performance objectives had been met to such date and recommended that our board of directors fully fund the cash bonus pool at 100% of target levels. After taking into consideration these recommendations and our board of directors' own review, our board of directors approved the full 2016 bonus pool funding, and the payment of 100% of target bonuses to our named executive officers from such pool, subject to each such officer's continued employment through the bonus payment date. Each of our named executive officers received 100% of his or her target bonus amount in January 2017. Following the end of 2016, management assessed the full year achievement against the 2016 corporate goals, and determined that 76% of such goals had ultimately been achieved. The amounts in the Summary Compensation Table under the column "Non-Equity Incentive Plan Compensation" are based on the bonuses awarded under the above-described 2016 bonus program.

Employment Arrangements with Our Named Executive Officers

Ryan J. Watts, Ph.D.

On November 10, 2017, we entered into a confirmatory employment letter with Dr. Watts, our President and Chief Executive Officer. The confirmatory employment letter has no specific term and provides for at-will employment. Dr. Watts' current annual base salary is $504,250 and Dr. Watts is considered annually for a target bonus of 55% of his annual base salary, subject to the terms and conditions of a bonus plan approved by our board of directors. The confirmatory offer letter also provides that we may, in our discretion, grant additional bonus amounts to Dr. Watts.

Alexander O. Schuth, M.D.

On November 10, 2017, we entered into a confirmatory employment letter with Dr. Schuth, our Chief Operating Officer and Secretary. The confirmatory employment letter has no specific term and provides for at-will employment. Dr. Schuth's current annual base salary is $380,250 and Dr. Schuth is considered annually for a target bonus of 40% of his annual base salary, subject to the terms of the applicable bonus plan developed by our chief executive officer and approved by our board of directors. The confirmatory offer letter also provides that we may, in our discretion, grant additional bonus amounts to Dr. Schuth.

Steve E. Krognes

On November 10, 2017, we entered into a confirmatory employment letter with Mr. Krognes, our Chief Financial Officer and Treasurer. The confirmatory employment letter has no specific term and provides for at-will employment. Mr. Krognes' current annual base salary is $437,750 and Mr. Krognes is considered annually for a target bonus of 40% of his annual base salary, subject to the terms of the applicable bonus plan developed by our chief executive officer and approved by our board of directors.

In addition, Mr. Krognes was previously awarded a one-time signing bonus of $500,000. Had Mr. Krognes' employment been terminated by us for cause or by Mr. Krognes other than for good reason, in each case before October 1, 2016, he would have been required to repay the signing bonus paid to him. The confirmatory offer letter also provides that we may, in our discretion, grant additional bonus amounts to Dr. Krognes.

Carole Ho, M.D.

On November 10, 2017, we entered into a confirmatory employment letter with Dr. Ho, our Chief Medical Officer. The confirmatory employment letter has no specific term and provides for at-will employment. Dr. Ho's current annual base salary is $406,850 and Dr. Ho is considered annually for a target bonus of 40% of her annual base salary, subject to the terms of the applicable bonus plan developed by our chief executive officer and approved by our board of directors.

In addition, Dr. Ho was previously awarded a one-time signing bonus of $199,033. Had Dr. Ho's employment been terminated by us for cause or by Dr. Ho other than for good reason, in each case before June 25, 2016, she would have been required to repay the signing bonus paid to her. The confirmatory offer letter also provides that we may, in our discretion, grant additional bonus amounts to Dr. Ho.

Potential Payments upon Termination or Change of Control

Our board of directors approved the following change of control and severance benefits for our executive officers (Dr. Watts, Dr. Schuth, Mr. Krognes and Dr. Ho) and other key employees pursuant to our Key Executive Change in Control and Severance Plan, or the Severance Plan.

If we terminate an executive officer's employment other than for "cause," death or "disability" or such participant resigns for "good reason" during the period beginning on a "change in control" (as such terms are defined in the Severance Plan) and ending 12 months following a change in control (the "change in control period"), such executive officer will be eligible to receive the following severance benefits (less applicable tax withholdings):

- 100% (150% for Dr. Watts) of the executive officer's annual base salary as in effect immediately prior to the termination (or if the termination is due to a resignation for good reason based on a material reduction in base salary, then the executive officer's annual base salary in effect immediately prior to such reduction) paid over 12 months (18 months for Dr. Watts);
- A lump sum payment equal to 100% of the annual target bonus the executive officer would otherwise be eligible to receive for the fiscal year in which the termination occurs, assuming achievement of all target levels at 100%;
- A lump sum cash payment in an aggregate amount equal to 12 months (18 months for Dr. Watts) of the applicable monthly premium cost that the executive officer otherwise would be required to pay to continue qualifying health coverage under COBRA (provided that if the Company determines in its sole discretion that these payments cannot be provided without violating applicable law, these payments will not be made); and

- 100% of the executive officer's then-outstanding and unvested equity awards that are subject to vest solely on the executive officer's continued service through the scheduled vesting dates will become vested in full and, if applicable, exercisable.

If we terminate an executive officer's employment other than for cause, death or disability or such participant resigns for good reason outside of the change in control period, such executive officer will be eligible to receive the following severance benefits (less applicable tax withholdings):

- 75% (100% for Dr. Watts) of the executive officer's annual base salary as in effect immediately prior to the termination (or if the termination is due to a resignation for good reason based on a material reduction in base salary, then the executive officer's annual base salary in effect immediately prior to such reduction) paid over nine months (12 months for Dr. Watts);
- A lump sum payment equal to the annual target bonus the executive officer would otherwise be eligible to receive for the fiscal year in which the termination occurs, assuming achievement of all annual targets at 100%, prorated for the portion of the year during which the executive officer was employed; and
- A lump sum cash payment in an aggregate amount equal to nine months (12 months for Dr. Watts) of the applicable monthly premium cost that the executive officer otherwise would be required to pay to continue qualifying health coverage under COBRA (provided that if the Company determines in its sole discretion that these payments cannot be provided without violating applicable law, these payments will not be made).

To receive the severance benefits upon a qualifying termination, an executive officer must sign and not revoke a form of separation agreement and release of claims in a form reasonably satisfactory to us within the timeframe set forth in the Severance Plan and must continue to comply with the provisions of such release and the terms of any confidentiality, proprietary information and inventions agreement and any other written agreement or agreements between the executive officer and us under which the executive officer has a material duty or obligation to us.

In addition, in the event of a change in control, the vesting schedule of any then-outstanding and unvested equity awards that are subject to time-based vesting and were granted to an executive officer prior to the effective date of the Severance Plan, will be accelerated in part so that the number of shares, if any, subject to each such award that would otherwise have first become vested in the period between the date of the consummation of the change in control and the date on which all but the final 12 months of the vesting period will have first become vested will immediately become vested and exercisable, as applicable. The remaining shares subject to each such award will continue to be eligible to vest in accordance with the original vesting schedule within the next 12 months as set forth in the applicable award agreement, and may accelerate in connection with certain terminations of employment, as described above.

If any of the payments provided for under the Severance Plan or otherwise payable to an executive officer would constitute "parachute payments" within the meaning of Section 280G of the Code and would be subject to the related excise tax under Section 4999 of the Code, then the executive officer will be entitled to receive either full payment of benefits or such lesser amount which would result in no portion of the benefits being subject to the excise tax, whichever results in the greater amount of after-tax benefits to him or her. The Severance Plan does not require us to provide any tax gross-up payments to any executive officer.

Employee Benefit and Stock Plans

2017 Equity Incentive Plan

Our board of directors adopted, and our stockholders approved, our 2017 Plan. Our 2017 Plan will be effective on the business day immediately prior to the effective date of the registration statement of which this prospectus forms a part. Our 2017 Plan provides for the grant of incentive stock options, within the meaning of Section 422 of the Code, to our employees and any parent and subsidiary corporations' employees, and for the grant of nonstatutory stock options, restricted stock, restricted stock units, stock appreciation rights, performance units and performance shares to our employees, directors and consultants and our parent and subsidiary corporations' employees and consultants.

Authorized Shares. A total of 6,210,000 shares of our common stock has been reserved for issuance pursuant to our 2017 Plan. In addition, the shares reserved for issuance under our 2017 Plan also will include (a) those shares reserved but unissued under our 2015 Plan as of immediately prior to the termination of the 2015 Plan, and (b) shares subject to awards under our 2015 Plan that, on or after the termination of the 2015 Plan, expire or terminate and shares previously issued pursuant to our 2015 Plan, as applicable, that, on or after the termination of the 2015 Plan, are forfeited or repurchased by us (provided that the maximum number of shares that may be added to our 2017 Plan pursuant to (a) and (b) is 8,325,000 shares). The number of shares available for issuance under our 2017 Plan will also include an annual increase on the first day of each fiscal year beginning on January 1, 2019, equal to the least of:

- 10,000,000 shares;
- five percent (5%) of the outstanding shares of our common stock as of the last day of the immediately preceding fiscal year; or
- such other amount as our board of directors may determine.

If an award expires or becomes unexercisable without having been exercised in full, is surrendered pursuant to an exchange program, or, with respect to restricted stock, restricted stock units, performance units or performance shares, is forfeited to or repurchased due to failure to vest, the unpurchased shares (or for awards other than stock options or stock appreciation rights, the forfeited or repurchased shares) will become available for future grant or sale under the 2017 Plan. With respect to stock appreciation rights, only the net shares actually issued will cease to be available under the 2017 Plan and all remaining shares under stock appreciation rights will remain available for future grant or sale under the 2017 Plan. Shares that have actually been issued under the 2017 Plan under any award will not be returned to the 2017 Plan; provided, however, that if shares issued pursuant to awards of restricted stock, restricted stock units, performance shares or performance units are repurchased or forfeited, such shares will become available for future grant under the 2017 Plan. Shares used to pay the exercise price of an award or satisfy the tax withholding obligations related to an award will become available for future grant or sale under the 2017 Plan. To the extent an award is paid out in cash rather than shares, such cash payment will not result in a reduction in the number of shares available for issuance under the 2017 Plan.

Plan Administration. The compensation committee of our board of directors will administer our 2017 Plan. In the case of awards intended to qualify as ''performance-based compensation'' within the meaning of Section 162(m) of the Code, the committee will consist of two or more ''outside directors'' within the meaning of Section 162(m) of the Code. In addition, if we determine it is desirable to qualify transactions under our 2017 Plan as exempt under Rule 16b-3 of the Exchange Act, such transactions will be structured to satisfy the requirements for exemption under Rule 16b-3. Subject to the provisions of our 2017 Plan, the administrator has the power to administer our 2017 Plan and make all determinations deemed necessary or advisable for administering the 2017 Plan, including but not

limited to, the power to determine the fair market value of our common stock, select the service providers to whom awards may be granted, determine the number of shares covered by each award, approve forms of award agreements for use under the 2017 Plan, determine the terms and conditions of awards (including, but not limited to, the exercise price, the times or times at which the awards may be exercised, any vesting acceleration or waiver or forfeiture restrictions, and any restriction or limitation regarding any award or the shares relating thereto), construe and interpret the terms of our 2017 Plan and awards granted under it, to prescribe, amend and rescind rules relating to our 2017 Plan, including creating sub-plans, and to modify or amend each award, including but not limited to the discretionary authority to extend the post-termination exercisability period of awards (provided that no option or stock appreciation right will be extended past its original maximum term), and to allow a participant to defer the receipt of payment of cash or the delivery of shares that would otherwise be due to such participant under an award). The administrator also has the authority to allow participants the opportunity to transfer outstanding awards to a financial institution or other person or entity selected by the administrator and to institute an exchange program by which outstanding awards may be surrendered or cancelled in exchange for awards of the same type which may have a higher or lower exercise price and/or different terms, awards of a different type and/or cash, or by which the exercise price of an outstanding award is increased or reduced. The administrator's decisions, interpretations and other actions are final and binding on all participants.

Stock Options. Stock options may be granted under our 2017 Plan. The exercise price of options granted under our 2017 Plan must at least be equal to the fair market value of our common stock on the date of grant. The term of an option may not exceed ten years. With respect to any participant who owns more than 10% of the voting power of all classes of our outstanding stock, the term of an incentive stock option granted to such participant must not exceed five years and the exercise price must equal at least 110% of the fair market value on the grant date. The administrator will determine the methods of payment of the exercise price of an option, which may include cash, shares or other property acceptable to the administrator, as well as other types of consideration permitted by applicable law. After the termination of service of an employee, director or consultant, he or she may exercise his or her option for the period of time stated in his or her option agreement. In the absence of a specified time in an award agreement, if termination is due to death or disability, the option will remain exercisable for 12 months. In all other cases, in the absence of a specified time in an award agreement, the option will remain exercisable for three months following the termination of service. An option may not be exercised later than the expiration of its term. Subject to the provisions of our 2017 Plan, the administrator determines the other terms of options.

Stock Appreciation Rights. Stock appreciation rights may be granted under our 2017 Plan. Stock appreciation rights allow the recipient to receive the appreciation in the fair market value of our common stock between the exercise date and the date of grant. Stock appreciation rights may not have a term exceeding ten years. After the termination of service of an employee, director or consultant, he or she may exercise his or her stock appreciation right for the period of time stated in his or her stock appreciation rights agreement. In the absence of a specified time in an award agreement, if termination is due to death or disability, the stock appreciation rights will remain exercisable for 12 months. In all other cases, in the absence of a specified time in an award agreement, the stock appreciation rights will remain exercisable for three months following the termination of service. However, in no event may a stock appreciation right be exercised later than the expiration of its term. Subject to the provisions of our 2017 Plan, the administrator determines the other terms of stock appreciation rights, including when such rights become exercisable and whether to pay any increased appreciation in cash or with shares of our common stock, or a combination thereof, except that the per share exercise price for the shares to be issued pursuant to the exercise of a stock appreciation right will be no less than 100% of the fair market value per share on the date of grant.

Restricted Stock. Restricted stock may be granted under our 2017 Plan. Restricted stock awards are grants of shares of our common stock that vest in accordance with terms and conditions established by the administrator. The administrator will determine the number of shares of restricted stock granted to any employee, director or consultant and, subject to the provisions of our 2017 Plan, will determine the terms and conditions of such awards. The administrator may impose whatever conditions to vesting it determines to be appropriate (for example, the administrator may set restrictions based on the achievement of specific performance goals or continued service to us); provided, however, that the administrator, in its sole discretion, may accelerate the time at which any restrictions will lapse or be removed. Recipients of restricted stock awards generally will have voting and dividend rights with respect to such shares upon grant without regard to vesting, unless the administrator provides otherwise. Shares of restricted stock that do not vest are subject to our right of repurchase or forfeiture.

RSUs. RSUs may be granted under our 2017 Plan. RSUs are bookkeeping entries representing an amount equal to the fair market value of one share of our common stock. Subject to the provisions of our 2017 Plan, the administrator determines the terms and conditions of RSUs, including the vesting criteria and the form and timing of payment. The administrator may set vesting criteria based upon the achievement of company-wide, divisional, business unit or individual goals (including, but not limited to, continued employment or service), applicable federal or state securities laws or any other basis determined by the administrator in its discretion. The administrator, in its sole discretion, may pay earned restricted stock units in the form of cash, in shares or in some combination thereof. Notwithstanding the foregoing, the administrator, in its sole discretion, may accelerate the time at which any restrictions will lapse or be removed.

Performance Units and Performance Shares. Performance units and performance shares may be granted under our 2017 Plan. Performance units and performance shares are awards that will result in a payment to a participant only if performance goals established by the administrator are achieved or the awards otherwise vest. The administrator will establish performance objectives or other vesting criteria in its discretion, which, depending on the extent to which they are met, will determine the number and/or the value of performance units and performance shares to be paid out to participants. The administrator may set performance objectives based on the achievement of company-wide, divisional, business unit or individual goals (including, but not limited to, continued employment or service), applicable federal or state securities laws or any other basis determined by the administrator in its discretion. After the grant of a performance unit or performance share, the administrator, in its sole discretion, may reduce or waive any performance criteria or other vesting provisions for such performance units or performance shares. Performance units shall have an initial dollar value established by the administrator on or prior to the grant date. Performance shares shall have an initial value equal to the fair market value of our common stock on the grant date. The administrator, in its sole discretion, may pay earned performance units or performance shares in the form of cash, in shares or in some combination thereof.

Outside Directors. Our 2017 Plan provides that all outside (non-employee) directors will be eligible to receive all types of awards (except for incentive stock options) under our 2017 Plan. We have adopted a formal policy pursuant to which our outside directors will be eligible to receive equity awards under our 2017 Plan, and they may also receive discretionary awards not covered by the policy. In order to provide a maximum limit on the awards that can be made to our outside directors, our 2017 Plan provides that in any given fiscal year, an outside director will not be granted awards having a grant-date fair value greater than $1,000,000, but this limit is increased to $1,600,000 in connection with his or her initial service (in each case, excluding awards granted to him or her as a consultant or employee). The grant-date fair values will be determined according to GAAP. The maximum limits do not reflect the intended size of any potential grants or a commitment to make grants to our outside directors under our 2017 Plan in the future.

Non-Transferability of Awards. Unless the administrator provides otherwise, our 2017 Plan generally does not allow for the transfer of awards and only the recipient of an award may exercise an award during his or her lifetime. If the administrator makes an award transferrable, such award will contain such additional terms and conditions as the administrator deems appropriate.

Certain Adjustments. In the event of certain changes in our capitalization, to prevent diminution or enlargement of the benefits or potential benefits available under our 2017 Plan, the administrator will adjust the number and class of shares that may be delivered under our 2017 Plan and/or the number, class and price of shares covered by each outstanding award and the numerical share limits set forth in our 2017 Plan.

Dissolution or Liquidation. In the event of our proposed liquidation or dissolution, the administrator will notify participants as soon as practicable and all awards will terminate immediately prior to the consummation of such proposed transaction.

Merger or Change in Control. Our 2017 Plan provides that in the event of a merger or change in control, as defined under our 2017 Plan, each outstanding award will be treated as the administrator determines, without a participant's consent. The administrator is not required to treat all awards, all awards held by a participant or all awards of the same type, similarly.

In the event that a successor corporation or its parent or subsidiary does not assume or substitute an equivalent award for any outstanding award, then such award will fully vest, all restrictions on such award will lapse, all performance goals or other vesting criteria applicable to such award will be deemed achieved at 100% of target levels and such award will become fully exercisable, if applicable, for a specified period prior to the transaction, unless specifically provided for otherwise under the applicable award agreement or other written agreement with the participant. The award will then terminate upon the expiration of the specified period of time. If an option or stock appreciation right is not assumed or substituted, the administrator will notify the participant in writing or electronically that such option or stock appreciation right will be exercisable for a period of time determined by the administrator in its sole discretion and the option or stock appreciation right will terminate upon the expiration of such period.

If an outside director's awards are assumed or substituted for in a merger or change in control and the service of such outside director is terminated on or following a change in control, other than pursuant to a voluntary resignation, his or her options and stock appreciation rights, if any, will vest fully and become immediately exercisable, all restrictions on his or her restricted stock and restricted stock units will lapse and all performance goals or other vesting requirements for his or her performance shares and units will be deemed achieved at 100% of target levels and all other terms and conditions met.

Amendment; Termination. The administrator has the authority to amend, suspend or terminate our 2017 Plan provided such action does not impair the existing rights of any participant. Our 2017 Plan automatically will terminate in 2027, unless we terminate it sooner.

2017 Employee Stock Purchase Plan

Our board of directors adopted, and our stockholders approved, our 2017 Employee Stock Purchase Plan, or ESPP. Our ESPP will be effective on the business day immediately prior to the effective date of the registration statement of which this prospectus forms a part. We believe that allowing our employees to participate in our ESPP provides them with a further incentive towards ensuring our success and accomplishing our corporate goals.

Authorized Shares. A total of 1,000,000 shares of our common stock will be available for sale under our ESPP. The number of shares of our common stock that will be available for sale under our ESPP also includes an annual increase on the first day of each fiscal year beginning on January 1, 2019, equal to the least of:

- 2,000,000 shares;
- one percent (1%) of the outstanding shares of our common stock as of the last day of the immediately preceding fiscal year; or
- such other amount as the administrator may determine.

Plan Administration. The compensation committee of our board of directors will administer our ESPP, and have full but non-exclusive authority to interpret the terms of our ESPP and determine eligibility to participate, subject to the conditions of our ESPP, as described below. The administrator will have full and exclusive discretionary authority to construe, interpret and apply the terms of the ESPP, to delegate ministerial duties to any of our employees, to designate separate offerings under the ESPP, to designate our subsidiaries and affiliates as participating in the ESPP, to determine eligibility, to adjudicate all disputed claims filed under the ESPP and to establish procedures that it deems necessary or advisable for the administration of the ESPP, including, but not limited to, adopting such procedures, sub-plans and appendices to the enrollment agreement as are necessary or appropriate to permit participation in the ESPP by employees who are foreign nationals or employed outside the U.S. The administrator's findings, decisions and determinations are final and binding on all participants to the full extent permitted by law.

Eligibility. Generally, all of our employees will be eligible to participate if they are customarily employed by us, or any participating subsidiary, for at least 20 hours per week and more than five months in any calendar year. The administrator, in its discretion, may, prior to an enrollment date for all options granted on such enrollment date in an offering, determine that an employee who (i) has not completed at least two years of service (or a lesser period of time determined by the administrator) since his or her last hire date, (ii) customarily works not more than 20 hours per week (or a lesser period of time determined by the administrator), (iii) customarily works not more than five months per calendar year (or a lesser period of time determined by the administrator), (iv) is a highly compensated employee within the meaning of Section 414(q) of the Code or (v) is a highly compensated employee within the meaning of Section 414(q) of the Code with compensation above a certain level or is an officer or subject to disclosure requirements under Section 16(a) of the Exchange Act, is or is not eligible to participate in such offering period.

However, an employee may not be granted rights to purchase shares of our common stock under our ESPP if such employee:

- immediately after the grant would own capital stock possessing 5% or more of the total combined voting power or value of all classes of our capital stock; or
- hold rights to purchase shares of our common stock under all of our employee stock purchase plans that accrue at a rate that exceeds $25,000 worth of shares of our common stock for each calendar year.

Offering Periods. Our ESPP includes a component that allows us to make offerings intended to qualify under Section 423 of the Code and a component that allows us to make offerings not intended to qualify under Section 423 of the Code to designated companies, as described in our ESPP. Our ESPP provides for consecutive, overlapping 12-month offering periods. The offering periods are scheduled to start on the first trading day on or after May 31 and November 30 of each year, except for the first offering period, which will commence on the first trading day on or after the effective date of

the registration statement of which this prospectus forms a part and will end on the first trading day on or after November 30, 2018. Each offering period will include purchase periods, which will be the approximately six-month period commencing with one exercise date and ending with the next exercise date; provided, however, that the first exercise date under the ESPP will be the first trading day on or after May 31, 2018.

Contributions. Our ESPP permits participants to purchase shares of our common stock through contributions (in the form of payroll deductions or otherwise to the extent permitted by the administrator) of up to 15% of their eligible compensation. A participant may purchase a maximum of 2,000 shares of our common stock during a purchase period.

Exercise of Purchase Right. Amounts contributed and accumulated by the participant are used to purchase shares of our common stock at the end of each six-month purchase period. The purchase price of the shares will be 85% of the lower of the fair market value of our common stock on the first trading day of each offering period or on the exercise date. If the fair market value of our common stock on the exercise date is less than the fair market value on the first trading day of the offering period, participants will be withdrawn from the current offering period following their purchase of shares of our common stock on the purchase date and will be automatically re-enrolled in a new offering period. Participants may end their participation at any time during an offering period and will be paid their accrued contributions that have not yet been used to purchase shares of our common stock. Participation ends automatically upon termination of employment with us.

Non-Transferability. A participant may not transfer rights granted under our ESPP. If our compensation committee permits the transfer of rights, it may only be done by will, the laws of descent and distribution or as otherwise provided under our ESPP.

Merger or Change in Control. Our ESPP provides that in the event of a merger or change in control, as defined under our ESPP, a successor corporation may assume or substitute each outstanding purchase right. If the successor corporation refuses to assume or substitute for the outstanding purchase right, the offering period then in progress will be shortened, and a new exercise date will be set that will be before the date of the proposed merger or change in control. The administrator will notify each participant that the exercise date has been changed and that the participant's option will be exercised automatically on the new exercise date unless prior to such date the participant has withdrawn from the offering period.

Amendment; Termination. The administrator has the authority to amend, suspend or terminate our ESPP, except that, subject to certain exceptions described in our ESPP, no such action may adversely affect any outstanding rights to purchase shares of our common stock under our ESPP. Our ESPP automatically will terminate in 2037, unless we terminate it sooner.

2015 Stock Incentive Plan

On April 21, 2015, our board of directors adopted and our stockholders approved our 2015 Plan. The 2015 Plan has been amended from time to time to increase the aggregate number of shares of our common stock reserved for issuance under the 2015 Plan, and was most recently amended on November 11, 2016, which amendment was approved by our stockholders on December 12, 2016. The 2015 Plan permits the grant of incentive stock options, within the meaning of Section 422 of the Code, to our employees and the employees of any parent and subsidiary corporation or other entities the employees of which are eligible to receive incentive stock options under the Code, and for the grant of nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock units and other stock-based awards to our employees, officers, directors, consultants and advisors or any parent or subsidiary of ours. It is expected that as of one business day prior to the effectiveness of the

registration statement of the registration statement of which this prospectus forms a part, the 2015 Plan will be terminated and we will not grant any additional awards under the 2015 Plan thereafter. However, the 2015 Plan will continue to govern the terms and conditions of the outstanding awards previously granted thereunder.

Authorized Shares. The maximum aggregate number of shares issuable under the 2015 Plan was 8,325,000 shares of our common stock. As of September 30, 2017, options to purchase 6,179,687 shares of our common stock were outstanding under the 2015 Plan, 505,731 shares of restricted stock were outstanding under the 2015 Plan, no shares subject to stock appreciation rights were outstanding under the 2015 Plan, no restricted stock units were outstanding under the 2015 Plan and no other stock-based awards were outstanding under the 2015 Plan.

Plan Administration. Our board of directors or a committee or subcommittee delegated by our board of directors administers the 2015 Plan. Subject to the provisions of the 2015 Plan, the administrator has the authority to grant awards and to adopt, amend and repeal such administrative rules, guidelines and practices relating to the 2015 Plan as it deems advisable, including to establish one or more sub-plans for purposes of satisfying applicable securities, tax or other laws of various jurisdictions. The administrator may amend or terminate any outstanding award, including substituting an award for another award of the same or a different type, changing the date of exercise or realization and converting an incentive stock option into a nonstatutory stock option, although the affected participant's consent will be required unless the administrator determines that the action does not materially adversely affect the participant's rights under the 2015 Plan, or the change is permitted under the adjustment, merger or Reorganization Event provisions of the 2015 Plan. The administrator may also amend any outstanding award granted under the 2015 Plan to provide an exercise price per share that is lower than the then-current exercise price per share of the outstanding award, and may cancel any outstanding award (whether or not granted under the 2015 Plan) and grant new, substitute awards under the 2015 Plan covering the same or a different number of shares and having an exercise price per share that is lower than the then-current exercise price per share of the cancelled award. The administrator may correct any defect, supply any omission or reconcile any inconsistency in the 2015 Plan or award in the manner and to the extent it deems expedient to carry the 2015 Plan into effect and is the sole and final judge of such expediency. All decisions by the administrator are made in the administrator's sole discretion and are final and binding on all persons having or claiming any interest in the 2015 Plan or in any award.

Stock Options. Stock options may be granted under our 2015 Plan. The exercise price of options granted under our 2015 Plan must at least be equal to 100% of the fair market value of our common stock on the date of grant. The term of a stock option may not exceed 10 years. The administrator will determine the methods of payment of the exercise price of an option, which may include cash or check, owned shares, a broker-assisted cashless exercise, "net exercise," a promissory note, as well as other types of consideration permitted by applicable law.

If a participant's service terminates other than for cause or the participant's death or disability, the participant may exercise his or her option within at least 30 days of termination or such longer period as reflected in the individual award agreement. If a participant's service terminates due to the participant's death or disability, the participant may exercise his or her option within at least six months of termination or such longer period as reflected in the individual award agreement. However, in no event may an option be exercised later than the expiration of its term. Subject to the provisions of the 2015 Plan, the administrator determines the other terms of options.

Stock Appreciation Rights. Stock appreciation rights may be granted under our 2015 Plan. Stock appreciation rights allow the recipient to receive the appreciation in the fair market value of our common stock between the exercise date and the date of grant. Stock appreciation rights may not

have a term exceeding 10 years. After the termination of service of an employee, director or consultant, he or she may exercise his or her stock appreciation right for the period of time stated in his or her stock appreciation right agreement. However, in no event may a stock appreciation right be exercised later than the expiration of its term. Subject to the provisions of our 2015 Plan, the administrator determines the other terms of stock appreciation rights, including when such rights become exercisable and whether to pay any increased appreciation in cash or with shares of our common stock, or a combination thereof, except that the per share measurement price for the shares to be issued pursuant to the exercise of a stock appreciation right will be no less than 100% of the fair market value per share on the date of grant.

Restricted Stock. Restricted stock may be granted under our 2015 Plan. Restricted stock awards are grants of shares of our common stock that vest in accordance with terms and conditions established by the administrator. The administrator will determine the number of shares of restricted stock granted to any employee, director or consultant and, subject to the provisions of our 2015 Plan, will determine the terms and conditions of such awards. The administrator may impose whatever conditions for lapse of the restriction on the shares it determines to be appropriate. Unless otherwise provided in the applicable award agreement, any dividends declared and paid by us with respect to shares of restricted stock will be paid to the participant only if and when such shares become free from the restrictions on transferability and forfeitability that apply to such shares. Shares of restricted stock as to which the restrictions have not lapsed are subject to our right of repurchase or forfeiture.

Restricted Stock Units. Restricted stock units may be granted under our 2015 Plan. Restricted stock units are bookkeeping entries representing an amount equal to the fair market value of one share of our common stock. Subject to the provisions of our 2015 Plan, the administrator will determine the terms and conditions of restricted stock units, including the vesting criteria and the form and timing of payment. The administrator, in its sole discretion, may pay earned restricted stock units in the form of cash, in shares or in some combination thereof. Participants who receive restricted stock units have no voting rights with respect to the restricted stock units. The award agreement for restricted stock units may provide participants with the right to receive an amount equal to any dividends or other distributions declared and paid on an equal number of outstanding shares of our common stock, which may be settled in cash and/or shares, and may be subject to the same restrictions on transfer and forfeitability as the restricted stock units to which they relate, as may be provided in the award agreement.

Other Stock-Based Awards. Other stock based awards may be granted under our 2015 Plan. Other stock-based awards are also available as a form of payment in the settlement of other awards granted under our 2015 Plan or as payment in lieu of compensation to which a participant is otherwise entitled. Other stock-based awards may be paid in shares of our common stock or cash, as determined by the administrator. Subject to the provisions of the 2015 Plan, the administrator determines the terms and conditions of other stock-based awards granted under the 2015 Plan.

Non-Transferability of Awards. Our 2015 Plan generally does not allow for the transfer of awards and only the recipient of an award may exercise an award during his or her lifetime. However, awards that are not subject to Section 409A of the Code may be transferred to family members through gifts or (other than incentive stock options) domestic relations orders, or to an executor or guardian upon the death of a participant.

Certain Adjustments. In the event of certain changes in our capitalization, the administrator will adjust the number and class of shares that may be delivered under the 2015 Plan and/or the number, class, price, repurchase price and other per-share-related provisions, as applicable, of shares covered by, each outstanding award.

Merger or Reorganization Event. The 2015 Plan provides that in the event of a merger or other Reorganization Event, as defined under the 2015 Plan, each outstanding award, except restricted stock, will be treated as the administrator determines, including, without limitation, that awards shall be assumed or substituted, that, upon written notice to a participant; that awards will terminate immediately prior to the consummation of the transaction; that awards will become fully exercisable or restrictions applicable to the award will lapse in whole or in part upon the transaction; or, upon a Reorganization Event under which the holders of shares of common stock will receive a cash payment for each share surrendered in the Reorganization Event, that awards will be terminated in exchange for a cash payment equal to the number of shares subject to the award multiplied by the acquisition price minus the exercise, measurement, or purchase price of the award. In addition, in the event of a Reorganization Event that is a liquidation or dissolution, the administrator may provide that awards will be converted into the right to receive liquidation proceeds (if applicable, net of the exercise, measurement, or purchase price thereof and applicable tax withholdings). Certain additional restrictions apply to restricted stock units to which Section 409A of the Code apply. On a Reorganization Event, our repurchase rights with respect to restricted stock will inure to the benefit of the successor and shall, unless the administrator determines otherwise, apply to the property into which the shares are converted. In the event of our proposed liquidation or dissolution, restrictions on restricted stock then outstanding will be automatically deemed satisfied.

Amendment, Termination. The administrator has the authority to amend the 2015 Plan, provided that if at any time the approval of our stockholders is required as to any modification or amendment under Section 422 of the Code or any successor provision with respect to incentive stock options, our board of directors may not effect such modification or amendment without such approval. As noted above our 2015 Plan will terminate in connection with our adoption of our 2017 Plan and no further awards will be granted thereunder. All outstanding awards will continue to be governed by their existing terms.

Executive Incentive Compensation Plan

In November 2017, our board of directors adopted our Executive Incentive Compensation Plan, or our Incentive Compensation Plan. Our Incentive Compensation Plan allows our compensation committee to provide incentive awards, generally payable in cash, to employees selected by our compensation committee, including our named executive officers, based upon performance goals established by our compensation committee.

Under our Incentive Compensation Plan, our compensation committee determines the performance goals applicable to any award, which goals may include, without limitation, goals related to research and development, regulatory milestones or regulatory-related goals, gross margin, financial milestones, new product or business development, operation margin, product release timelines or other product release milestones, publications, cash flow, procurement, savings, internal structure, leadership development, project, function or portfolio-specific milestones, license or research collaboration agreements, capital raising, initial public offering preparations, patentability and individual objectives such as peer reviews or other subjective or objective criteria. The performance goals may differ from participant to participant and from award to award.

Our compensation committee will administer our Incentive Compensation Plan. The administrator of our Incentive Compensation Plan may, in its sole discretion and at any time, increase, reduce or eliminate a participant's actual award, and/or increase, reduce or eliminate the amount allocated to the bonus pool for a particular performance period. The actual award may be below, at or above a participant's target award, in the discretion of the administrator. The administrator may determine the amount of any reduction on the basis of such factors as it deems relevant, and it is not required to establish any allocation or weighting with respect to the factors it considers.

Actual awards will be paid in cash (or its equivalent) only after they are earned, and, unless otherwise determined by the administrator, a participant must be employed by us through the date the actual award is paid. The compensation committee reserves the right to settle an actual award with a grant of an equity award under our then-current equity compensation plan, which equity award may have such terms and conditions, including vesting, as the compensation committee determines. Payment of awards occurs as soon as administratively practicable after they are earned, but no later than the dates set forth in our Incentive Compensation Plan.

Our board of directors and our compensation committee will have the authority to amend, alter, suspend or terminate our Incentive Compensation Plan, provided such action does not impair the existing rights of any participant with respect to any earned awards.

401(k) Plan

We maintain a 401(k) retirement savings plan for the benefit of our employees, including our named executive officers, who satisfy certain eligibility requirements. Under the 401(k) plan, eligible employees may elect to defer a portion of their compensation, within the limits prescribed by the Code, on a pre-tax or after-tax (Roth) basis through contributions to the 401(k) plan. The 401(k) plan authorizes employer safe harbor contributions. The 401(k) plan is intended to qualify under Sections 401(a) and 501(a) of the Code. As a tax-qualified retirement plan, pre-tax contributions to the 401(k) plan and earnings on those pre-tax contributions are not taxable to the employees until distributed from the 401(k) plan, and earnings on Roth contributions are not taxable when distributed from the 401(k) plan.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

In addition to the compensation arrangements, including employment, termination of employment and change in control arrangements, with our directors and executive officers, including those discussed in the sections titled “Management” and “Executive Compensation,” and the registration rights described in the section titled “Description of Capital Stock—Registration Rights,” the following is a description of each transaction since January 1, 2014 and each currently proposed transaction in which:

- we have been or are to be a participant;
- the amount involved exceeded or exceeds $120,000; and
- any of our directors, executive officers or holders of more than 5% of our outstanding capital stock, or any immediate family member of, or person sharing the household with, any of these individuals or entities, had or will have a direct or indirect material interest.

Sales of Securities

Common stock

From March 2015 through August 2015, we sold an aggregate of 2,815,787 shares of our common stock at a purchase price of $0.04 per share, for an aggregate purchase price of $0.1 million, to six accredited investors and we issued an aggregate of 3,339,043 shares of our common stock at $0.04 to $0.68 per share, with an aggregate fair market value of $0.4 million, to four of our directors, each an accredited investor, in exchange for services to us. The following table summarizes purchases of our common stock by related persons:

Stockholder	Affiliated Director(s) or Officer(s)	Shares of Common Stock	Total Purchase Price
5% Stockholders:			
Entities associated with AKDL, L.P.(1)		312,500	$ 12,500
ARCH Venture Fund VIII, L.P.	Robert Nelsen	312,500	$ 12,500
Flagship Ventures Fund V, L.P.	Douglas Cole, M.D.	312,500	$ 12,500
Entities associated with F-Prime Capital Partners Healthcare Fund IV L.P.(2)	Stephen Knight, M.D.; Stacie Weninger, Ph.D(3)	1,812,499	$ 72,500
Directors and Executive Officers:			
Marc Tessier-Lavigne, Ph.D.		3,114,043	$ 367,550
Vicki Sato, Ph.D.		75,000	$ 3,000
Jay Flatley		75,000	$ 3,000
David Schenkein, M.D.		75,000	$ 3,000

(1) Entities associated with AKDL, L.P. holding our securities whose shares are aggregated for purposes of reporting share ownership information are AKDL, L.P. and Neuro Line Partners, L.P.

(2) Entities associated with F-Prime Capital Partners Healthcare Fund IV L.P. holding our securities whose shares are aggregated for purposes of reporting share ownership information are Impresa Fund III Limited Partnership, F-Prime Capital Partners Healthcare Fund IV L.P. (f/k/a Beacon Bioventures Fund IV Limited Partnership), F-Prime Capital Partners Healthcare Advisors Fund IV LP and F-Prime Capital (f/k/a Fidelity Biosciences Corp.).

(3) Each of Drs. Knight and Weninger resigned as members of our board of directors on August 11, 2017.

Series A-1 Convertible Preferred Stock

In May 2015, we issued and sold an aggregate of 9,777,055 shares of our Series A-1 convertible preferred stock at a purchase price of $4.00 per share, for aggregate proceeds of $39.1 million, to a total of 30 accredited investors.

In July 2015, we issued and sold an aggregate of 2,420,825 shares of our Series A-1 convertible preferred stock at a purchase price of $4.00 per share, for aggregate proceeds of $9.7 million, to a total of 11 accredited investors.

In January 2016, we issued and sold an aggregate of 11,749,997 shares of our Series A-1 convertible preferred stock at a purchase price of $4.00 per share, for aggregate proceeds of $47.0 million, to a total of nine accredited investors.

In June 2016, we issued and sold an aggregate of 22,166,546 shares of our Series A-1 convertible preferred stock at a purchase price of $4.00 per share, for aggregate proceeds of $88.7 million, to a total of eight accredited investors. The following table summarizes purchases of our Series A-1 convertible preferred stock by related persons:

Stockholder	Affiliated Director(s) or Officer(s)	Shares of Series A-1 Convertible Preferred Stock	Total Purchase Price
5% Stockholders:			
Entities associated with AKDL, L.P.(1)		15,243,598	$ 60,974,400
ARCH Venture Fund VIII, L.P.	Robert Nelsen	10,068,749	$ 40,275,000
Flagship Ventures Fund V, L.P.	Douglas Cole, M.D.	8,324,999	$ 33,300,000
Entities associated with F-Prime Capital Partners Healthcare Fund IV L.P.(2)	Stephen Knight, M.D.; Stacie Weninger, Ph.D.(7)	4,468,003	$ 17,872,000
Entities associated with FIL Limited(3)		1,606,995	$ 6,428,000
Executive Officers and Directors:			
Steve E. Krognes(4)		500,000	$ 2,000,000
Vicki Sato, Ph.D.		62,500	$ 250,000
Jay Flatley(5)		250,000	$ 1,000,000
David Schenkein, M.D.(6)		250,000	$ 1,000,000
Marc Tessier-Lavigne, Ph.D.		25,000	$ 100,000

(1) Entities associated with AKDL, L.P. holding our securities whose shares are aggregated for purposes of reporting share ownership information are AKDL, L.P. and Neuro Line Partners, L.P.

(2) Entities associated with F-Prime Capital Partners Healthcare Fund IV L.P. holding our securities whose shares are aggregated for purposes of reporting share ownership information are Impresa Fund III Limited Partnership, F-Prime Capital Partners Healthcare Fund IV L.P. (f/k/a Beacon Bioventures Fund IV Limited Partnership), F-Prime Capital Partners Healthcare Advisors Fund IV LP and F-Prime Capital (f/k/a Fidelity Biosciences Corp.).

(3) Entities associated with FIL Limited holding our securities whose shares are aggregated for purposes of reporting share ownership information are FIL Limited, Asia Ventures III L.P., Japan Ventures I L.P., FIL Capital Investments (Mauritius) II Limited, Asia Partners III LP, Japan Partners I LP and India Partners II LP.

(4) Consists of 500,000 shares of Series A-1 convertible preferred stock held of record by The Steve Edward Krognes Revocable Trust, for which Mr. Krognes serves as trustee.

(5) Consists of 250,000 shares of Series A-1 convertible preferred stock held by The Flatley Family Trust, for which Mr. Flatley serves as trustee.

(6) Consists of (a) 116,011 shares of Series A-1 convertible preferred stock held by the David P. Schenkein 2015 Denali Qualified Annuity Trust, for which Dr. Schenkein serves as trustee,

(b) 8,988 shares of Series A-1 convertible preferred stock held by the David P. Schenkein 2004 Revocable Trust, for which Dr. Schenkein serves as trustee, (c) 116,011 shares of Series A-1 convertible preferred stock held by the Amy P. Schenkein 2015 Denali Qualified Annuity Trust and (d) 8,988 shares of Series A-1 convertible preferred stock held by the Amy P. Schenkein 2004 Revocable Trust. Dr. Schenkein shares voting and dispositive power over the shares held by the Amy P. Schenkein 2015 Denali Qualified Annuity Trust and the Amy P. Schenkein 2004 Revocable Trust.

(7) Each of Drs. Knight and Weninger resigned as members of our board of directors on August 11, 2017.

Series A-2 Convertible Preferred Stock

In June 2016, we issued and sold an aggregate of 4,361,527 shares of our Series A-2 convertible preferred stock at a purchase price of $8.00 per share, for aggregate proceeds of $34.9 million, to a total of 15 accredited investors. The following table summarizes purchases of our Series A-2 convertible preferred stock by related persons:

Stockholder	Affiliated Director(s) or Officer(s)	Shares of Series A-2 Convertible Preferred Stock	Total Purchase Price
5% Stockholders:			
Entities associated with AKDL, L.P.(1)		2,628,200	$ 21,025,600
ARCH Venture Fund VIII, L.P.	Robert Nelsen	375,000	$ 3,000,000
Flagship Ventures Fund V, L.P.	Douglas Cole, M.D.	125,000	$ 1,000,000
Entities associated with F-Prime Capital Partners Healthcare Fund IV L.P.(2)	Stephen Knight, M.D.; Stacie Weninger, Ph.D.(4)	83,123	$ 664,990
Entities associated with FIL Limited(3)		41,876	$ 335,010

(1) Entities associated with AKDL, L.P. holding our securities whose shares are aggregated for purposes of reporting share ownership information are AKDL, L.P. and Neuro Line Partners, L.P.

(2) Entities associated with F-Prime Capital Partners Healthcare Fund IV L.P. holding our securities whose shares are aggregated for purposes of reporting share ownership information are Impresa Fund III Limited Partnership, F-Prime Capital Partners Healthcare Fund IV L.P. (f/k/a Beacon Bioventures Fund IV Limited Partnership), F-Prime Capital Partners Healthcare Advisors Fund IV LP and F-Prime Capital (f/k/a Fidelity Biosciences Corp.).

(3) Entities associated with FIL Limited holding our securities whose shares are aggregated for purposes of reporting share ownership information are FIL Limited, Asia Ventures III L.P., Japan Ventures I L.P., FIL Capital Investments (Mauritius) II Limited, Asia Partners III LP, Japan Partners I LP and India Partners II LP.

(4) Each of Drs. Knight and Weninger resigned as members of our board of directors on August 11, 2017.

Series B-1 Convertible Preferred Stock

In June 2016, we issued and sold an aggregate of 7,646,241 shares of our Series B-1 convertible preferred stock at a purchase price of $16.00 per share, for aggregate proceeds of $122.3 million, to a total of 17 accredited investors.

In August 2016, we issued and sold an aggregate of 478,124 shares of our Series B-1 convertible preferred stock at a purchase price of $16.00 per share, for aggregate proceeds of $7.7 million, to a total of 10 accredited investors. The following table summarizes purchases of our Series B-1 convertible preferred stock by related persons:

Stockholder	Affiliated Director(s) or Officer(s)	Shares of Series B-1 Convertible Preferred Stock	Total Purchase Price
5% Stockholders:			
Entities associated with AKDL, L.P.(1)		2,115,000	$33,840,000
ARCH Venture Fund VIII, L.P.	Robert Nelsen	312,500	$ 5,000,000
Flagship Ventures Fund V, L.P.	Douglas Cole, M.D.	156,250	$ 2,500,000
Entities associated with F-Prime Capital Partners Healthcare Fund IV L.P.(2)	Stephen Knight, M.D.; Stacie Weninger, Ph.D.(4)	207,809	$ 3,325,000
Entities associated with FIL Limited(3)		104,690	$ 1,675,000
Executive Officers and Directors:			
Ryan J. Watts, Ph.D.		12,500	$ 200,000

(1) Entities associated with AKDL, L.P. holding our securities whose shares are aggregated for purposes of reporting share ownership information are AKDL, L.P. and Neuro Line Partners, L.P.

(2) Entities associated with F-Prime Capital Partners Healthcare Fund IV L.P. holding our securities whose shares are aggregated for purposes of reporting share ownership information are Impresa Fund III Limited Partnership, F-Prime Capital Partners Healthcare Fund IV L.P. (f/k/a Beacon Bioventures Fund IV Limited Partnership), F-Prime Capital Partners Healthcare Advisors Fund IV LP and F-Prime Capital (f/k/a Fidelity Biosciences Corp.).

(3) Entities associated with FIL Limited holding our securities whose shares are aggregated for purposes of reporting share ownership information are FIL Limited, Asia Ventures III L.P., Japan Ventures I L.P., FIL Capital Investments (Mauritius) II Limited, Asia Partners III LP, Japan Partners I LP and India Partners II LP.

(4) Each of Drs. Knight and Weninger resigned as members of our board of directors on August 11, 2017.

Investors' Rights Agreement

We are party to an investors' rights agreement, as amended, with certain holders of our capital stock, including Ryan J. Watts, Ph.D., Alexander O. Schuth, M.D., Marc Tessier-Lavigne, Ph.D., Jay Flatley, Vicki Sato, Ph.D., David Schenkein, M.D., entities associated with AKDL, L.P., ARCH Venture Fund VIII, L.P., an entity affiliated with Robert Nelsen, entities associated with F-Prime Capital Partners Healthcare Fund IV L.P., entities associated with FIL Limited and Flagship Ventures Fund V, L.P., an entity affiliated with Douglas Cole, M.D. Under our investors' rights agreement, certain holders of our capital stock have the right to demand that we file a registration statement or request that their shares of our capital stock be covered by a registration statement that we are otherwise filing. See the section titled "Description of Capital Stock—Registration Rights" for additional information regarding these registration rights.

Right of First Refusal and Co-Sale Agreement

Pursuant to our equity compensation plans and certain agreements with certain holders of our capital stock, including Ryan J. Watts, Ph.D., Alexander O. Schuth, M.D., Steve E. Krognes, Marc Tessier-Lavigne, Ph.D., Jay Flatley, Vicki Sato, Ph.D., David Schenkein, M.D., entities associated with AKDL, L.P., ARCH Venture Fund VIII, L.P., an entity affiliated with Robert Nelsen, entities associated with F-Prime Capital Partners Healthcare Fund IV L.P., entities associated with FIL Limited and Flagship Ventures Fund V, L.P., an entity affiliated with Douglas Cole, M.D., including a right of first

refusal and co-sale agreement, as amended, we or our assignees have a right to purchase shares of our common stock which stockholders propose to sell to other parties. This right will terminate upon the completion of this offering. See the section titled “Principal Stockholders” for additional information regarding beneficial ownership of our capital stock.

Voting Agreement

We are party to a voting agreement, as amended under which certain holders of our capital stock, including Ryan J. Watts, Ph.D., Alexander O. Schuth, M.D., Steve E. Krognes, Marc Tessier-Lavigne, Ph.D., Jay Flatley, Vicki Sato, Ph.D., David Schenkein, M.D., entities associated with AKDL, L.P., ARCH Venture Fund VIII, L.P., an entity affiliated with Robert Nelsen, entities associated with F-Prime Capital Partners Healthcare Fund IV L.P., entities associated with FIL Limited and Flagship Ventures Fund V, L.P., an entity affiliated with Douglas Cole, M.D., have agreed as to the manner in which they will vote their shares of our capital stock on certain matters, including with respect to the election of directors. This agreement will terminate upon the completion of this offering, and thereafter none of our stockholders will have any special rights regarding the election or designation of members of our board of directors after the completion of this offering.

Indemnification Agreements

We have entered, and intend to continue to enter, into separate indemnification agreements with each of our directors and executive officers, in addition to the indemnification that will be provided for in our amended and restated certificate of incorporation and amended and restated bylaws. The indemnification agreements and our amended restated certificate of incorporation and amended and restated bylaws that will be in effect upon the completion of this offering require us to indemnify our directors, executive officers and certain controlling persons to the fullest extent permitted by Delaware law. See the section titled “Executive Compensation—Limitation of Liability and Indemnification” for additional information.

Participation in this Offering

Certain of our existing stockholders, including one that beneficially owns more than 5% of our outstanding common stock, have indicated an interest in purchasing an aggregate of $50.0 million or more in shares of our common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no shares in this offering to any of these stockholders, or any of these stockholders may determine to purchase more, less or no shares in this offering.

Related Party Transaction Policy

Our audit committee will have the primary responsibility for reviewing and approving or disapproving “related party transactions,” which are transactions between us and related persons in which the aggregate amount involved exceeds or may be expected to exceed $120,000 and in which a related person has or will have a direct or indirect material interest. The written charter of our audit committee will provide that our audit committee shall review and approve in advance any related party transaction.

Prior to the completion of this offering, we intend to adopt a formal written policy providing that we are not permitted to enter into any transaction that exceeds $120,000 and in which any related person has a direct or indirect material interest without the consent of our audit committee. In approving or rejecting any such transaction, our audit committee is to consider the relevant facts and circumstances available and deemed relevant to our audit committee, including whether the transaction is on terms no less favorable than terms generally available to an unaffiliated third party under the same or similar circumstances and the extent of the related person's interest in the transaction.

PRINCIPAL STOCKHOLDERS

The following table sets forth the beneficial ownership of our common stock as of November 24, 2017 by:

- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our common stock;
- each of the named executive officers;
- each of our directors; and
- all of our current executive officers and directors as a group.

We have determined beneficial ownership in accordance with the rules of the SEC, and thus it represents sole or shared voting or investment power with respect to our securities. Unless otherwise indicated below, to our knowledge, the persons and entities named in the table have sole voting and sole investment power with respect to all shares that they beneficially owned, subject to community property laws where applicable. The information does not necessarily indicate beneficial ownership for any other purpose, including for purposes of Sections 13(d) and 13(g) of the Exchange Act.

Certain of our existing stockholders, including one that beneficially owns more than 5% of our outstanding common stock, have indicated an interest in purchasing an aggregate of $50.0 million or more in shares of our common stock in this offering at the initial public offering price. The information set forth in the table below does not reflect the potential purchase of any shares in this offering by these stockholders.

We have based our calculation of the percentage of beneficial ownership prior to this offering on 74,090,587 shares of our common stock outstanding as of November 24, 2017, which includes 60,365,020 shares of our common stock resulting from the conversion of all outstanding shares of our convertible preferred stock (including our Series B-2 convertible preferred stock issued in November 2017) into our common stock immediately prior to the completion of this offering, as if this conversion had occurred as of November 24, 2017. We have based our calculation of the percentage of beneficial ownership after this offering on 82,423,920 shares of our common stock outstanding immediately after the completion of this offering, assuming no exercise by the underwriters of their option to purchase additional shares. We have deemed shares of our common stock subject to stock options that are currently exercisable or exercisable within 60 days of November 24, 2017, to be outstanding and to be beneficially owned by the person holding the stock option for the purpose of computing the percentage ownership of that person. We did not deem these shares outstanding, however, for the purpose of computing the percentage ownership of any other person.

Unless otherwise indicated, the address of each beneficial owner listed in the table below is c/o Denali Therapeutics Inc., 151 Oyster Point Blvd., 2nd Floor, South San Francisco, CA 94080.

	Shares Beneficially Owned Prior to this Offering		Shares Beneficially Owned After this Offering	
Name of Beneficial Owner	Shares	Percentage	Shares	Percentage
5% Stockholders:				
Entities associated with AKDL, L.P. (1)	20,299,298	27.4%	20,299,298	24.6%
ARCH Venture Fund VIII, L.P. (2)	11,068,749	14.9%	11,068,749	13.4%
Flagship Ventures Fund V, L.P. (3)	8,918,749	12.0%	8,918,749	10.8%
Entities associated with F-Prime Capital Partners Healthcare Fund IV L.P. (4)	4,889,994	6.6%	4,889,994	5.9%
Entities associated with FIL Limited (5)	4,184,982	5.6%	4,184,982	5.1%
Named Executive Officers and Directors:				
Ryan J. Watts, Ph.D. (6)	2,815,138	3.8%	2,815,138	3.4%
Alexander O. Schuth, M.D. (7)	810,089	1.1%	810,089	1.0%
Steve E. Krognes (8)	1,000,000	1.3%	1,000,000	1.2%
Carole Ho, M.D. (9)	484,375	*	484,375	*
Vicki Sato, Ph.D. (10)	150,000	*	150,000	*
Douglas Cole, M.D. (11)	—	—	—	—
Jay Flatley (12)	325,000	*	325,000	*
Robert Nelsen (13)	11,068,749	14.9%	11,068,749	13.4%
David Schenkein, M.D. (14)	324,998	*	324,998	*
Marc Tessier-Lavigne, Ph.D. (15)	3,139,043	4.2%	3,139,043	3.8%
All executive officers and directors as a group (10 persons) (16)	20,117,392	27.0%	20,117,392	24.3%

* Represents beneficial ownership of less than one percent (1%) of the outstanding shares of our common stock.

(1) Consists of (a) 19,187,499 shares held of record by AKDL, L.P. and (b) 1,111,799 shares held of record by Neuro Line Partners, L.P. Crestline SI (GP), L.P., or Crestline SI, is the general partner of AKDL, L.P. and Crestline Investors, Inc., or Crestline, is the general partner of Crestline SI. Bratton Capital Management, L.P. is the general partner of Neuro Line Partners, L.P. and Bratton Capital, Inc. is the general partner of Bratton Capital Management, L.P. Douglas K. Bratton, as the sole director of Crestline and Bratton Capital, Inc., has sole voting and investment control with respect to the shares held by AKDL, L.P. and Neuro Line Partners, L.P. The address of these entities is 201 Main Street, Suite 1900, Fort Worth, TX 76102.

(2) Consists of 11,068,749 shares held of record by ARCH Venture Fund VIII, L.P., or ARCH Venture Fund VIII. ARCH Venture Partners VIII, L.P., or AVP VIII LP, as the sole general partner of ARCH Venture Fund VIII, may be deemed to beneficially own certain of the shares held by ARCH Venture Fund VIII. AVP VIII LP disclaims beneficial ownership of all shares held by ARCH Venture Fund VIII in which AVP VIII LP does not have an actual pecuniary interest. ARCH Venture Partners VIII, LLC, or AVP VIII LLC, as the sole general partner of AVP VIII LP, may be deemed to beneficially own certain of the shares held by ARCH Venture Fund VIII. AVP VIII LLC disclaims beneficial ownership of all shares held by ARCH Venture Fund VIII in which AVP VIII LLC does not have an actual pecuniary interest. As the managing directors of AVP VIII LLC, Keith Crandell, Robert Nelsen, one of our directors, and Clinton Bybee (collectively, the Managing Directors), share voting and investment control with respect to the shares held by ARCH Venture Fund VIII. The Managing Directors disclaim beneficial ownership of all shares held by ARCH Venture Fund VIII except to the extent of any pecuniary interest therein. The address of these entities is 8755 West Higgins Road, Suite 1025, Chicago, IL 60631.

(3) Consists of 8,918,749 shares held of record by Flagship Ventures Fund V, L.P., or Flagship V. Flagship Ventures Fund V General Partner LLC, or Flagship V GP, is the general partner of Flagship V. As the manager of Flagship V GP, Noubar B. Afeyan, Ph.D. has sole voting and investment control with respect to the shares held by Flagship V. In addition, Dr. Cole, a member of our board of directors, is a member of Flagship V GP but does not have voting or investment control with respect to the shares held by Flagship V. Dr. Cole disclaims beneficial ownership of all shares held by Flagship V. The address of these entities is 55 Cambridge Parkway, Suite 800E, Cambridge, MA 02142.

(4) Consists of (a) 2,999,521 shares held of record by Impresa Fund III Limited Partnership, (b) 1,107,257 shares held of record by F-Prime Capital Partners Healthcare Fund IV LP (f/k/a Beacon Bioventures Fund IV Limited Partnership), (c) 33,215 shares held of record by F-Prime Capital Partners Healthcare Advisors Fund IV LP, and (d) 750,001 shares held of record by F-Prime Inc. (f/k/a Fidelity Biosciences Corp.) (collectively, the Entities associated with F-Prime Capital Partners Healthcare Fund IV LP). The general partner of F-Prime Capital

Partners Healthcare Fund IV LP is F-Prime Capital Partners Healthcare Advisors Fund IV LP. F-Prime Capital Partners Healthcare Advisors Fund IV LP is solely managed by Impresa Management LLC, the general partner of its general partner and its investment manager. Impresa Management LLC is owned, directly or indirectly, by various shareholders and employees of FMR LLC. The general partner of Impresa Fund III Limited Partnership is Impresa Management LLC. F-Prime Inc. is a wholly-owned subsidiary of FMR LLC. Each of the entities listed above expressly disclaims beneficial ownership of the securities listed above except to the extent of any pecuniary interest therein. The address of these entities is 245 Summer Street, Boston, MA 02210.

(5) Consists of (a) 1,914,833 shares held of record by FIL Limited, (b) 1,460,570 shares held of record by Asia Ventures III L.P., (c) 401,692 shares held of record by Japan Ventures I L.P., (d) 400,456 shares held of record by FIL Capital Investments (Mauritius) II Limited, (e) 5,146 shares held of record by Asia Partners III LP, (f) 906 shares held of record by Japan Partners I LP and (g) 1,379 shares held of record by India Partners II LP (collectively, the Entities associated with FIL Limited). The general partner of Asia Ventures III L.P. is Asia Partners III LP. The general partner of Japan Ventures I L.P. is Japan Partners I LP. The general partner of Asia Partners III LP is FIL Capital Management Ltd. The general partner of Japan Partners I LP is FIL Capital Management Ltd. The general partner of India Partners II LP is FIL Capital Management Ltd. Each of the entities listed above expressly disclaims beneficial ownership of the securities listed above except to the extent of any pecuniary interest therein. The address of each of these entities except for FIL Capital Investments (Mauritius) II Limited is Pembroke Hall, 42 Crow Lange, Pembroke, Bermuda HM 19. The address of FIL Capital Investments (Mauritius) II Limited is c/o Cim Fund Services Ltd, 33 Edith Cavell Street, Port Louis, Mauritius.

(6) Consists of (a) 12,500 shares held of record by Dr. Watts and (b) 2,802,638 shares of restricted stock held of record by the Watts Family 2015 Trust dated July 7, 2015, for which Dr. Watts serves as trustee and which vest on February 23, 2019.

(7) Consists of (a) 685,089 shares of restricted stock held of record by the Schuth Family Trust, for which Dr. Schuth serves as trustee, which vest on March 17, 2019 and (b) 125,000 shares subject to options exercisable within 60 days of November 24, 2017, none of which have vested as of such date.

(8) Consists of 1,000,000 shares held of record by The Steve Edward Krognes Revocable Trust, for which Mr. Krognes serves as a trustee, of which 239,584 shares are subject to repurchase by us at the original purchase price as of November 24, 2017.

(9) Consists of (a) 46,875 shares held of record by Dr. Ho, all of which are subject to repurchase by us at the original purchase price as of November 24, 2017, (b) 235,890 shares held of record by the Rohatgi-Ho Family 2009 Revocable Trust, for which Dr. Ho serves as trustee, of which 89,063 shares are subject to repurchase by us at the original purchase price as of November 24, 2017, (c) 25,000 shares held of record by The Rohatgi-Ho Irrevocable GST Trust, for which Dr. Ho serves as trustee, of which 9,896 shares are subject to repurchase by us at the original purchase price as of November 24, 2017 and (d) 176,610 shares subject to options exercisable within 60 days of November 24, 2017, of which 46,875 have vested as of such date.

(10) Consists of (a) 62,500 shares held of record by Dr. Sato, (b) 75,000 shares of restricted stock held of record by Dr. Sato, which vest on April 17, 2019 and (c) 12,500 shares subject to options exercisable within 60 days of November 24, 2017, all of which have vested as of such date.

(11) Dr. Cole, a member of our board of directors, is a member of Flagship V GP but does not have voting or investment control with respect to the shares held by Flagship V. Dr. Cole disclaims beneficial ownership of all shares held by Flagship V.

(12) Consists of (a) 75,000 shares of restricted stock held of record by Mr. Flatley, which vest on April 17, 2019 and (b) 250,000 shares held of record by The Flatley Family Trust, for which Mr. Flatley serves as a trustee.

(13) Consists of the shares described in footnote (2) above. Mr. Nelsen is a managing director of AVP VIII LLC and shares voting and investment control with respect to these shares. Mr. Nelsen disclaims beneficial ownership of all shares held by ARCH Venture Fund VIII except to the extent of any pecuniary interest therein.

(14) Consists of (a) 75,000 shares of restricted stock held of record by Dr. Schenkein, which vest on April 17, 2019, (b) 105,225 shares held of record by the David P. Schenkein 2015 Denali Qualified Annuity Trust, for which Dr. Schenkein serves as a trustee, (c) 19,774 shares held of record by the David P. Schenkein 2004 Revocable Trust, for which Dr. Schenkein serves as a trustee, (d) 105,225 shares held of record by the Amy P. Schenkein 2015 Denali Qualified Annuity Trust, for which Dr. Schenkein serves as a trustee and (e) 19,774 shares held of record by the Amy P. Schenkein 2004 Revocable Trust, for which Dr. Schenkein serves as a trustee.

(15) Consists of (a) 25,000 shares held of record by Dr. Tessier-Lavigne and (b) 3,114,043 shares of restricted stock held of record by Dr. Tessier-Lavigne, which vest on March 24, 2019.

(16) Consists of (a) 20,117,392 shares beneficially owned by our current executive officers and directors, of which 385,418 shares may be repurchased by us at the original purchase price as of such date, and (b) 314,110 shares subject to options exercisable within 60 days of November 24, 2017, of which 59,375 have vested as of such date.

DESCRIPTION OF CAPITAL STOCK

The following descriptions of our capital stock and certain provisions of our amended and restated certificate of incorporation and amended and restated bylaws are summaries and are qualified by reference to the amended and restated certificate of incorporation and the amended and restated bylaws that will be in effect upon completion of this offering. Copies of these documents will be filed with the SEC as exhibits to our registration statement, of which this prospectus forms a part. The descriptions of the common stock and preferred stock reflect changes to our capital structure that will occur upon the completion of this offering.

Upon the completion of this offering and the filing of our amended and restated certificate of incorporation to be effective upon completion of this offering, our authorized capital stock will consist of 440,000,000 shares of capital stock, par value $0.01 per share, of which:

- 400,000,000 shares are designated as common stock; and
- 40,000,000 shares are designated as preferred stock.

Assuming the conversion of all outstanding shares of our convertible preferred stock issued as of Septermber 30, 2017 into shares of our common stock, which will occur upon the completion of this offering, as of September 30, 2017 there are 72,325,882 shares of our common stock outstanding held by 148 stockholders of record, and no shares of our preferred stock outstanding. Our board of directors is authorized, without stockholder approval except as required by the listing standard of NASDAQ, to issue additional shares of our capital stock.

Common Stock

Voting Rights

Each holder of common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors. Our certificate of incorporation and bylaws to be in effect upon the completion of this offering do not provide for cumulative voting rights. Because of this, the holders of a plurality of the shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they should so choose. With respect to matters other than the election of directors, at any meeting of the stockholders at which a quorum is present or represented, the affirmative vote of a majority of the voting power of the shares present in person or represented by proxy at such meeting and entitled to vote on the subject matter shall be the act of the stockholders, except as otherwise required by law. The holders of a majority of the stock issued and outstanding and entitled to vote, present in person or represented by proxy, shall constitute a quorum for the transaction of business at all meetings of the stockholders.

Dividends

Subject to preferences that may be applicable to any then-outstanding preferred stock, holders of our common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then-outstanding shares of preferred stock.

Rights and Preferences

Holders of our common stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of our preferred stock that we may designate in the future.

Fully Paid and Nonassessable

All of our outstanding shares of common stock are, and the shares of common stock to be issued in this offering, upon payment and delivery in accordance with the underwriting agreement, will be fully paid and nonassessable.

Preferred Stock

Upon the closing of this offering, our board of directors will have the authority, without further action by the stockholders, to issue up to 40,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, redemption rights, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of such series, any or all of which may be greater than the rights of common stock. The issuance of preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing change in our control or other corporate action. Upon closing of this offering, no shares of preferred stock will be outstanding, and we have no present plan to issue any shares of preferred stock.

Options

As of September 30, 2017, we had outstanding options to purchase an aggregate of 6,179,687 shares of our common stock, with a weighted-average exercise price of approximately $3.06 per share, under our 2015 Plan. After September 30, 2017, we issued options to purchase an aggregate of 194,000 shares of our common stock, with a weighted-average exercise price of $11.64 per share, under our 2015 Plan.

Registration Rights

After the completion of this offering, under our investors' rights agreement, as amended, the holders of approximately 64,913,502 shares of common stock or their transferees, have the right to require us to register the offer and sale of their shares, or to include their shares in any registration statement we file, in each case as described below.

Demand Registration Rights

After the completion of this offering, the holders of up to 64,913,502 shares of our common stock will be entitled to certain demand registration rights. At any time beginning 180 days after the effective date of this offering, holders of at least a majority of the shares having registration rights then outstanding can request that we file a registration statement to register the offer and sale of their shares. We are obligated to effect only two such registrations. Each such request for registration must cover securities the anticipated aggregate public offering price of which, before payment of underwriting discounts and commissions, is at least $10 million. These demand registration rights are

subject to specified conditions and limitations, including the right of the underwriters to limit the number of shares included in any such registration under certain circumstances. If we determine that it would be seriously detrimental to us and our stockholders to effect such a demand registration, we have the right to defer such registration, not more than twice in any 12-month period, for a period of up to 60 days.

Form S-3 Registration Rights

After the completion of this offering, the holders of up to 64,913,502 shares of our common stock will be entitled to certain Form S-3 registration rights. At any time we are eligible to file a registration statement on Form S-3, at least twenty percent of the shares having these rights then outstanding can request that we register the offer and sale of their shares of our common stock on a registration statement on Form S-3 so long as the request covers securities the anticipated aggregate public offering price of which, before payment of underwriting discounts and commissions, is at least $5 million. These stockholders may make an unlimited number of requests for registration on a registration statement on Form S-3. However, we will not be required to effect a registration on Form S-3 if we have effected two such registrations within the 12-month period preceding the date of the request. Additionally, if we determine that it would be seriously detrimental to us and our stockholders to effect such a demand registration, we have the right to defer such registration, not more than twice in any 12-month period, for a period of up to 60 days.

Piggyback Registration Rights

After the completion of this offering, the holders of up to 64,913,502 shares of our common stock will be entitled to certain “piggyback” registration rights. If we propose to register the offer and sale of shares of our common stock under the Securities Act, all holders of these shares then outstanding can request that we include their shares in such registration, subject to certain marketing and other limitations, including the right of the underwriters to limit the number of shares included in any such registration statement under certain circumstances. As a result, whenever we propose to file a registration statement under the Securities Act, other than with respect to (1) a registration related to any employee benefit plan or a corporate reorganization or other transaction covered by Rule 145 promulgated under the Securities Act, (2) a registration in which the only stock being registered is common stock issuable upon conversion of debt securities also being registered or (3) a registration on any form that does not include substantially the same information as would be required to be included in a registration statement covering the sale of our common stock, the holders of these shares are entitled to notice of the registration and have the right, subject to certain limitations, to include their shares in the registration.

Expenses of Registration

We will pay all expenses relating to any demand registrations, Form S-3 registrations and piggyback registrations, subject to specified exceptions.

Termination

The registration rights terminate upon the earliest of (1) the date that is five years after the closing of this offering, (2) as to a given holder of registration rights, when such holder of registration rights can sell all of such holder’s registrable securities in a three-month period pursuant to Rule 144 promulgated under the Securities Act and (3) the closing of a deemed liquidation event.

Anti-Takeover Effects of Certain Provisions of Delaware Law, Our Amended and Restated Certificate of Incorporation and Our Amended and Restated Bylaws

Certain provisions of Delaware law and certain provisions that will be included in our amended and restated certificate of incorporation and amended and restated bylaws summarized below may be deemed to have an anti-takeover effect and may delay, deter, or prevent a tender offer or takeover attempt that a stockholder might consider to be in its best interests, including attempts that might result in a premium being paid over the market price for the shares held by stockholders.

Preferred Stock

Our amended and restated certificate of incorporation will contain provisions that permit our board of directors to issue, without any further vote or action by the stockholders, shares of preferred stock in one or more series and, with respect to each such series, to fix the number of shares constituting the series and the designation of the series, the voting rights (if any) of the shares of the series, and the powers, preferences or relative, participation, optional and other special rights, if any, and any qualifications, limitations or restrictions, of the shares of such series.

Classified Board of Directors

Our amended and restated certificate of incorporation will provide that our board of directors is divided into three classes, designated Class I, Class II, and Class III. Each class will be an equal number of directors, as nearly as possible, consisting of one-third of the total number of directors constituting our entire board of directors. The term of initial Class I directors shall terminate on the date of the 2018 annual meeting, the term of the initial Class II directors shall terminate on the date of the 2019 annual meeting, and the term of the initial Class III directors shall terminate on the date of the 2020 annual meeting. At each annual meeting of stockholders beginning in 2018, successors to the class of directors whose term expires at that annual meeting will be elected for a three-year term.

Removal of Directors

Our amended and restated certificate of incorporation will provide that stockholders may only remove a director for cause by a vote of no less than a majority of the shares present in person or by proxy at the meeting and entitled to vote.

Director Vacancies

Our amended and restated certificate of incorporation will authorize only our board of directors to fill vacant directorships.

No Cumulative Voting

Our amended and restated certificate of incorporation will provide that stockholders do not have the right to cumulate votes in the election of directors.

Special Meetings of Stockholders

Our amended and restated certificate of incorporation and amended and restated bylaws will provide that, except as otherwise required by law, special meetings of the stockholders may be called only by an officer at the request of a majority of our board of directors, by the chairperson of our board of directors, or by our Chief Executive Officer.

Advance Notice Procedures for Director Nominations

Our bylaws will provide that stockholders seeking to nominate candidates for election as directors at an annual or special meeting of stockholders must provide timely notice thereof in writing. To be timely, a stockholder's notice generally will have to be delivered to and received at our principal executive offices before notice of the meeting is issued by the secretary of the company, with such notice being served not less than 90 nor more than 120 days before the meeting. Although the amended and restated bylaws will not give our board of directors the power to approve or disapprove stockholder nominations of candidates to be elected at an annual meeting, the amended and restated bylaws may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed or may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect its own slate of directors or otherwise attempting to obtain control of the company.

Action by Written Consent

Our amended and restated certificate of incorporation and amended and restated bylaws will provide that any action to be taken by the stockholders must be effected at a duly called annual or special meeting of stockholders and may not be effected by written consent.

Amending our Certificate of Incorporation and Bylaws

Our amended and restated certificate of incorporation may be amended or altered in any manner provided by the DGCL. Our amended and restated bylaws may be adopted, amended, altered, or repealed by stockholders only upon approval of at least majority of the voting power of all the then outstanding shares of the common stock, except for any amendment of the above provisions, which would require the approval of a two-thirds majority of our then outstanding common stock. Additionally, our amended and restated certificate of incorporation will provide that our bylaws may be amended, altered, or repealed by our board of directors.

Authorized but Unissued Shares

Our authorized but unissued shares of common stock and preferred stock will be available for future issuances without stockholder approval, except as required by the listing standards of NASDAQ, and could be utilized for a variety of corporate purposes, including future offerings to raise additional capital, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved common stock and preferred stock could render more difficult or discourage an attempt to obtain control of the company by means of a proxy contest, tender offer, merger or otherwise.

Exclusive Jurisdiction

Our amended and restated bylaws will provide that, unless we consent to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of fiduciary duty, any action asserting a claim arising pursuant to the DGCL, any action regarding our amended and restated certificate of incorporation or our amended and restated bylaws or any action asserting a claim against us that is governed by the internal affairs doctrine. Our amended and restated certificate of incorporation further provides that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act.

Business Combinations with Interested Stockholders

Subject to certain exceptions, Section 203 of the DGCL prohibits a public Delaware corporation from engaging in a business combination (as defined in such section) with an "interested stockholder"

(defined generally as any person who beneficially owns 15% or more of the outstanding voting stock of such corporation or any person affiliated with such person) for a period of three years following the time that such stockholder became an interested stockholder, unless (i) prior to such time the board of directors of such corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder; (ii) upon consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of such corporation at the time the transaction commenced (excluding for purposes of determining the voting stock of such corporation outstanding (but not the outstanding voting stock owned by the interested stockholder) those shares owned (A) by persons who are directors and also officers of such corporation and (B) by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer); or (iii) at or subsequent to such time the business combination is approved by the board of directors of such corporation and authorized at a meeting of stockholders (and not by written consent) by the affirmative vote of at least 66 2/3% of the outstanding voting stock of such corporation not owned by the interested stockholder.

Our amended and restated certificate of incorporation and our amended and restated bylaws will provide that we must indemnify our directors and officers to the fullest extent authorized by the DGCL. We are expressly authorized to carry, and we intend to carry, directors' and officers' insurance providing coverage for our directors, officers and certain employees for some liabilities. We believe that these indemnification provisions and insurance are useful to attract and retain qualified directors and executive directors.

The limitation on liability and indemnification provisions in our certificate of incorporation and bylaws may discourage stockholders from bringing a lawsuit against directors for breach of their fiduciary duty. These provisions may also have the effect of reducing the likelihood of derivative litigation against directors and officers, even though such an action, if successful, might otherwise benefit us and our stockholders. In addition, your investment may be adversely affected to the extent we pay the costs of settlement and damage awards against directors and officers pursuant to these indemnification provisions.

Listing

We have applied to list our common stock on the NASDAQ Global Select Market under the symbol "DNLI."

Transfer Agent and Registrar

Upon completion of this offering, the transfer agent and registrar for our common stock will be American Stock Transfer & Trust Company, LLC. The transfer agent and registrar's address is 6201 15th Avenue, Brooklyn, New York 11219.

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common stock, and although we expect that our common stock will be approved for listing on NASDAQ, we cannot assure investors that there will be an active public market for our common stock following this offering. We cannot predict what effect, if any, sales of our shares in the public market or the availability of shares for sale will have on the market price of our common stock. Future sales of substantial amounts of common stock in the public market, including shares issued upon exercise of outstanding options, or the perception that such sales may occur, however, could adversely affect the market price of our common stock and also could adversely affect our future ability to raise capital through the sale of our common stock or other equity-related securities of ours at times and prices we believe appropriate.

Upon completion of this offering, based on our shares outstanding as of September 30, 2017 and after giving effect to the conversion of all outstanding shares of our convertible preferred stock (including 1,764,705 shares issuable upon conversion of our Series B-2 convertible preferred stock), 82,423,920 shares of our common stock will be outstanding, or 83,673,920 shares of common stock if the underwriters exercise their option to purchase additional shares in full. All of the shares of common stock expected to be sold in this offering will be freely tradable without restriction or further registration under the Securities Act unless held by our “affiliates,” as that term is defined in Rule 144 under the Securities Act. The remaining outstanding shares of our common stock will be deemed “restricted securities” as that term is defined under Rule 144. Restricted securities may be sold in the public market only if their offer and sale is registered under the Securities Act or if the offer and sale of those securities qualify for an exemption from registration, including exemptions provided by Rules 144 and 701 under the Securities Act, which are summarized below.

As a result of the lock-up agreements and market stand-off provisions described below and the provisions of Rules 144 or 701 and no exercise of the underwriters’ option to purchase additional shares, the shares of our common stock that will be deemed “restricted securities” will be available for sale in the public market following the completion of this offering as follows:

- 8,333,333 shares will be eligible for sale on the date of this prospectus; and
- 74,090,587 shares will be eligible for sale upon expiration of the lock-up agreements and market stand-off provisions described below, beginning more than 180 days after the date of this prospectus.

Lock-Up Agreements and Market Standoff Agreements

Our officers, directors and the holders of substantially all of our capital stock and options have entered into lock-up agreements with the underwriters or market standoff agreements with us under which they have agreed, subject to certain exceptions, not to dispose of or hedge any of their common stock or securities convertible into or exchangeable for shares of common stock during the period from the date of this prospectus continuing through the date 180 days after the date of this prospectus, except with the prior consent of Goldman Sachs & Co. LLC, Morgan Stanley & Co. LLC and J.P. Morgan Securities LLC. See the section titled “Underwriting” for additional information.

Rule 144

Rule 144, as currently in effect, generally provides that, once we have been subject to the public company reporting requirements of Section 13 or Section 15(d) of the Exchange Act for at least 90 days, a stockholder who is not deemed to have been one of our affiliates at any time during the preceding 90 days and who has beneficially owned the shares of our capital stock proposed to be sold for at least six months is entitled to sell such shares in reliance upon Rule 144 without complying with

the volume limitation, manner of sale or notice conditions of Rule 144. If such stockholder has beneficially owned the shares of our capital stock proposed to be sold for at least one year, then such person is entitled to sell such shares in reliance upon Rule 144 without complying with any of the conditions of Rule 144.

Rule 144 also provides that a stockholder who is deemed to have been one of our affiliates at any time during the preceding 90 days and who has beneficially owned the shares of our common stock proposed to be sold for at least six months is entitled to sell such shares in reliance upon Rule 144 within any three-month period beginning 90 days after the date of this prospectus a number of shares that does not exceed the greater of the following:

- 1% of the number of shares of our capital stock then outstanding, which will equal 824,239 shares immediately after the completion of this offering; or
- the average weekly trading volume of our common stock during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Sales of our capital stock made in reliance upon Rule 144 by a stockholder who is deemed to have been one of our affiliates at any time during the preceding 90 days are also subject to the current public information, manner of sale, and notice conditions of Rule 144.

Rule 701

Rule 701 generally provides that, once we have been subject to the public company reporting requirements of Section 13 or Section 15(d) of the Exchange Act for at least 90 days, a stockholder who purchased shares of our common stock pursuant to a written compensatory benefit plan or contract and who is not deemed to have been one of our affiliates at any time during the preceding 90 days may sell such shares in reliance upon Rule 144 without complying with the current public information or holding period conditions of Rule 144. Rule 701 also provides that a stockholder who purchased shares of our common stock pursuant to a written compensatory benefit plan or contract and who is deemed to have been one of our affiliates during the preceding 90 days may sell such shares under Rule 144 without complying with the holding period condition of Rule 144. However, all stockholders who purchased shares of our common stock pursuant to a written compensatory benefit plan or contract are required to wait until 90 days after the date of this prospectus before selling such shares pursuant to Rule 701.

Registration Rights

After the completion of this offering, the holders of up to 64,913,502 shares of our common stock will be entitled to certain rights with respect to the registration of such shares under the Securities Act. The registration of these shares of our common stock under the Securities Act would result in these shares becoming eligible for sale in the public market without restriction under the Securities Act immediately upon the effectiveness of such registration, subject to the Rule 144 limitations applicable to affiliates. See the section titled “Description of Capital Stock—Registration Rights” for a description of these registration rights.

Registration Statement

In connection with this offering, we intend to file a registration statement on Form S-8 under the Securities Act to register all of the shares of our common stock subject to equity awards outstanding or reserved for issuance under our equity compensation plans. The shares of our common stock covered by such registration statement will be eligible for sale in the public market without restriction under the Securities Act immediately upon the effectiveness of such registration statement, subject to vesting restrictions, the conditions of Rule 144 applicable to affiliates and any applicable market standoff agreements and lock-up agreements. See the section titled “Executive Compensation—Employee Benefit and Stock Plans” for a description of our equity compensation plans.

MATERIAL U.S. FEDERAL INCOME AND ESTATE TAX CONSIDERATIONS FOR NON-U.S. HOLDERS OF OUR COMMON STOCK

The following is a summary of the material U.S. federal income tax consequences of the ownership and disposition of our common stock acquired in this offering by a "non-U.S. holder" (as defined below), but does not purport to be a complete analysis of all the potential tax considerations relating thereto. This summary is based upon the provisions of the United States Internal Revenue Code of 1986, as amended, or the Code, Treasury Regulations promulgated thereunder, administrative rulings and judicial decisions, all as of the date hereof. These authorities may be changed, possibly retroactively, so as to result in U.S. federal income tax consequences different from those set forth below. We have not sought, and do not intend to seek, any ruling from the Internal Revenue Service, or IRS, with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS or a court will agree with such statements and conclusions.

This summary also does not address the tax considerations arising under the laws of any non-U.S., state or local jurisdiction or under U.S. federal gift and estate tax rules, except to the limited extent set forth below. In addition, this discussion does not address tax considerations applicable to an investor's particular circumstances or to investors that may be subject to special tax rules, including, without limitation:

- banks, insurance companies, regulated investment companies, real estate investment trusts or other financial institutions;
- persons subject to the alternative minimum tax or the tax on net investment income;
- tax-exempt organizations;
- pension plans and tax-qualified retirement plans;
- controlled foreign corporations, passive foreign investment companies and corporations that accumulate earnings to avoid U.S. federal income tax;
- brokers or dealers in securities or currencies;
- traders in securities that elect to use a mark-to-market method of accounting for their securities holdings;
- persons that own, or are deemed to own, more than five percent of our capital stock (except to the extent specifically set forth below);
- certain former citizens or long-term residents of the United States;
- persons who hold our common stock as a position in a hedging transaction, "straddle," "conversion transaction" or other risk reduction transaction;
- persons who hold or receive our common stock pursuant to the exercise of any option or otherwise as compensation;
- persons who do not hold our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, property held for investment); or
- persons deemed to sell our common stock under the constructive sale provisions of the Code.

In addition, if a partnership, entity or arrangement classified as a partnership or flow-through entity for U.S. federal income tax purposes holds our common stock, the tax treatment of a partner generally will depend on the status of the partner and upon the activities of the partnership or other entity. A partner in a partnership or other such entity that will hold our common stock should consult his, her or its own tax advisor regarding the tax consequences of the ownership and disposition of our common stock through a partnership or other such entity, as applicable.

You are urged to consult your tax advisor with respect to the application of the U.S. federal income tax laws to your particular situation, as well as any tax consequences of the purchase, ownership and disposition of our common stock arising under the U.S. federal gift or estate tax rules or under the laws of any state, local, non-U.S. or other taxing jurisdiction or under any applicable tax treaty.

Non-U.S. Holder Defined

For purposes of this discussion, you are a "non-U.S. holder" if you are a beneficial owner of our common stock that, for U.S. federal income tax purposes, is not a partnership or:

- an individual who is a citizen or resident of the United States;
- a corporation or other entity taxable as a corporation created or organized in the United States or under the laws of the United States or any political subdivision thereof, or otherwise treated as such for U.S. federal income tax purposes;
- an estate whose income is subject to U.S. federal income tax regardless of its source; or
- a trust (x) whose administration is subject to the primary supervision of a U.S. court and that has one or more U.S. persons who have the authority to control all substantial decisions of the trust or (y) that has made a valid election under applicable Treasury Regulations to be treated as a U.S. person.

Distributions

As described in the section titled "Dividend Policy," we have never declared or paid cash dividends on our common stock, and we do not anticipate paying any dividends on our common stock following the completion of this offering. However, if we do make distributions on our common stock, those payments will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent those distributions exceed both our current and our accumulated earnings and profits, the excess will constitute a return of capital and will first reduce your basis in our common stock, but not below zero, and then will be treated as gain from the sale of stock.

Subject to the discussions below on effectively connected income and Foreign Account Tax Compliance Act, or FATCA, withholding, any dividend paid to you generally will be subject to U.S. federal withholding tax either at a rate of 30% of the gross amount of the dividend or such lower rate as may be specified by an applicable income tax treaty between the United States and your country of residence. In order to receive a reduced treaty rate, you must provide the applicable withholding agent with an IRS Form W-8BEN or W-8BEN-E or other appropriate version of IRS Form W-8 certifying qualification for the reduced rate. A non-U.S. holder of shares of our common stock eligible for a reduced rate of U.S. federal withholding tax pursuant to an income tax treaty may obtain a refund of any excess amounts withheld by filing an appropriate claim for refund with the IRS. If the non-U.S. holder holds our common stock through a financial institution or other agent acting on the non-U.S. holder's behalf, the non-U.S. holder will be required to provide appropriate documentation to the agent, which then will be required to provide certification to the applicable withholding agent, either directly or through other intermediaries.

Dividends received by you that are treated as effectively connected with your conduct of a U.S. trade or business (and, if required by an applicable income tax treaty, such dividends are attributable to a permanent establishment or fixed base maintained by you in the United States) are generally exempt from the 30% U.S. federal withholding tax, subject to the discussion below on backup withholding and FATCA withholding. In order to obtain this exemption, you must provide the applicable withholding

agent with a properly executed IRS Form W-8ECI or other applicable IRS Form W-8 properly certifying such exemption. Such effectively connected dividends, although not subject to U.S. federal withholding tax, are taxed at the same graduated rates applicable to U.S. persons, net of certain deductions and credits, subject to an applicable income tax treaty providing otherwise. In addition, if you are a corporate non-U.S. holder, dividends you receive that are effectively connected with your conduct of a U.S. trade or business may also be subject to a branch profits tax at a rate of 30% or such lower rate as may be specified by an applicable income tax treaty between the United States and your country of residence. You should consult your tax advisor regarding the tax consequences of the ownership and disposition of our common stock, including any applicable tax treaties that may provide for different rules.

Gain on Disposition of Common Stock

Subject to the discussion below regarding backup withholding and FATCA withholding, you generally will not be required to pay U.S. federal income tax on any gain realized upon the sale or other disposition of our common stock unless:

- the gain is effectively connected with your conduct of a U.S. trade or business (and, if an applicable income tax treaty so provides, the gain is attributable to a permanent establishment or fixed base maintained by you in the United States);
- you are an individual who is present in the United States for a period or periods aggregating 183 days or more during the calendar year in which the sale or disposition occurs and certain other conditions are met; or
- our common stock constitutes a United States real property interest by reason of our status as a “United States real property holding corporation,” or USRPHC, for U.S. federal income tax purposes at any time within the shorter of the five-year period preceding your disposition of, or your holding period for, our common stock.

We believe that we are not currently and will not become a USRPHC for U.S. federal income tax purposes, and the remainder of this discussion so assumes. However, because the determination of whether we are a USRPHC depends on the fair market value of our U.S. real property interests relative to the fair market value of our U.S. and worldwide real property interests plus our other business assets, there can be no assurance that we will not become a USRPHC in the future. Even if we become a USRPHC, however, as long as our common stock is regularly traded on an established securities market, your common stock will be treated as U.S. real property interests only if you actually (directly or indirectly) or constructively hold more than five percent of such regularly traded common stock at any time during the shorter of the five-year period preceding your disposition of, or your holding period for, our common stock.

If you are a non-U.S. holder described in the first bullet above, you will be required to pay tax on the gain derived from the sale (net of certain deductions and credits) under regular graduated U.S. federal income tax rates, and a corporate non-U.S. holder described in the first bullet above also may be subject to the branch profits tax at a 30% rate, or such lower rate as may be specified by an applicable income tax treaty. If you are an individual non-U.S. holder described in the second bullet above, you will be subject to tax at 30% (or such lower rate specified by an applicable income tax treaty) on the gain derived from the sale, which gain may be offset by U.S. source capital losses for the year, provided you have timely filed U.S. federal income tax returns with respect to such losses. You should consult your tax advisor regarding any applicable income tax or other treaties that may provide for different rules.

Federal Estate Tax

Our common stock beneficially owned by an individual who is not a citizen or resident of the United States (as defined for U.S. federal estate tax purposes) at the time of his or her death will generally be includable in the decedent's gross estate for U.S. federal estate tax purposes. Such stock, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax treaty provides otherwise.

Backup Withholding and Information Reporting

Generally, we must report annually to the IRS the amount of dividends paid to you, your name and address, and the amount of tax withheld, if any. A similar report will be sent to you. Pursuant to applicable income tax treaties or other agreements, the IRS may make these reports available to tax authorities in your country of residence.

Payments of dividends on or of proceeds from the disposition of our common stock made to you may be subject to information reporting and backup withholding at a current rate of 28% unless you establish an exemption, for example, by properly certifying your non-U.S. status on a properly completed IRS Form W-8BEN or W-8BEN-E or another appropriate version of IRS Form W-8. Notwithstanding the foregoing, backup withholding and information reporting may apply if the applicable withholding agent has actual knowledge, or reason to know, that you are a U.S. person.

Backup withholding is not an additional tax; rather, the U.S. federal income tax liability of persons subject to backup withholding will be reduced by the amount of tax withheld. If withholding results in an overpayment of taxes, a refund or credit may generally be obtained from the IRS, provided that the required information is furnished to the IRS in a timely manner.

Foreign Account Tax Compliance Act (FATCA)

Provisions of the Code commonly referred to as FATCA, Treasury Regulations issued thereunder and official IRS guidance generally impose a U.S. federal withholding tax of 30% on dividends on, and the gross proceeds from a sale or other disposition of our common stock, paid to a "foreign financial institution" (as specially defined under these rules), unless such institution enters into an agreement with the U.S. government to, among other things, withhold on certain payments and to collect and provide to the U.S. tax authorities substantial information regarding the U.S. account holders of such institution (which includes certain equity and debt holders of such institution, as well as certain account holders that are foreign entities with U.S. owners) or otherwise establishes an exemption. FATCA also generally imposes a U.S. federal withholding tax of 30% on dividends on, and the gross proceeds from, a sale or other disposition of our common stock paid to a "non-financial foreign entity" (as specially defined under these rules), unless such entity provides the withholding agent with a certification identifying the substantial direct and indirect U.S. owners of the entity, certifies that it does not have any substantial U.S. owners, or otherwise establishes an exemption.

The withholding obligations under FATCA generally apply to dividends on our common stock and under current transition rules are expected to apply to the payment of gross proceeds of a sale or other disposition of our common stock made on or after January 1, 2019. The withholding tax will apply regardless of whether the payment otherwise would be exempt from U.S. nonresident and backup withholding tax, including under the other exemptions described above. Under certain circumstances, a non-U.S. holder might be eligible for refunds or credits of such taxes. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this section. Prospective investors are encouraged to consult with their own tax advisors regarding the application of FATCA withholding to their investment in, and ownership and disposition of, our common stock.

The preceding discussion of U.S. federal tax considerations is for general information only. It is not tax advice to investors in their particular circumstances. Each prospective investor should consult its own tax advisor regarding the particular U.S. federal, state and local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed change in applicable laws.

UNDERWRITING

We and the underwriters named below have entered into an underwriting agreement with respect to the shares being offered. Subject to certain conditions, each underwriter has severally agreed to purchase the number of shares indicated in the following table. Goldman Sachs & Co. LLC, Morgan Stanley & Co. LLC and J.P. Morgan Securities LLC are the representatives of the underwriters.

Underwriters	Number of Shares
Goldman Sachs & Co. LLC	
Morgan Stanley & Co. LLC	
J.P. Morgan Securities LLC	
Evercore Group L.L.C.	
Total	8,333,333

The underwriters will be committed to take and pay for all of the shares being offered, if any are taken, other than the shares covered by the option described below unless and until this option is exercised.

Certain of our existing stockholders, including one that beneficially owns more than 5% of our outstanding common stock, have indicated an interest in purchasing an aggregate of $50.0 million or more in shares of our common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no shares in this offering to any of these stockholders, or any of these stockholders may determine to purchase more, less or no shares in this offering. The underwriters will receive the same underwriting discounts and commissions on any shares purchased by these stockholders as they will on any other shares sold to the public in this offering.

The underwriters will have an option to buy up to an additional 1,250,000 shares from us to cover sales by the underwriters of a greater number of shares than the total number set forth in the table above. They may exercise that option for 30 days. If any shares are purchased pursuant to this option, the underwriters will severally purchase shares in approximately the same proportion as set forth in the table above.

The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters by us. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase 1,250,000 additional shares.

Paid by the Company	No Exercise	Full Exercise
Per Share	$	$
Total	$	$

Shares sold by the underwriters to the public will initially be offered at the initial public offering price set forth on the cover of this prospectus. Any shares sold by the underwriters to securities dealers may be sold at a discount of up to $ per share from the initial public offering price. After the initial offering of the shares, the representatives may change the offering price and the other selling terms. The offering of the shares by the underwriters is subject to receipt and acceptance and subject to the underwriters' right to reject any order in whole or in part.

We, our officers, directors, and holders of substantially all of our common stock and securities convertible into or exchangeable for our common stock have agreed that, without the prior written consent of the representatives on behalf of the underwriters, we and they will not, subject to certain exceptions, dispose of or hedge any common stock or securities convertible into or exchangeable for shares of common stock during the period from the date of this prospectus continuing through the date 180 days after the date of this prospectus. This agreement does not apply to any existing employee benefit plans. See the section titled “Shares Eligible for Future Sale” for a discussion of certain transfer restrictions.

Prior to the offering, there has been no public market for the shares. The initial public offering price will be negotiated among the representatives and us. Among the factors to be considered in determining the initial public offering price of the shares, in addition to prevailing market conditions, will be our historical performance, estimates of our business potential and earnings prospects, an assessment of our management and the consideration of the above factors in relation to market valuation of companies in related businesses.

We have applied to list our common stock on NASDAQ under the symbol “DNLI.”

In connection with the offering, the underwriters may purchase and sell shares of common stock in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering, and a short position represents the amount of such sales that have not been covered by subsequent purchases. A “covered short position” is a short position that is not greater than the amount of additional shares for which the underwriters’ option described above may be exercised. The underwriters may cover any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to cover the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase additional shares pursuant to the option described above. “Naked” short sales are any short sales that create a short position greater than the amount of additional shares for which the option described above may be exercised. The underwriters must cover any such naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of common stock made by the underwriters in the open market prior to the completion of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it, because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Purchases to cover a short position and stabilizing transactions, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of our stock, and together with the imposition of the penalty bid, may stabilize, maintain or otherwise affect the market price of the common stock. As a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. The underwriters are not required to engage in these activities and may end any of these activities at any time. These transactions may be effected on NASDAQ, in the over-the-counter market or otherwise.

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State), an offer to the public of our common stock may

not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of our common stock may be made at any time under the following exemptions under the Prospectus Directive:

(a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;

(b) to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), subject to obtaining the prior consent of the representatives for any such offer; or

(c) in any other circumstances falling within Article 3(2) of the Prospectus Directive;

provided that no such offer of shares of our common stock shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to our common stock in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and our common stock to be offered so as to enable an investor to decide to purchase our common stock, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression "Prospectus Directive" means Directive 2003/71/EC (as amended), including by Directive 2010/73/EU and includes any relevant implementing measure in the Relevant Member State.

This European Economic Area selling restriction is in addition to any other selling restrictions set out below.

United Kingdom

In the United Kingdom, this prospectus is only addressed to and directed as qualified investors who are (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the Order); or (ii) high net worth entities and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as "relevant persons"). Any investment or investment activity to which this prospectus relates is available only to relevant persons and will only be engaged with relevant persons. Any person who is not a relevant person should not act or relay on this prospectus or any of its contents.

Canada

The common stock may be sold in Canada only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions, and Ongoing Registrant Obligations. Any resale of the common stock must be made in accordance with an exemption form, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Hong Kong

The common stock may not be offered or sold in Hong Kong by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32 of the Laws of Hong Kong), or Companies (Winding Up and Miscellaneous Provisions) Ordinance, or which do not constitute an invitation to the public within the meaning of the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong), or Securities and Futures Ordinance, or (ii) to "professional investors" as defined in the Securities and Futures Ordinance and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance, and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares of common stock which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" in Hong Kong as defined in the Securities and Futures Ordinance and any rules made thereunder.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the common stock may not be circulated or distributed, nor may the common stock be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor (as defined under Section 4A of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, under Section 274 of the SFA, (ii) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to conditions set forth in the SFA.

Where the shares of common stock are subscribed or purchased under Section 275 of the SFA by a relevant person which is a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor, the securities (as defined in Section 239(1) of the SFA) of that corporation shall not be transferable for 6 months after that corporation has acquired the common stock under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer in that corporation's securities pursuant to Section 275(1A) of the SFA, (3) where no consideration is or will be given for the transfer, (4) where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore, or Regulation 32.

Where the shares of common stock are subscribed or purchased under Section 275 of the SFA by a relevant person which is a trust (where the trustee is not an accredited investor (as defined in Section 4A of the SFA)) whose sole purpose is to hold investments and each beneficiary of the trust is

an accredited investor, the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferable for 6 months after that trust has acquired the common stock under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer that is made on terms that such rights or interest are acquired at a consideration of not less than S$200,000 (or its equivalent in a foreign currency) for each transaction (whether such amount is to be paid for in cash or by exchange of securities or other assets), (3) where no consideration is or will be given for the transfer, (4) where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32.

Japan

The common stock has not been and will not be registered under the Financial Instruments and Exchange Act of Japan (Act No. 25 of 1948, as amended), or the FIEA. The common stock may not be offered or sold, directly or indirectly, in Japan or to or for the benefit of any resident of Japan (including any person resident in Japan or any corporation or other entity organized under the laws of Japan) or to others for reoffering or resale, directly or indirectly, in Japan or to or for the benefit of any resident of Japan, except pursuant to an exemption from the registration requirements of the FIEA and otherwise in compliance with any relevant laws and regulations of Japan.

We estimate that our share of the total expenses of the offering, excluding underwriting discounts and commissions, will be approximately $3,500,000. We will agree to reimburse the underwriters for expenses related to any applicable state securities filings and to the Financial Industry Regulatory Authority incurred by them in connection with this offering in an amount up to $35,000. The underwriters will agree to reimburse us, or will pay and not seek reimbursement from us, for certain out-of-pocket expenses incurred by us in connection with this offering.

We will agree to indemnify the several underwriters against certain liabilities, including liabilities under the Securities Act.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. Certain of the underwriters and their respective affiliates have provided, and may in the future provide, a variety of these services to the issuer and to persons and entities with relationships with the issuer, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and their respective affiliates, officers, directors and employees may purchase, sell or hold a broad array of investments and actively trade securities, derivatives, loans, commodities, currencies, credit default swaps and other financial instruments for their own account and for the accounts of their customers, and such investment and trading activities may involve or relate to assets, securities and/or instruments of the issuer (directly, as collateral securing other obligations or otherwise) and/or persons and entities with relationships with the issuer. The underwriters and their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

LEGAL MATTERS

The validity of the issuance of our common stock offered in this prospectus will be passed upon for us by Wilson Sonsini Goodrich & Rosati, Professional Corporation, Palo Alto, California. Davis Polk & Wardwell LLP, Menlo Park, California, is acting as counsel for the underwriters.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements at December 31, 2016 and 2015, and for each of the two years in the period ended December 31, 2016, as set forth in their report. We have included our consolidated financial statements in the prospectus and elsewhere in the registration statement in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of our common stock offered by this prospectus. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement, as permitted by the rules and regulations of the SEC. For further information with respect to us and our common stock, we refer you to the registration statement, including the exhibits filed as a part of the registration statement. Statements contained in this prospectus concerning the contents of any contract or any other document is not necessarily complete. If a contract or document has been filed as an exhibit to the registration statement, please see the copy of the contract or document that has been filed. Each statement in this prospectus relating to a contract or document filed as an exhibit is qualified in all respects by the filed exhibit. You may obtain copies of this information by mail from the Public Reference Section of the SEC, 100 F Street, N.E., Room 1580, Washington, D.C. 20549, at prescribed rates or view them online. You may obtain information on the operation of the public reference rooms by calling the SEC at 1-800-SEC-0330. The SEC also maintains an Internet website that contains the registration statement of which this prospectus forms a part, as well as the exhibits thereto. These documents, along with future reports, proxy statements and other information about us, are available at the SEC's website, www.sec.gov.

As a result of this offering, we will become subject to the information and reporting requirements of the Exchange Act, as amended, and, in accordance with this law, will file periodic reports, proxy statements and other information with the SEC. These periodic reports, proxy statements and other information will be available for inspection and copying at the SEC's public reference facilities and the website of the SEC referred to above. We also maintain a website at www.denalitherapeutics.com. Upon the completion of this offering, you may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. Information contained on our website is not a part of this prospectus, and the inclusion of our website address in this prospectus is an inactive textual reference only.

GLOSSARY

Abeta	amyloid beta
ALS	amyotrophic lateral sclerosis
AMP	average manufacturer price
Amyloid	complex proteins deposited in tissues that form the primary component of plaques characteristic of Alzheimer's disease
Amyloid plaques	accumulations of amyloid
ANDA	abbreviated new drug application to the FDA
APP	amyloid precursor protein
Assay	procedure to assess the amount or activity of a target entity
aSyn	alpha-synuclein
ATV	antibody transport vehicle
BACE1	beta-secretase 1
BBB	blood-brain barrier
Biomarker	a biological molecule found in blood, other bodily fluids or tissues that is a sign of a normal or abnormal process or of a condition or disease
BLA	biologics license application to the FDA
cGCPs	current good clinical practices promulgated by the FDA
cGMPs	current good manufacturing practices promulgated by the FDA
CHMP	Committee for Medicinal Products for Human Use
Cmax	predicted maximum concentration
CMO	third-party contract manufacturer
CMS	Centers for Medicare & Medicaid Services
CRO	contract research organization
CSF	cerebrospinal fluid
CTA	clinical trial application to the EMA
DAT	dopamine transporter imaging
Degenogenes	genes, that when mutated, cause, or are major risk factors for, neurodegenerative diseases
DLB	dementia with Lewy bodies
DNA	deoxyribonucleic acid
EEA	European Economic Area
EMA	European Medicines Agency
ETV	enzyme transport vehicle
Fabs	targets bound by the variable domains of an antibody or other therapeutic modalities

Fcabs	constant Fc domains of an antibody with non-native antigen binding activity
FDA	U.S. Food and Drug Administration
GAGs	glycosaminoglycans
GBA	glucocerebrosidase, a lysosomal enzyme
GCP	good clinical practice promulgated by the FDA
Glial cells	non-neuronal cells that maintain homeostasis, form myelin and support, protect and provide nutrition to neurons
GLP	good laboratory practice promulgated by the FDA
Homeostasis	the ability of cellular or molecular pathways to seek and maintain a condition of equilibrium or stability within its internal environment when dealing with cellular stress and genetic variation
IDS	iduronate 2-sulfatase, a lysosomal enzyme
IMM	irreversible morbidity or mortality
IND	investigational new drug
IRB	Institutional Review Board
Kinase	an enzyme that catalyzes the addition of a phosphate group to substrates, usually proteins
LRRK2	leucine-rich repeat kinase 2
LSD	lysosomal storage disease
Lysosomal system	the disposal and recycling compartment of a cell, which is involved in the digestion and processing of proteins and lipids in brain cells
MA	Marketing Authorization
MAA	marketing authorization application
Microglial cells	types of glial cells that are the resident macrophages of the brain and spinal cord, and thus act as the first and main form of active immune defense in the central nervous system
MPS II	mucopolysaccharidosis type II, also known as Hunter Syndrome
MSA	multiple system atrophy
NDA	new drug application to the FDA
Neurodegenerative disease	a condition defined by progressive nervous system dysfunction, degeneration and/or death of neurons causing cognitive decline, functional impairment and eventually death
Neurofibrillary tangles	aggregates of hyperphosphorylated Tau protein that are a marker of Alzheimer’s disease and other diseases known as tauopathies
OPTN	Optineurin
Orange Book	Approved Drug Products with Therapeutic Equivalence Evaluations
PBMC	peripheral blood mononuclear cell
PD	pharmacodynamic

PK	pharmacokinetic
PK/PD	pharmacokinetic/pharmacodynamic
Proteinopathy	disease that results from disorders of protein synthesis, trafficking, folding, processing or degradation in cells
pRab10	phosphorylation of Rab10 on Threonine 73
pS166	phosphorylation of RIPK1 at Serine 166
pS935	phosphorylation of LRRK2 at Serine 935
Reagent	substance used to characterize or quantify a biological process or component
REMS	Risk Evaluation and Mitigation Strategy
RIPK1	receptor interacting serine/threonine protein kinase 1
RMS	Reference Member State
RMT	receptor-mediated transcytosis
RNA	ribonucleic acid
SPC	summary of product characteristics
TBK	Tank Binding Kinase
TfR	transferrin receptor
TNIP1	TNFAIP3-interacting protein 1
TREM2	triggering receptor expressed in myeloid cells 2
TSPO	translocator protein
TV	transport vehicle

DENALI THERAPEUTICS INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of Denali Therapeutics Inc.

We have audited the accompanying consolidated balance sheets of Denali Therapeutics Inc. as of December 31, 2016 and 2015, and the related consolidated statements of operations and comprehensive loss, stockholders' (deficit) and cash flows for each of the two years in the period ended December 31, 2016. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Denali Therapeutics Inc. at December 31, 2016 and 2015, and the consolidated results of its operations and its cash flows for each of the two years in the period ended December 31, 2016, in conformity with U.S. generally accepted accounting principles.

Ernst & Young LLP

Redwood City, California
September 8, 2017, except for the second paragraph of Note 1 and for Note 13, as to which the date is December , 2017

The foregoing report is in the form that will be signed upon the completion of the reverse stock split described in the second paragraph of Note 1 to the consolidated financial statements.

/s/ Ernst & Young LLP

Redwood City, California
November 27, 2017

Denali Therapeutics Inc.

Consolidated Balance Sheets
(In thousands, except share amounts)

	December 31,		Pro Forma Stockholders' Equity as of December 31,
	2015	2016	2016 (Unaudited)
Assets			
Current assets:			
Cash and cash equivalents	$ 30,740	$ 39,853	
Short-term marketable securities	—	138,478	
Prepaid expenses and other current assets	2,691	3,624	
Total current assets	33,431	181,955	
Long-term marketable securities	—	72,580	
Property and equipment, net	3,168	15,262	
Other non-current assets	84	1,270	
Total assets	$ 36,683	$ 271,067	
Liabilities, convertible preferred stock and stockholders' equity (deficit)			
Current liabilities:			
Accounts payable	$ 1,713	$ 1,963	
Accrued liabilities	603	3,850	
Accrued compensation	1,017	2,592	
Deferred rent and other current liabilities	148	701	
Total current liabilities	3,481	9,106	
Deferred rent	18	7,045	
Other non-current liabilities	510	397	
Total liabilities	4,009	16,548	
Commitments and contingencies (Note 7)			
Convertible preferred stock, $0.01 par value; 61,028,466 and 63,288,466 shares authorized as of December 31, 2015 and 2016, respectively; 12,197,880 and 58,600,315 shares issued and outstanding as of December 31, 2015 and 2016, respectively; aggregate liquidation preference of $51,131 and $370,071 as of December 31, 2015 and 2016, respectively; no shares issued and outstanding, pro forma (unaudited)	48,308	348,673	$ —
Stockholders' equity (deficit):			
Common stock, $0.01 par value; 79,527,362 and 83,587,362 shares authorized as of December 31, 2015 and 2016, respectively; 4,260,560 and 8,597,316 shares issued and outstanding, as of December 31, 2015 and 2016, respectively; 67,197,631 shares issued and outstanding, pro forma (unaudited)	170	344	2,688
Additional paid-in capital	1,056	9,387	355,716
Accumulated other comprehensive loss	—	(373)	(373)
Accumulated deficit	(16,860)	(103,512)	(103,512)
Total stockholders' equity (deficit)	(15,634)	(94,154)	254,519
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	$ 36,683	$ 271,067	$ 271,067

See accompanying notes to consolidated financial statements.

Denali Therapeutics Inc.

Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except share and per share amounts)

	Year ended December 31,	
	2015	2016
Operating expenses:		
Research and development	$ 11,571	$ 75,702
General and administrative	5,108	11,731
Total operating expenses	16,679	87,433
Loss from operations	(16,679)	(87,433)
Interest income (expense), net	(109)	781
Net loss	(16,788)	(86,652)
Other comprehensive loss:		
Net unrealized loss on marketable securities, net of tax	—	(373)
Comprehensive loss	$ (16,788)	$ (87,025)
Net loss per share, basic and diluted	$ (5.58)	$ (13.49)
Weighted average number of shares outstanding, basic and diluted	3,006,379	6,424,720
Pro forma net loss per share, basic and diluted (unaudited)		$ (1.77)
Weighted-average number of shares used in computing pro forma net loss per share, basic and diluted (unaudited)		48,924,244

See accompanying notes to consolidated financial statements.

Denali Therapeutics Inc.

Consolidated Statements of Convertible Preferred Stock and Stockholders' (Deficit)
(In thousands, except share amounts)

	Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' (Deficit)
	Shares	Amount	Shares	Amount				
Balance at December 31, 2014	—	$ —	887,324	$ 35	$ —	$ —	$ (70)	$ (35)
Issuance of common stock	—	—	2,815,787	113	(1)	—	(2)	110
Issuance of common stock as consideration in asset acquisition	—	—	472,942	19	581	—	—	600
Issuance of series A-1 convertible preferred stock, net of issuance costs of $484	12,197,880	48,308	—	—	—	—	—	—
Vesting of restricted stock awards	—	—	84,507	3	(3)	—	—	—
Stock-based compensation	—	—	—	—	479	—	—	479
Net loss	—	—	—	—	—	—	(16,788)	(16,788)
Balance at December 31, 2015	**12,197,880**	**48,308**	**4,260,560**	**170**	**1,056**	**—**	**(16,860)**	**(15,634)**
Issuance of series A-1 convertible preferred stock, net of issuance costs of $23	33,916,543	135,643	—	—	—	—	—	—
Issuance of series A-2 convertible preferred stock, net of issuance costs of $7	4,361,527	34,885	—	—	—	—	—	—
Issuance of series B-1 convertible preferred stock, net of issuance costs of $153	8,124,365	129,837	—	—	—	—	—	—
Issuance of common stock as contingent consideration in asset acquisition	—	—	945,880	38	5,242	—	—	5,280
Issuance of common stock upon exercise of stock options	—	—	162,665	6	105	—	—	111
Vesting of early exercised common stock	—	—	239,580	10	153	—	—	163
Vesting of restricted stock awards	—	—	2,988,631	120	(120)	—	—	—
Stock-based compensation	—	—	—	—	2,951	—	—	2,951
Net loss	—	—	—	—	—	—	(86,652)	(86,652)
Other comprehensive loss	—	—	—	—	—	(373)	—	(373)
Balance at December 31, 2016	**58,600,315**	**$348,673**	**8,597,316**	**$ 344**	**$ 9,387**	**$ (373)**	**$ (103,512)**	**$ (94,154)**

See accompanying notes to consolidated financial statements.

Denali Therapeutics Inc.

Consolidated Statements of Cash Flows
(In thousands)

	Year ended December 31, 2015	2016
Operating activities		
Net loss	$(16,788)	$ (86,652)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	121	1,469
Stock-based compensation expense	479	2,951
Non-cash interest expense	110	—
Net amortization of premiums and discounts on marketable securities	—	304
Loss on disposal of property and equipment	—	3
Fair value of common stock issued in connection with asset acquisition	600	5,280
Changes in operating assets and liabilities:		
Restricted cash	(84)	(451)
Prepaid expenses and other assets	(2,691)	(533)
Accounts payable	1,678	161
Accrued and other current liabilities	1,607	5,357
Other non-current liabilities	(84)	(248)
Net cash used in operating activities	(15,052)	(72,359)
Investing activities		
Purchase of marketable securities	—	(226,370)
Purchase of property and equipment	(3,062)	(6,134)
Purchase of other investments	—	(500)
Maturities and sales of marketable securities	—	14,000
Net cash used in investing activities	(3,062)	(219,004)
Financing activities		
Proceeds from convertible promissory note received from a related party	5,000	—
Proceeds from exercise of common stock options	510	111
Proceeds from issuance of common stock	110	—
Proceeds from issuance of convertible preferred stock, net of issuance costs	43,234	300,365
Net cash provided by financing activities	48,854	300,476
Net increase in cash and cash equivalents	30,740	9,113
Cash and cash equivalents at beginning of year	—	30,740
Cash and cash equivalents at end of year	$ 30,740	$ 39,853
Supplemental disclosures of cash flow information		
Convertible preferred stock issuance costs incurred but not yet paid	$ 36	$ —
Property and equipment purchases accrued but not yet paid	$ 126	$ 233
Conversion of convertible promissory note and interest into convertible preferred stock	$ 5,110	$ —

See accompanying notes to consolidated financial statements.

Denali Therapeutics Inc.
Notes to Consolidated Financial Statements

1. Significant Accounting Policies

Organization and Description of Business

Denali Therapeutics Inc. ("Denali" or the "Company") is a biopharmaceutical company, incorporated in Delaware, that discovers and develops therapeutics to defeat degeneration. The Company was incorporated in October 2013 as SPR Pharma Inc. The Company's name was changed to Denali Therapeutics Inc. in March 2015. The Company is headquartered in South San Francisco, California.

Basis of Presentation

These consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP"). All share and per share information included in the accompanying consolidated financial statements has been adjusted to reflect a 4-for-1 reverse stock split to be effected prior to the completion of this offering.

Principles of Consolidation

These consolidated financial statements include the accounts of the Company and its wholly-owned subsidiary. This subsidiary was dissolved in September 2016. All intercompany balances and transactions have been eliminated on consolidation.

The Company assesses whether it is the primary beneficiary of a variable interest entity ("VIE") at the inception of the arrangement and at each reporting date. This assessment is based on the Company's power to direct the activities of the VIE that most significantly impact the VIE's economic performance and the Company's obligation to absorb losses or the right to receive benefits from the VIE that could potentially be significant to the VIE.

Unaudited Pro Forma Information

Immediately prior to the completion of this offering, all outstanding shares of convertible preferred stock will automatically convert into common stock. Unaudited pro forma balance sheet information as of December 31, 2016 assumes the conversion of all outstanding convertible preferred stock into shares of common stock. The shares of common stock issuable and the proceeds expected to be received in the initial public offering are excluded from such pro forma financial information. Pro forma basic and diluted net loss per share has been computed to give effect to the conversion of all outstanding convertible preferred stock into shares of common stock. The unaudited pro forma net loss per share does not include the shares expected to be sold and related proceeds to be received from the initial public offering. The unaudited pro forma net loss per share for the year ended December 31, 2016 was computed using the weighted-average number of shares of common stock outstanding, including the pro forma effect of the conversion of all outstanding shares of convertible preferred stock into shares of common stock, as if such conversion had occurred at the beginning of the period, or their issuance dates if later.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires the Company to make certain estimates, judgments, and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial

statements, as well as the reported amounts of expenses during the reporting period. Actual results could differ from those estimates, and such differences could be material to the consolidated financial position and results of operations.

Concentration of Credit Risk and Other Risks and Uncertainties

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist primarily of cash, cash equivalents and marketable securities. Substantially all of the Company's cash and cash equivalents are deposited in accounts with three financial institutions that management believes are of high credit quality. Such deposits have and will continue to exceed federally insured limits. The Company maintains its cash with accredited financial institutions and accordingly, such funds are subject to minimal credit risk. The Company has not experienced any losses on its cash deposits.

The Company's investment policy limits investments to certain types of securities issued by the U.S. government, its agencies and institutions with investment-grade credit ratings and places restrictions on maturities and concentration by type and issuer. The Company is exposed to credit risk in the event of a default by the financial institutions holding its cash, cash equivalents and marketable securities and issuers of marketable securities to the extent recorded on the consolidated balance sheets. As of December 31, 2016, the Company has no off-balance sheet concentrations of credit risk.

The Company is subject to a number of risks similar to other early-stage biopharmaceutical companies, including, but not limited to, the need to obtain adequate additional funding, possible failure of current or future preclinical testing or clinical trials, its reliance on third parties to conduct its clinical trials, the need to obtain regulatory and marketing approvals for its product candidates, competitors developing new technological innovations, the need to successfully commercialize and gain market acceptance of the Company's product candidates, its right to develop and commercialize its product candidates pursuant to the terms and conditions of the licenses granted to the Company, protection of proprietary technology, the ability to make milestone, royalty or other payments due under any license or collaboration agreements, and the need to secure and maintain adequate manufacturing arrangements with third parties. If the Company does not successfully commercialize or partner any of its product candidates, it will be unable to generate product revenue or achieve profitability.

Need for Additional Capital

Since inception, the Company has incurred net losses and negative cash flows from operations. During the year ended December 31, 2016, the Company incurred a net loss of $86.7 million and used $72.4 million of cash in operations. At December 31, 2016, the Company had an accumulated deficit of $103.5 million and does not expect to experience positive cash flows in the foreseeable future. The Company has financed its operations to date primarily through the sale and issuance of convertible preferred stock. Management expects to incur additional operating losses in the future as the Company continues the development of, and seeks regulatory approvals for, its product candidates, and begins to commercialize any approved products, and recognizes the need to raise additional capital to fully implement its business plan. The Company intends to raise such capital through public or private equity financings, strategic alliances with third parties and potentially through debt financings. The Company had $250.9 million of cash, cash equivalents and marketable securities at December 31, 2016. Based on the Company's business plans, management believes that this is sufficient to meet its obligations for at least the next twelve months from the issuance date of these consolidated financial statements.

Denali Therapeutics Inc.
Notes to Consolidated Financial Statements

Segments

The Company has one operating segment. The Company's chief operating decision maker, its Chief Executive Officer, manages the Company's operations on a consolidated basis for the purposes of allocating resources.

Fair Value of Financial Instruments

ASC Topic 820, Fair Value Measurement ("ASC 820"), establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability, and are developed based on the best information available in the circumstances.

ASC 820 identifies fair value as the exchange price, or exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions in fair value measurements, ASC 820 establishes a three-tier fair value hierarchy that distinguishes between the following:

Level 1 – inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities.

Level 2 – inputs are inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly.

Level 3 – inputs are unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability. Financial assets and liabilities are classified in their entirety based on the lowest level of input that is significant to the fair value measurement.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The carrying amounts reflected in the consolidated balance sheets for cash and cash equivalents, prepaid expenses and other current assets, accounts payable and accrued liabilities approximate their fair values, due to their short-term nature.

Cash and Cash Equivalents

The Company considers all highly liquid investments with original maturities of 90 days or less at the date of purchase to be cash and cash equivalents. Cash equivalents, which consist primarily of highly liquid investments with maturities of three months or less when purchased, are stated at fair value.

Marketable Securities

The Company generally invests its excess cash in money market funds and investment grade short to intermediate-term fixed income securities. Such investments are included in cash and cash

equivalents, short-term marketable securities, or long-term marketable securities on the balance sheets, are considered available-for-sale, and reported at fair value with unrealized gains and losses included as a component of stockholders' deficit. The amortized cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity, which is included in interest income (expense), net on the consolidated statements of operations. Realized gains and losses and declines in value judged to be other-than-temporary, if any, on marketable securities are included in interest income (expense), net. The cost of securities sold is determined using specific identification.

The Company periodically evaluates whether declines in fair values of its marketable securities below their book value are other-than-temporary. This evaluation consists of several qualitative and quantitative factors regarding the severity and duration of the unrealized loss as well as the Company's ability and intent to hold the marketable security until a forecasted recovery occurs. Additionally, the Company assesses whether it has plans to sell the security or it is more likely than not it will be required to sell any marketable securities before recovery of its amortized cost basis. Factors considered include quoted market prices, recent financial results and operating trends, implied values from any recent transactions or offers of investee securities, credit quality of debt instrument issuers, other publicly available information that may affect the value of the marketable security, duration and severity of the decline in value, and management's strategy and intentions for holding the marketable security.

Restricted Cash

The Company's restricted cash consists of restricted cash in connection with the building leases for the Company's former and current headquarters. The current portion of $0.1 million is classified within prepaid expenses and other current assets and the non-current portion of $0.5 million is classified within other non-current assets on the accompanying consolidated balance sheets.

Property and Equipment, Net

Property and equipment are stated at cost, net of accumulated depreciation. Depreciation is computed using the straight-line method over the related estimated useful lives as presented in the table below. Significant additions and improvements are capitalized, while repairs and maintenance are charged to expense as incurred.

Leasehold improvements	Shorter of life of asset or lease term
Manufacturing and laboratory equipment	5 years
Computer hardware and software	3 years
Office furniture and equipment	5 years

Impairment of Long-Lived Assets

The Company periodically evaluates property and equipment for impairment whenever events or changes in circumstances indicate that a potential impairment may have occurred. If such events or changes in circumstances arise, the Company compares the carrying amount of the long-lived assets to the estimated future undiscounted cash flows expected to be generated by the long-lived assets. If the estimated aggregate undiscounted cash flows are less than the carrying amount of the long-lived assets, an impairment charge, calculated as the amount by which the carrying amount of the assets exceeds the fair value of the assets, is recorded. The fair value of the long-lived assets is determined based on the estimated discounted cash flows expected to be generated from the long-lived assets. The Company has not recorded any such impairment charges during the years presented.

Denali Therapeutics Inc.
Notes to Consolidated Financial Statements

Deferred Rent

Certain of the Company's operating lease agreements include scheduled rent escalations over the lease term, as well as tenant improvement allowances. Rent expense is charged ratably over the life of the lease. Deferred rent consists of the difference between cash payments and the recognition of rent expense on a straight-line basis for the buildings the Company occupies. Tenant improvement allowances are recorded as a deferred rent liability and are amortized on a straight-line basis over the term of the lease as a reduction to rent expense.

Research and Development Expenses

Research and development costs are expensed as incurred. Research and development costs consist of salaries and other personnel related expenses, including associated stock-based compensation, consulting fees, lab supplies, and facility costs, as well as fees paid to other entities that conduct certain research, development and manufacturing activities on behalf of the Company.

Nonrefundable advance payments for goods and services that will be used or rendered in future research and development activities are deferred and recognized as expense in the period in which the related goods are delivered or services are performed.

The Company has and may continue to acquire the rights to develop and commercialize new product candidates from third parties. The upfront payments to acquire license, product or rights, as well as any future milestone payments, are immediately recognized as research and development expense provided that there is no alternative future use of the rights in other research and development projects.

Stock-Based Compensation

The Company measures employee and director stock-based compensation expense for all stock-based awards at the grant date based on the fair value measurement of the award. The expense is recorded on a straight-line basis over the requisite service period, which is generally the vesting period, for the entire award. Expense is adjusted for actual forfeitures of unvested awards as they occur. The Company calculates the fair value measurement of stock options using the Black-Scholes valuation model.

The Company granted restricted stock awards that vest in conjunction with certain performance and market conditions to certain key employees and directors. At each reporting date, the Company is required to evaluate whether achievement of the performance conditions is probable. Compensation expense is recorded over the appropriate service period based upon the Company's assessment of accomplishing each performance provision.

The Company accounts for stock options issued to non-employees in accordance with the provisions of ASC 505-50, Equity-Based Payments to Non-employees, which requires valuing the stock options on their grant date and remeasuring such stock options at the current fair value at the end of each reporting period until they vest.

Income Taxes

Income taxes are accounted for using the liability method, under which deferred tax assets and liabilities are determined based on the differences between the financial reporting and tax bases of

assets and liabilities and consideration is given to net operating losses and tax credit carryforwards. Deferred tax assets and liabilities are measured using the enacted tax rates that are expected to be in effect when the differences are expected to reverse.

The Company assesses the likelihood that deferred tax assets will be recovered from future taxable income, and a valuation allowance is established when necessary to reduce deferred tax assets to the amounts more likely than not expected to be realized.

The Company recognizes and measures uncertain tax positions using a two–step approach. The first step is to evaluate the tax position taken or expected to be taken by determining whether the weight of available evidence indicates that it is more likely than not that the tax position will be sustained in an audit, including resolution of any related appeals or litigation processes. The second step is to measure the tax benefit as the largest amount that is more than 50% likely to be realized upon ultimate settlement. Significant judgment is required to evaluate uncertain tax positions. The Company evaluates uncertain tax positions on a regular basis. The evaluations are based on a number of factors, including changes in facts and circumstances, changes in tax law, correspondence with tax authorities during the course of the audit, and effective settlement of audit issues.

Comprehensive Loss

Comprehensive loss includes net loss and certain changes in stockholders' deficit that are excluded from net loss, primarily unrealized losses on the Company's marketable securities.

Net Loss per Share

Basic net loss per share is calculated by dividing the net loss by the weighted-average number of shares of common stock outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is the same as basic net loss per share, since the effects of potentially dilutive securities are antidilutive given the net loss for each period presented.

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2014-09 ("ASU 2014-09"), Revenue from Contracts with Customers (Topic 606), and further updated through ASU 2016-12 ("ASU 2016-12"), which amends the existing accounting standards for revenue recognition. ASU 2014-09 is based on principles that govern the recognition of revenue at an amount to which an entity expects to be entitled when products are transferred to customers. This guidance is effective for annual reporting periods, and interim periods within those years, beginning after December 15, 2017, for public entities and no later than for annual reporting periods beginning after December 15, 2018, for non-public entities. The new revenue standard may be applied retrospectively to each prior period presented or retrospectively with the cumulative effect recognized as of the date of adoption. While the Company continues to assess all potential impacts under ASU 2014-09, it does not believe adopting the new revenue standard will have a material impact on its consolidated financial statements as the Company is not yet generating revenues.

In February 2016, the FASB issued ASU No. 2016-02 ("ASU 2016-02"), Leases (Topic 842), which supersedes the guidance in former ASC 840, Leases. The new standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will

determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than 12 months regardless of their classification. Leases with a term of 12 months or less will be accounted for similar to existing guidance for operating leases today. The standard is effective for interim and annual periods beginning after December 15, 2018, with early adoption permitted. The ASU is expected to impact the Company's consolidated financial statements as the Company has certain operating lease arrangements for which the Company is the lessee. Management is currently evaluating the impact the adoption of ASU 2016-02 will have on the Company's financial position and results of operations. Management expects that the adoption of this standard will result in the recognition of an asset for the right to use the leased facility on the Company's balance sheet, as well as the recognition of a liability for the lease payments remaining on the lease. While the balance sheet presentation is expected to change, management does not expect a material change to the consolidated statement of operations.

In November 2016, the FASB issued ASU 2016-18, Statement of Cash Flows (Topic 230): Restricted Cash. The purpose of Update No. 2016-18 is to clarify guidance and presentation related to restricted cash in the statement of cash flows. The amendment requires beginning-of-period and end-of-period total amounts shown on the statement of cash flows to include cash and cash equivalents as well as restricted cash and restricted cash equivalents. The update is effective for fiscal years beginning after December 15, 2017, including interim reporting periods within those fiscal years. Early adoption is permitted. The Company is currently evaluating the impact of adopting this standard on the consolidated financial statements and disclosures, but does not expect it to be material.

In May 2017, the FASB issued ASU 2017-09, Compensation - Stock Compensation (Topic 718): Scope of Modification Accounting, which clarifies when to account for a change to the terms or conditions of a share-based payment award as a modification. Under the new guidance, modification accounting is required only if the fair value, the vesting conditions, or the classification of the award (as equity or liability) changes as a result of the change in terms or conditions. It is effective for annual and interim periods beginning after December 15, 2017. Early adoption is permitted. The Company is currently evaluating the impact of adopting this standard on the consolidated financial statements and disclosures, but does not expect it to have a significant impact.

Denali Therapeutics Inc.
Notes to Consolidated Financial Statements

2. Fair Value Measurements

Assets measured at fair value as of December 31, 2016 are as follows (in thousands):

	Fair Value Measurements			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	$28,705	$ —	$ —	$ 28,705
Short-term:				
U.S. government treasuries	22,268	—	—	22,268
U.S. government agency securities	—	70,787	—	70,787
Corporate debt securities	—	38,941	—	38,941
Commercial paper	—	6,482	—	6,482
Long-term:				
U.S. government treasuries	4,989	—	—	4,989
U.S. government agency securities	—	52,868	—	52,868
Corporate debt securities	—	14,723	—	14,723
Total marketable securities	27,257	183,801	—	211,058
Total fair value measurements	**$55,962**	**$183,801**	**$ —**	**$239,763**

The carrying amounts of accounts payable and accrued liabilities approximate their fair values due to their short-term maturities.

The Company's Level 2 securities are valued using third-party pricing sources. The pricing services utilize industry standard valuation models, including both income and market-based approaches, for which all significant inputs are observable, either directly or indirectly.

There were no transfers of assets or liabilities between the fair value measurement levels during the year ended December 31, 2016.

Denali Therapeutics Inc.
Notes to Consolidated Financial Statements

3. Marketable Securities

All marketable securities were considered available-for-sale at December 31, 2016. The amortized cost, unrealized holding gains or losses, and fair value of the Company's marketable securities by major security type at December 31, 2016 are summarized in the table below (in thousands):

	Amortized Cost	Unrealized Holding Gains	Unrealized Holding Losses	Aggregate Fair Value at December 31, 2016
Short-term marketable securities:				
U.S. government treasuries	$ 22,277	$ —	$ (9)	$ 22,268
U.S. government agency securities	70,835	—	(48)	70,787
Corporate debt securities	39,037	—	(96)	38,941
Commercial paper	6,482	—	—	6,482
Total short-term marketable securities	138,631	—	(153)	138,478
Long-term marketable securities:				
U.S. government treasuries	4,996	1	(8)	4,989
U.S. government agency securities	53,005	—	(137)	52,868
Corporate debt securities	14,799	—	(76)	14,723
Total long-term marketable securities	72,800	1	(221)	72,580
Total	**$211,431**	**$ 1**	**$ (374)**	**$ 211,058**

As of December 31, 2016, some of the Company's marketable securities were in an unrealized loss position. The Company determined that it did have the ability and intent to hold all marketable securities that have been in a continuous loss position until maturity or recovery, thus there has been no recognition of any other-than-temporary impairment in the year ended December 31, 2016. All marketable securities with unrealized losses as of December 31, 2016 have been in a loss position for less than twelve months or the loss is not material.

All of the Company's short-term marketable securities have an effective maturity date of less than one year, and all of the Company's long-term marketable securities have an effective maturity of less than two years.

4. Acquisition

In June 2015, the Company acquired Incro Pharmaceuticals Corporation ("Incro"), a preclinical private biotechnology company incorporated in Delaware. The primary asset purchased in the acquisition was an in-process research and development license agreement which would allow the Company to further its RIPK1 program. The Company concluded that the assets acquired and liabilities assumed did not meet the accounting definition of a business as a limited number of inputs were acquired but no processes were acquired, and the licensed technology had not achieved technological feasibility. As such, the acquisition was accounted for as an asset purchase and the Company recorded the purchase price as $1.5 million in research and development expense in the accompanying statement of operations and comprehensive loss in the year ended December 31, 2015.

As purchase consideration the Company issued an aggregate of 472,942 shares of common stock, valued at $0.6 million on the transaction date, to the former Incro stockholders, and recognized

within additional paid-in capital an obligation to issue an additional 27,054 shares of common stock, valued at $32,466, to one former Incro stockholder. The deemed fair value (see Note 10) of the Company's common stock was $1.20 per common share as of the date of the transaction. In addition to the issuance of this equity, the Company assumed liabilities of $0.9 million.

The Company also agreed to issue an additional 945,880 shares of common stock to the former Incro stockholders, and to recognize an obligation to issue 54,110 shares of common stock to one former Incro shareholder ("Milestone Shares"), upon acceptance of an investigational new drug ("IND") application by the U.S. Food and Drug Administration or an equivalent in the EU, Canada, Australia, or New Zealand within six years of the date of the acquisition. Of these shares, 350,000 shares of common stock ("Indemnification Shares") were to be held in escrow by Denali, and would be released to former stockholders of Incro within 30 days of the later of (i) expiration of 18 months after the closing; and (ii) the date the Milestone Shares vest as noted above. The number of Indemnification Shares to be released to Incro's stockholders were to be reduced to the extent of breaches of standard representations by Incro's stockholders. As this transaction was accounted for as an asset purchase rather than a business combination, no amounts were recognized on the acquisition date relating to the contingent consideration.

In August 2016, the Company filed a Clinical Trial Application ("CTA") in Europe to initiate a Phase 1 clinical trial. Upon acceptance of the CTA in September 2016, the issuance of the Milestone Shares was triggered. The Company issued a total of 595,880 shares of common stock, recognized an obligation to issue 54,110 shares of common stock, and recorded a liability for the 350,000 Indemnification Shares held in escrow. The Company recognized $5.3 million of research and development expense related to the estimated fair value of these shares of $5.28 per share during the year ended December 31, 2016. In December 2016, the 350,000 Indemnification Shares were released and issued and the related liability was extinguished upon the expiration of the 18-month period after the closing of the acquisition.

5. License and Collaboration Agreements

F-star

On August 24, 2016, the Company entered into a License and Collaboration Agreement ("Collaboration Agreement") with F-star Gamma Limited ("F-star Gamma"), f-star Biotechnologische Forschungs-und Entwicklungsges m.b.H and F-star Biotechnology Limited (collectively, "F-star"). The goal of the collaboration is the development of certain constant Fc-domains of an antibody with non-native antigen binding activity ("Fcabs"), to enhance delivery of therapeutics across the blood-brain barrier ("BBB") into the brain. The collaboration leverages F-star's modular antibody technology and the Company's expertise in the development of therapies for neurodegenerative diseases.

Under the terms of the Collaboration Agreement, the Company can nominate up to three Fcab targets ("Accepted Fcab Targets"), within the first three years of the date of the Collaboration Agreement; and the Company has selected transferrin receptor ("TfR") as the first Accepted Fcab Target. With respect to each Accepted Fcab Target, the Company can nominate up to eight Fab targets ("Accepted Fab Targets"), which are targets bound by the variable domains of an antibody or other therapeutic modalities ("Fabs"). For each accepted Fcab target, the Company is obligated to use commercially reasonable efforts during the research term to perform development activities in accordance with certain specified development plans. Under the terms of the Collaboration Agreement, the Company received non-exclusive licenses under certain intellectual property to conduct technology

development to discover and develop Fcabs. The Company is obligated to assign to F-star certain patents and know-how that the Company generates under the Collaboration Agreement related to F-star's platform technology or certain Fcabs identified solely by F-star and the Company received a non-exclusive license under certain of F-star Biotechnology's platform patents and know-how to develop and commercialize products in connection with the delivery of therapeutics across the BBB, subject to certain specified restrictions. F-star retains the right to use its intellectual property, including any intellectual property that the Company and F-star jointly own pursuant to the terms of the Collaboration Agreement, outside the scope of the licenses granted to the Company.

Under the terms of the Collaboration Agreement, the Company paid F-star Gamma an upfront fee of $5.5 million, which includes selection of the first Accepted Fcab Target. The Company is obligated to pay a one-time fixed fee in the low single-digit millions for each additional Accepted Fcab Target the Company selects, technical milestone payments for each Accepted Fcab Target, up to a maximum of $15.0 million in the aggregate for all Accepted Fcab Targets, and, at specified times, monthly exclusivity fees for Accepted Fcab Targets and Accepted Fab Targets, which may be eliminated in certain circumstances. The Company is also responsible for certain research costs incurred by F-star in conducting activities under each agreed development plan, for up to 24 months. These research costs for the agreed TfR development plan will be up to $2.1 million.

Either party may terminate the agreement if the other party materially breaches the agreement, subject to specified notice and cure provisions, or for the other party's bankruptcy or insolvency. In addition, F-star Gamma may terminate the agreement if the Company challenges any of the patent rights licensed to it by F-star. The Company is able to terminate the agreement for convenience, either in its entirety or on an Accepted Fcab Target-by-Accepted Fcab Target basis or an Accepted Fab Target-by-Accepted Fab Target basis, on 90 days' prior written notice to F-star. Unless earlier terminated, the agreement with F-star will remain in effect until all royalty and milestone payment obligations to F-star Gamma expire.

In connection with the entry into the Collaboration Agreement, the Company also purchased an option for an upfront option fee of $0.5 million (the "buy-out-option"), to acquire all of the outstanding shares of F-star Gamma pursuant to a pre-negotiated buy-out option agreement (the "Option Agreement"). The Company must elect whether to exercise its buy-out option before the earlier of (i) dosing of the fifth patient dosed in the first Phase 1 trial of an antibody that binds to an Accepted Fab Target and an Accepted Fcab Target, (ii) the fourth anniversary of the first delivery by F-star of an Fcab meeting certain delivery criteria, and (iii) five and one half years after the delivery by the Company of a notice that it is progressing an Fcab identified from the Company's library that binds to an Accepted Fcab Target. If the Company exercises this buy-out option, it will be obligated to make inital exercise payments ranging from $18.0 million to $50.0 million plus the estimated net cash held by F-star Gamma at the time of such exercise. In addition, it will be required to make certain contingent payments upon the achievement of certain preclinical, clinical, regulatory and commercial milestones, up to a maximum amount of $447.0 million in the aggregate. The amount of the initial exercise and contingent payments varies based on whether F-star delivers an Fcab that meets pre-defined criteria, whether the Fcab has been identified solely by the Company or solely by F-star or jointly by the Company and F-star and the timing of the Company's exercise of the buy-out option. Following exercise of the buy-out option, the Company will not be required to make any further milestone or royalty payments under the Collaboration Agreement. If the Company exercises the buy-out option, then f-star Biotechnologische Forschungs-und Entwicklungsges m.b.H and F-star Biotechnology will continue to be prohibited from developing, commercializing and manufacturing any antibody or other molecule that incorporates any Selected Fcab, or any Selected Fcab as a standalone product, and

from authorizing any third party to take any such action. If the Company does not exercise its option to acquire F-star Gamma prior to the expiration of the buy-out option period, then, from the lapse of the buy-out option period until the Company's rights with respect to an Accepted Fab Target expire or terminate, F-star is prohibited from developing, commercializing and manufacturing any antibody or other molecule that contains both a Selected Fcab and a Fab that specifically binds to the relevant Accepted Fab Target.

If the Company does not exercise the buy-out option, then with respect to each Accepted Fab Target, the Company has the right to obtain from F-star an exclusive, worldwide license to certain intellectual property to develop and commercialize licensed products that contain (i) a Fab that specifically binds to such Accepted Fab Target and (ii) an Fcab that the Company or F-star identifies, either solely or jointly, and that specifically binds to an Accepted Fcab Target, for up to eight Accepted Fab Targets per each Accepted Fcab Target. Each time the Company exercises such license option, it will be obligated to pay F-star Gamma (i) a one-time fixed fee in the low single-digit millions, (ii) milestone payments upon the achievement of certain clinical development and commercial milestones, up to a maximum of $362.5 million in the aggregate; (iii) additional sales-based milestones if net sales of licensed products achieve certain specified levels, up to a maximum amount payable to F-star of $650.0 million in the aggregate and (iv) low-to-mid single-digit percentage royalties on net sales of licensed products. Such amounts may be reduced by a specified percentage depending on the origin of the Fcab incorporated in the applicable licensed product and whether F-star delivers to the Company an Fcab that meets pre-defined criteria. The Company has the right to credit a certain amount of royalty payments that it pays to third parties with respect to certain licensed products against the Company's royalty obligation to F-star Gamma, up to a maximum reduction of fifty percent. The Company's royalty payment obligations will expire on a country-by-country and licensed product-by-licensed product basis upon the later of (a) the expiration of the last valid claim of a licensed patent covering such licensed product in such country, (b) the expiration of regulatory exclusivity for such licensed product in such country and (c) the twelfth anniversary of the first commercial sale of such licensed product in such country.

The Company recognized the upfront option fee of $0.5 million within other non-current assets recorded at cost. This asset will be assessed for potential impairment on an ongoing basis. No impairment charge was recognized during the year ended December 31, 2016.

The Company determined that F-star Gamma is and continues to be a variable interest entity and that the Company holds a variable interest in F-star Gamma's intellectual property assets and the related potential future product candidates these assets may produce through the Collaboration Agreement and the Option Agreement. However, the Company concluded that its governance role in the collaboration, which is specified by the terms of a joint steering committee, does not provide the Company the power to direct the activities of F-star Gamma that most significantly impact F-star Gamma's economic performance. Based on this conclusion, the Company is not considered to be the primary beneficiary of F-star Gamma; and therefore F-star Gamma is not subject to consolidation by the Company.

The Company recognized the entirety of the $5.5 million upfront license fee in research and development expense for the year ended December 31, 2016. The Company recognized an additional $0.3 million of research and development expense related to the funding of F-star Gamma research costs during the year ended December 31, 2016.

The $0.5 million other non-current asset is the only asset or liability recorded in the Company's consolidated balance sheet that relates to the Company's variable interest in F-star Gamma at

December 31, 2016. The upfront payments of $0.5 million and $5.5 million, along with 1) the obligation to fund certain future research costs, 2) any future Fcab selection fee, technical milestone payments or monthly exclusivity fees and 3) any future license fees or pre-commercial milestone payments represent the Company's maximum exposure to loss under the arrangements with F-star. The ultimate expense that the Company incurs under the arrangements with F-Star cannot be quantified at this time as the amount will vary based on the timing and outcome of future research activities.

Genentech

On June 17, 2016, the Company entered into an Exclusive License Agreement with Genentech, Inc. ("Genentech"). The agreement gives the Company access to Genentech's preclinical stage LRRK2 small molecule program, which can be used to enhance and further progress the Company's in-house LRRK2 program for Parkinson's disease. Under the agreement, Genentech granted the Company (i) an exclusive, worldwide, sublicenseable license under Genentech's rights to certain patents and patent applications directed to small molecule compounds which bind to and inhibit LRRK2 and (ii) a non-exclusive, worldwide, sublicenseable license to certain related know-how, in each case, to develop and commercialize certain compounds and licensed products incorporating any such compound. The Company is obligated to use commercially reasonable efforts during the first three years of the agreement to research, develop and commercialize at least one licensed product.

As consideration, the Company paid an upfront fee of $8.5 million and a technology transfer fee of $1.5 million, both of which are included in research and development expense for the year ended December 31, 2016 as there is no alternative future use of the rights acquired in other research and development projects.

The Company may owe Genentech milestone payments upon the achievement of certain development, regulatory, and commercial milestones, up to a maximum of $315.0 million in the aggregate, as well as royalties on net sales of licensed products ranging from low to high single-digit percentages, with the exact royalty rate dependent on various factors, including (i) whether the compound incorporated in the relevant licensed product is a Genentech-provided compound or a compound acquired or developed by the Company, (ii) the date a compound was first discovered, derived or optimized by the Company, (iii) the existence of patent rights covering the relevant licensed product in the relevant country, (iv) the existence of orphan drug exclusivity covering a licensed product that is a Genentech-provided compound and (v) the level of annual net sales of the relevant licensed product. The Company also has the right to credit a certain amount of third-party royalty and milestone payments against royalty and milestone payments owed to Genentech, up to a maximum reduction of fifty percent. The Company's royalty payment obligations will expire on a country-by-country and licensed product-by-licensed product basis upon the later of (a) ten years after the first commercial sale of such licensed product in such country and (b) the expiration of the last valid claim of a licensed patent covering such licensed product in such country.

Genentech may terminate the agreement if the Company challenges any of the patent rights licensed to the Company by Genentech, or if the Company materially breaches the agreement, subject to specified notice and cure provisions, or enters into bankruptcy or insolvency proceedings. If Genentech terminates the agreement for the Company's material breach, bankruptcy or insolvency after the Company has made a milestone payment to Genentech, then the Company is obligated to grant to Genentech an exclusive right of first negotiation with respect to certain of the Company's patents, know-how and regulatory filings directed to Genentech-provided compounds. The Company does not have the right to terminate the agreement without cause, but may terminate the agreement for Genentech's material breach, subject to specified notice and cure provisions.

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Unless earlier terminated, the agreement with Genentech will continue in effect until all of the Company's royalty and milestone payment obligations to Genentech expire. Following expiration of the agreement, the Company will retain the licenses under the intellectual property Genentech licensed to the Company on a non-exclusive, royalty-free basis.

6. Balance Sheet Components:

Property and Equipment, Net

	December 31,	
	2015	2016
	(in thousands)	
Lab equipment	$3,034	$ 8,868
Leasehold improvements	101	7,543
Computers equipment and purchased software	146	373
Furniture and fixtures	8	66
	3,289	16,850
Less: accumulated depreciation	(121)	(1,588)
Total property and equipment, net	$3,168	$15,262

Depreciation expense was $0.1 million and $1.5 million for the years ended December 31, 2015 and 2016, respectively.

Prepaid Expenses and Other Current Assets

	December 31,	
	2015	2016
	(in thousands)	
Prepaid research and development expenses	$1,652	$2,396
Accrued interest on short-term marketable securities	—	438
Prepaid employee bonuses	973	234
Other prepaid and current assets	66	556
Total prepaid expenses and other current assets	$2,691	$3,624

Other Non-Current Assets

	December 31,	
	2015	2016
	(in thousands)	
Other investments	$—	$ 500
Restricted cash	84	451
Other prepaid and non-current assets	—	319
Total other non-current assets	$ 84	$1,270

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Deferred Rent and Other Current Liabilities

	December 31, 2015	December 31, 2016
	(in thousands)	
Current portion of deferred rent liability	$ —	$538
Other current liabilities	148	163
Total deferred rent and other current liabilities	$148	$701

7. Commitments and Contingencies

Lease Obligations

In September 2015, the Company entered into a non-cancelable operating lease for its corporate headquarters comprising 38,109 of rentable square feet in a building in South San Francisco (“Headquarters Lease”). The Headquarters Lease commenced on August 1, 2016 with a lease term of eight years. The Company has an option to extend the lease term for a period of five years by giving the landlord written notice of the election to exercise the option at least nine months, but not more than twelve months, prior to the original expiration of the lease term. The Headquarters Lease provides for monthly base rent amounts escalating over the term of the lease. In addition, the Headquarters Lease provides both a tenant improvement allowance (“TIA”) of up to $7.4 million, of which $1.9 million will be repaid to the landlord in the form of additional monthly rent with interest applied. This additional monthly rent commenced in November 2016 when the entire TIA was utilized, and results in an increase of base rent of $0.4 million per year.

The Company utilized $0.1 million and $7.3 million of the TIA in the years ended December 31, 2015 and 2016, respectively. The total $7.4 million TIA has been recorded as leasehold improvements and deferred rent liability on the consolidated balance sheet. The Company is amortizing the deferred rent liability as a reduction of rent expense and the leasehold improvement through an increase of depreciation expense of leasehold improvements ratably over the lease term. Under the terms of the Headquarters Lease, the Company was required to pay a security deposit of $0.5 million, which is recorded as other non-current assets in the accompanying consolidated balance sheets.

In May 2015, the Company entered into a non-cancelable operating lease for office and research and development space in South San Francisco that expires in December 2017 (the “First Lease”). The First Lease provides for 9,855 of rentable square feet at a base rent that increases annually. Under the terms of the First Lease, the Company was required to pay a security deposit of $0.1 million, which is recorded as prepaid expenses other current assets in the accompanying consolidated balance sheets.

On July 22, 2016, the Company entered into a sublease agreement with a third party for the entirety of the remaining term of the First Lease. The sublease commenced on August 22, 2016. The Company received sublease payments totaling $0.1 million through the year ended December 31, 2016 and expects to receive future minimum payments from this sublease of $0.4 million in 2017, which is recognized as an offset to rent expense.

The Company recognizes rent expense on a straight-line basis over the non-cancelable lease term and records the difference between cash rent payments and the recognition of rent expense as a deferred rent liability. Where leases contain escalation clauses, rent abatements, and/or concessions

such as rent holidays and landlord or tenant incentives or allowances, the Company applies them in the determination of straight-line rent expense over the lease term. The Company records tenant improvement allowances as deferred rent and associated expenditures as leasehold improvements that are being amortized over the shorter of their estimated useful life or the term of the lease. The Company does not assume renewals in its determination of the lease term unless the renewals are deemed by management to be reasonably assured at lease inception.

Rent expense for the years ended December 31, 2015 and 2016 was $0.2 million and $1.0 million, respectively.

As of December 31, 2016, the future minimum lease payments under non–cancelable operating leases are as follows (in thousands):

Year Ended December 31:	
2017	$ 2,510
2018	2,586
2019	2,664
2020	2,745
2021 and later	10,534
	$21,039

Indemnification

In the ordinary course of business, the Company may provide indemnifications of varying scope and terms to vendors, lessors, business partners, board members, officers, and other parties with respect to certain matters, including, but not limited to, losses arising out of breach of such agreements, services to be provided by the Company, negligence or willful misconduct of the Company, violations of law by the Company, or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with directors and certain officers and employees that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors, officers or employees. No demands have been made upon the Company to provide indemnification under such agreements, and thus, there are no claims that the Company is aware of that could have a material effect on the Company's balance sheet, statements of comprehensive loss, or statements of cash flows.

Commitments

In the normal course of business, the Company enters into various firm purchase commitments primarily related to research and development activities. As of December 31, 2016, the Company has non-cancelable purchase commitments of $1.0 million and contractual obligations under license agreements of $0.2 million. Pursuant to certain license and collaboration agreements, the Company has obligations to make future milestone and royalty payments to other third parties. However, because these amounts are contingent and not fixed or determinable, they have not been included on the Company's consolidated balance sheet.

8. Convertible Promissory Note

In January 2015, the Company entered into a convertible promissory note with a related party, a stockholder of the Company. The principal amount of the promissory note was $5.0 million at a fixed

interest rate of 8.0%, which was repayable in January 2016. Interest of $0.1 million accrued on the note and was recognized within interest income (expense), net in the consolidated statement of operations and comprehensive loss in the year ended December 31, 2015.

The entire amount due, including interest, was converted into 1,277,397 shares of Series A-1 convertible preferred stock in May 2015 (see Note 9).

9. Convertible Preferred Stock and Stockholders' Deficit

Convertible Preferred Stock

The Company is authorized to and has issued two classes of stock: convertible preferred stock and common stock. Convertible preferred stock is carried at the issuance price, net of issuance costs. The carrying value of the convertible preferred stock has not been accreted up to its redemption value as no redemption events are considered probable by management.

The Company entered into a preferred stock purchase agreement ("Preferred Stock Purchase Agreement"), with certain investors on May 8, 2015 (the "Initial Closing"), under which the Company agreed to sell up to 45,223,973 shares of Series A-1 convertible preferred stock and 4,361,532 shares of Series A-2 convertible preferred stock. Additionally, at the Initial Closing, the Company concurrently issued 6,295,805 shares of Series A-1 convertible preferred stock for net proceeds of $24.8 million.

The Preferred Stock Purchase Agreement provided that, upon Board of Directors approval, each investor would purchase its pro-rata portion of the shares to be issued in one or more additional series A-1 closings, and in any Series A-2 closings. Further, the Company agreed to sell and issue said shares of Series A-1 convertible preferred stock on the same terms as the first tranche, and to issue said shares of Series A-2 convertible preferred stock on the terms included in the Preferred Stock Purchase Agreement. The second and third Series A-1 closings added further obligations for new investors to participate in the Series A-2 tranches. The Company did not separately account for tranche purchase rights described above as they were not freestanding from the associated shares of convertible preferred stock.

On May 20, 2015 (the "First Additional Closing") the Company and the Series A convertible preferred stock shareholders amended the Preferred Stock Purchase Agreement pursuant to which the Company agreed to sell up to an additional 456,250 shares of Series A-1 convertible preferred stock. Additionally, at the First Additional Closing, the Company issued 3,481,250 shares of Series A-1 convertible preferred stock for net proceeds of $13.9 million and on July 22, 2015 ("Second Additional Closing"), the Company issued an additional 2,420,825 shares of Series A-1 convertible preferred stock for net proceeds of $9.6 million.

On January 6, 2016 (the "Third Additional Closing"), the Company issued 500,000 shares of Series A-1 convertible preferred stock, for net proceeds of $2.0 million. On January 26, 2016 (the "first Tranche Closing"), the Company issued 11,249,997 shares of Series A-1 convertible preferred stock, for net proceeds of $45.0 million. On June 6, 2016 (the "Second Tranche Closing and Series A-2 Closing"), the Company issued 22,166,546 shares of Series A-1 convertible preferred stock and 4,361,527 shares of Series A-2 convertible preferred stock, for net proceeds of $88.7 million and $34.9 million, respectively. All of these shares were sold under the Preferred Stock Purchase Agreement.

On June 23, 2016 (the "First Series B-1 Closing"), the Company entered into a preferred stock purchase agreement ("Series B Preferred Stock Purchase Agreement") with certain investors, under

which the Company sold 7,646,241 shares of Series B-1 convertible preferred stock at a price of $16.00 per share for net proceeds of $122.2 million. In connection with this financing, the Company amended and restated its certificate of incorporation to increase the authorized shares of its common stock to 81,787,362 shares and the authorized shares of its preferred stock to 63,288,466 shares, each with a par value of $0.01 per share. The authorized preferred shares consisted of 46,114,433 designated as Series A-1 convertible preferred stock, 4,361,533 designated as Series A-2 convertible preferred stock, 8,125,000 designated Series B-1 convertible preferred stock and 4,687,500 designated Series B-2 convertible preferred stock.

On August 26, 2016, (the “Second Series B-1 Closing”), the Company sold 478,124 shares of Series B-1 convertible preferred stock at a price of $16.00 per share for net proceeds of $7.6 million.

On December 23, 2016, upon the passing of six months from the First Series B-1 Closing, the shares authorized for Series B-2 were no longer available for issuance under the Series B Preferred Stock Purchase Agreement.

At December 31, 2015, convertible preferred stock consisted of the following (in thousands, except share and per share amounts):

	Shares Authorized	Shares Issued and Outstanding	Issuance Price per Share	Carrying Value	Liquidation Preference
Series A-1	46,114,433	12,197,880	$ 4.00	$48,308	$ 51,131
Series A-2	4,361,533	—	8.00	—	—
Series B	10,552,500	—	16.00	—	—
	61,028,466	12,197,880		$48,308	$ 51,131

At December 31, 2016, convertible preferred stock consisted of the following (in thousands, except share and per share amounts):

	Shares Authorized	Shares issued and Outstanding	Issuance Price per Share	Carrying Value	Liquidation Preference
Series A-1	46,114,433	46,114,423	$ 4.00	$183,951	$198,264
Series A-2	4,361,533	4,361,527	8.00	34,885	36,483
Series B-1	8,125,000	8,124,365	16.00	129,837	135,324
Series B-2	4,687,500	—	—	—	—
	63,288,466	58,600,315		$348,673	$370,071

The rights, preferences and privileges of the convertible preferred stock are as follows:

Dividend Rights

The holders of preferred stock are entitled to receive dividends, if and when declared by the Board of Directors, at the rate of $0.08 per share per annum for Series A-1, $0.16 per share per annum for Series A-2, and $0.32 per share per annum for Series B-1 from and after the date of issuance of such shares, subject to adjustment in the event of a stock split, combination, common stock dividend or distribution, reclassification, exchange, substitution or reorganization. As of December 31, 2015 and 2016, no such dividends had been declared or accrued.

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Dividends on any other class of capital stock cannot be paid unless the holders of the preferred stock first receive, or simultaneously receive, the preferred stock dividend. The holders of preferred stock also participate in dividends paid on common stock as if the shares of preferred stock had been converted into shares of common stock and are considered participating securities.

Conversion Rights

The holders of preferred stock have the right to convert at any time into shares of common stock initially at a one-for-one ratio. All shares of the preferred stock shall be automatically converted into shares common stock (i) upon the consent of the holders of at least a majority of the outstanding preferred stock, or (ii) upon the closing of a firmly underwritten initial public offering of common stock at a price of at least $5.00 per share resulting in at least $50.0 million of gross proceeds. The conversion price for each series of preferred stock is subject to an adjustment in the event of stock split, combination, common stock dividend or distribution, reclassification, exchange, substitution, or reorganization.

Liquidation Rights

In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company or a deemed liquidation event, the holders of shares of preferred stock then outstanding are entitled to be paid out of the assets of the Company available for distribution to its stockholders, before any payment can be made to the holders of common stock, an amount per share equal to the greater of (i) the original issue price for the Series of preferred stock held plus any dividends accrued but unpaid, whether or not declared; or (ii) such amount per share as would have been paid if all shares of preferred stock had been converted to common stock immediately prior to such liquidation, dissolution, winding up or deemed liquidation event. If assets of the Company available are insufficient to pay holders of Preferred Stock the full amount they are entitled to, the holders of preferred stock will share ratably in any distribution of the assets available for distribution in proportion to the amounts due such holders. After the payment of all preferential amounts required to be paid to the holders of shares of preferred stock, the remaining assets of the Company will be distributed among the holders of the shares of common stock, pro rata based on the number of shares held by each such holder.

The Company classifies its convertible preferred stock outside of stockholders' deficit as certain change in control events are outside the Company's control.

Voting Rights

Each share of preferred stock has voting rights equal to the number of shares of common stock into which the preferred stock could be converted immediately after the close of business on the record date.

As long as certain investors in Series A convertible preferred stock hold 100,000 or more shares of convertible preferred stock purchased pursuant to the Preferred Stock Purchase Agreement, subject to adjustment in the event of a stock split, combination, common stock dividend or distribution, reclassification, exchange, substitution or reorganization. They are entitled to elect individually one member of the Board totaling five Series A Directors. Series B convertible preferred stockholders are entitled to elect one member of the Board by majority vote of the Series B convertible preferred stockholders. Together, Series A and Series B convertible preferred stock investors shall be entitled to elect two additional members of the Board that are not otherwise an affiliate of the Company or of any investor.

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Redemption

Upon certain change in control events that are outside of the Company's control, including liquidation, sale or transfer of control of the Company, holders of the convertible preferred stock can cause its redemption. Shares of preferred stock must be redeemed by the Company at the original issue price for each series of preferred stock plus any dividends accrued but unpaid, whether or not declared, in three annual installments, upon a written request from the holders of a majority of the then outstanding shares of preferred stock, which request can be made at any time after the fifth anniversary of the Series B-1 original issue date (on or after June 22, 2021). On each of the three annual redemption dates the Company must redeem the number of outstanding shares of preferred stock determined by dividing the total number of outstanding shares of preferred stock by the number of remaining redemption dates.

Common Stock

As of December 31, 2016, the Company had reserved shares of common stock for issuance as follows:

Series A-1 convertible preferred stock	46,114,433
Series A-2 convertible preferred stock	4,361,533
Series B-1 convertible preferred stock	8,125,000
Series B-2 convertible preferred stock	4,687,500
Options issued and outstanding	5,374,014
Restricted shares subject to future vesting	3,922,638
Early exercised common stock subject to future vesting	510,417
Options available for future grants	1,813,321
Shares to be issued under Incro acquisition agreement	81,164
Total	74,990,020

10. Stock Incentive Plan

2015 Stock Incentive Plan

In May 2015, the Company adopted the 2015 Stock Incentive Plan (the "2015 Plan"), which as amended, reserved 8,325,000 shares for the issuance of stock options, non-qualified stock options, restricted stock and other stock awards, to employees, non-employee directors, and consultants under terms and provisions established by the Board of Directors and approved by the stockholders. Awards granted under the 2015 Plan expire no later than ten years from the date of grant. For incentive stock options and non-statutory stock options, the option price shall not be less than 100% of the estimated fair value on the day of grant. For all stock options granted between August 2015 and February 2016 with an exercise price of $0.68, a deemed fair value of $1.20 per share was used in calculating stock-based compensation expense, which was determined using management hindsight. Options granted typically vest over a four-year period but may be granted with different vesting terms

The Company permits early exercise of certain stock options prior to vesting by certain directors and officers. Any shares issued pursuant to unvested options are restricted and subject to repurchase by the Company until the conditions for vesting are met. The amounts paid for shares purchased under an early exercise of stock options and subject to repurchase by the Company are reported in stockholders' deficit once those shares vest. Upon termination of employment of an option holder, the Company has the right to repurchase, at the original purchase price, any unvested restricted shares.

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In 2015, there were 750,000 options exercised prior to vesting for total proceeds of $0.5 million to the Company which was recognized as a long-term liability as of December 31, 2015. No shares vested relating to these exercises in the year ended December 31, 2015. The Company reclassified $0.2 million to stockholders' deficit upon vesting during the year ended December 31, 2016 and the remaining proceeds related to the unvested options of $0.3 million as of December 31, 2016 will be reclassified to stockholders' deficit as the options vest.

As of December 31, 2015 and 2016, there were 2,024,871 shares and 1,813,321 shares, respectively, available for the Company to grant under the 2015 Plan.

Stock Option Activity

The following table summarizes option activity under the 2015 plan:

	Number of Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (Years)	Aggregate Intrinsic Value (in thousands)
Balance at December 31, 2014	—	$ —	—	
Options granted	4,275,121	0.68		
Options exercised	(750,000)	0.68		
Balance at December 31, 2015	3,525,121	0.68	9.73	
Options granted	2,112,808	3.45		
Options exercised	(162,665)	0.68		
Options forfeited	(101,250)	0.82		
Balance at December 31, 2016	5,374,014	$ 1.77	9.03	$ 18,873
Options vested and expected to vest at December 31, 2016	3,629,276	$ 2.29	9.21	$ 10,847
Options exercisable at December 31, 2016	419,085	$ 0.68	8.83	$ 1,926

Aggregate intrinsic value represents the difference between the Company's estimated fair value of its common stock and the exercise price of outstanding options. The total intrinsic value of options exercised was $0.4 million and $0.7 million for the years ended December 31, 2015 and 2016, respectively. The total intrinsic value of options exercisable was $1.9 million as of December 31, 2016. During the year ended December 31, 2016, the weighted-average grant-date fair value of the options vested was $1.36 per share. No options vested during the year ended December 31, 2015. The weighted-average grant date fair value of options granted during the years ended December 31, 2015 and 2016 was $2.03 and $2.83 per share, respectively.

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Stock Options Granted to Employees with Service-Based Vesting

The estimated fair value of stock options granted to employees were calculated using the Black-Scholes option-pricing model using the following assumptions:

	Year Ended December 31,	
	2015	2016
Expected term (in years)	6.08	6.00-6.08
Volatility	85.7%-90.2%	91.2%-92.2%
Risk-free interest rate	1.7%-1.9%	1.2%-2.1%
Dividend yield	—	—

Expected Term: The expected term represents the period that the options granted are expected to be outstanding and is determined using the simplified method (based on the mid-point between the vesting date and the end of the contractual term).

Expected Volatility: The Company used an average historical stock price volatility of comparable public companies within the biotechnology and pharmaceutical industry that were deemed to be representative of future stock price trends as the Company does not have any trading history for its common stock.

Risk-Free Interest Rate: The Company based the risk-free interest rate over the expected term of the options based on the constant maturity rate of U.S. Treasury securities with similar maturities as of the date of the grant.

Expected Dividend: The Company has not paid and does not anticipate paying any dividends in the near future. Therefore, the expected dividend yield was zero.

Performance Contingent Stock Options Granted to Employees

In August and November 2015, the Board of Directors granted 250,000 and 500,000 of stock option awards to certain executive officers, respectively. These awards have an exercise price of $0.68 per share. These awards vest over time and include a performance provision which states that upon the occurrence of a change in control event, the vesting term would accelerate. As of December 31, 2016, the Company determined that the achievement of the requisite performance condition was not probable and, as a result, the expense relating to these grants is being recognized over the initial time-based vesting period. If the performance goal is ever deemed to be probable of achievement, the recognition of compensation expense will be accelerated in accordance with the accelerated vesting schedule.

The estimated fair value of employee performance-contingent options was estimated at the date of grant using a Black-Scholes option-pricing model using the same assumptions as the Stock Options Granted to Employees with Service-based Vesting Valuation Assumptions.

Performance and Market Contingent Stock Options Granted to Employees

In August and November 2015, the Board of Directors granted 1,619,738 and 125,000 of performance- and market- contingent awards to members of the senior management team, respectively. These awards have an exercise price of $0.68 per share.

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These awards have two separate market triggers for vesting based upon either (i) the successful achievement of stepped target closing prices on a national securities exchange for 90 consecutive trading days later than 180 days after the Company's initial public offering for its common stock, or (ii) stepped target prices for a change in control transaction. By definition, the market condition in these awards can only be achieved after the performance condition of a liquidity event has been achieved. As such, the requisite service period is based on the estimated period over which the market condition can be achieved. When a performance goal is deemed to be probable of achievement, time-based vesting and recognition of stock-based compensation expense commences. In the event any the milestones are not achieved by the specified timelines, such vesting award will terminate and no longer be exercisable with respect to that portion of the shares. The maximum potential expense associated with the performance- and market- contingent awards is $6.2 million ($5.8 million and $0.4 million of general and administrative and research and development expense, respectively) if all of the performance and market conditions are achieved as stated in the option agreement. As of December 31, 2016, the Company determined that the achievement of the requisite performance conditions was not probable and, as a result, no compensation cost was recognized for these awards.

The Company uses a lattice model with a Monte Carlo simulation to value stock options with performance and market conditions. This valuation methodology utilizes the estimated fair value of the Company's common stock on grant date and several key assumptions, including expected volatility of the Company's stock price based on comparable public companies, risk-free rates of return and expected dividend yield.

Stock Options Granted to Non-Employees with Service-Based Vesting

Stock-based compensation related to stock options granted to non-employees is recognized as the stock options are earned. The estimated fair value of the stock options granted is calculated at each reporting date using the Black-Scholes option-pricing model with the following assumptions:

	Year Ended December 31,	
	2015	2016
Expected term (in years)	9.50-9.84	8.50-9.70
Volatility	88.6%-89.3%	95.3%-98.2%
Risk-free interest rate	2.0%-2.3%	2.4%
Dividend yield	—	—

The expected term for stock options granted to non-employees is equivalent to the remaining contractual term of the award.

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Restricted Stock Activity

The following table summarizes restricted stock activity:

	Shares	Weighted-Average Fair Value at Date of Grant per Share
Unvested at December 31, 2015	6,911,269	$ 0.18
Granted	—	—
Vested	(2,988,631)	0.17
Forfeited	—	—
Unvested at December 31, 2016	3,922,638	$ 0.18

At December 31, 2016, there was $0.7 million of total unrecognized compensation cost related to non-vested restricted stock, all which is expected to be recognized over a remaining weighted-average period of 2.5 years.

Stock-Based Compensation Expense

The Company's results of operations include expenses relating to employee and non-employee stock-based awards and restricted stock awards as follows (in thousands):

	Year Ended December 31,	
	2015	2016
Research and development	$ 94	$ 2,078
General and administrative	385	873
Total	$ 479	$ 2,951

As of December 31, 2016, total unamortized stock-based compensation expense related to unvested employee and non-employee awards that are expected to vest was $7.2 million and $0.4 million, respectively. The weighted-average period over which such stock-based compensation expense will be recognized is approximately 3.1 years and 3.2 years as of December 31, 2015 and 2016, respectively.

The Company recorded stock-based compensation expense for options issued to non-employees under the 2015 Plan of $0.1 million and $1.0 million for the years ended December 31, 2015 and 2016, respectively.

11. Income Taxes

The Company has incurred net operating losses for all the periods presented. The Company has not reflected any benefit of such net operating loss carryforwards in the accompanying financial statements. The Company has established a full valuation allowance against its deferred tax assets due to the uncertainty surrounding the realization of such assets.

The effective tax rate for the years ended December 31, 2015 and 2016 is different from the federal statutory tax rate primarily due to the valuation allowance against deferred tax assets as a

result of insufficient sources of income. The effective tax rate of the provision for income taxes differs from the federal statutory rate as follows:

	Year Ended December 31,	
	2015	2016
Taxes at the U.S. statutory tax rate	34.0%	34.0%
Change in valuation allowance	(34.1)	(32.0)
Contingent consideration issued in tax-free reorganization	—	(2.1)
Research tax credits	1.5	0.6
Stock-based compensation	(0.2)	(0.5)
Other	(1.2)	—
Total provision for income taxes	0.0%	0.0%

The components of the Company's net deferred tax assets are as follows (in thousands):

	December 31,	
	2015	2016
Deferred tax assets:		
Net operating loss carryforwards	$ 4,452	$ 26,044
Tax credit carryforwards	410	1,486
Reserves and accruals	370	4,038
Capitalized start-up costs	1,987	5,128
Intangibles	—	6,565
Share based compensation	67	390
Gross deferred tax assets	7,286	43,651
Valuation allowance	(6,823)	(40,113)
Net deferred tax assets	463	3,538
Deferred tax liabilities:		
Property and equipment	(65)	(3,379)
Stock-based compensation	(398)	(159)
Net deferred tax assets	$ —	$ —

Recognition of deferred tax assets is appropriate when realization of such assets is more likely than not. Based upon the weight of available evidence, especially the uncertainties surrounding the realization of deferred tax assets through future taxable income, the Company believes it is not more likely than not that the deferred tax assets will be fully realizable. Accordingly, the Company has provided a 100% valuation allowance against its net deferred tax assets as of December 31, 2015 and 2016.

As of December 31, 2016, the Company has federal net operating loss ("NOL") carryforwards of approximately $65.4 million, which are available to reduce future taxable income, and has federal tax credits of approximately $1.2 million which may be used to offset future tax liabilities. The federal NOL and federal tax credit carryforwards will begin to expire in 2035. The Company also has state NOL carryforwards of approximately $65.4 million, which are available to reduce future taxable income, and has state tax credits of approximately $1.4 million which may be used to offset future tax liabilities. The state NOL will begin to expire in 2035 and the state tax credit carryforwards will be carried forward

indefinitely. The NOL and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service ("IRS") and state tax authorities and may become subject to an annual limitation in the event of certain future cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code of 1986. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities.

The Company follows the provisions of ASC 740, Accounting for Income Taxes, and the accounting guidance related to accounting for uncertainty in income taxes. The Company determines its uncertain tax positions based on a determination of whether and how much of a tax benefit taken by the Company in its tax filings is more likely than not to be sustained upon examination by the relevant income tax authorities.

A reconciliation of the beginning and ending amounts of unrecognized tax benefits is as follows (in thousands):

	December 31,	
	2015	2016
Gross unrecognized tax benefits at January 1	$ —	$122
Additions for tax positions taken in a prior year	—	7
Additions for tax positions taken in the current year	122	411
Reductions for tax positions taken in the prior year	—	(9)
Gross unrecognized tax benefits at December 31	$122	$531

If recognized, none of the unrecognized tax benefits as of December 31, 2015 and 2016 would reduce the annual effective tax rate, primarily due to corresponding adjustments to the valuation allowance. The Company will recognize both accrued interest and penalties related to unrecognized benefits in income tax expense. As of December 31, 2016, no liability has been recorded for potential interest or penalties. The Company does not expect the unrecognized tax benefits to change significantly over the next 12 months.

Since the Company is in a loss carryforward position, the Company is generally subject to examination by the U.S. federal, state and local income tax authorities for all tax years in which a loss carryforward is available.

12. Net Loss and Unaudited Pro Forma Net Loss Per Share

The following table sets forth the computation of the basic and diluted net loss per share (in thousands, except share and per share data):

	Year Ended December 31,	
	2015	2016
Numerator:		
Net loss	$ (16,788)	$ (86,652)
Denominator:		
Weighted average common shares outstanding	3,006,379	6,424,720
Net loss per share, basic and diluted	$ (5.58)	$ (13.49)

Denali Therapeutics Inc.
Notes to Consolidated Financial Statements

Since the Company was in a loss position for all periods presented, basic net loss per share is the same as diluted net loss per share for all periods as the inclusion of all potential common shares outstanding would have been anti-dilutive. Potentially dilutive securities that were not included in the diluted per share calculations because they would be anti-dilutive were as follows:

	December 31,	
	2015	2016
Series A-1 convertible preferred stock	12,197,880	46,114,423
Series A-2 convertible preferred stock	—	4,361,527
Series B-1 convertible preferred stock	—	8,124,365
Options issued and outstanding	3,525,121	5,374,014
Restricted shares subject to future vesting	6,911,269	3,922,638
Early exercised common stock subject to future vesting	750,000	510,417
Shares to be issued under Incro acquisition agreement	27,054	81,164
Total	23,411,324	68,488,548

Unaudited Pro Forma Net Loss Per Share

The following table sets forth the computation of the Company's unaudited pro forma basic and diluted net loss per share (in thousands, except for share and per share amounts):

	Year ended December 31, 2016 (Unaudited)
Net loss	$ (86,652)
Shares used in computing net loss per share, basic and diluted	6,424,720
Pro forma adjustment to reflect assumed conversion of preferred stock	42,499,524
Shares used to compute pro forma net loss per share, basic and diluted	48,924,244
Pro forma net loss per share, basic and diluted	$ (1.77)

13. Subsequent event

In November 2017, the Company sold 1,764,705 shares of Series B-2 convertible preferred stock at a price of $17.00 per share for net proceeds of $29.9 million. In connection with this financing, the Company amended and restated its certificate of incorporation to reflect that the holders of preferred stock are entitled to receive dividends, if and when declared by the Board of Directors, at the rate of $0.34 per share per annum, and to establish the Series B-2 original issuance price at $4.25 per share, both subject to adjustment in the event of a stock split, combination, common stock dividend or distribution, reclassification, exchange, substitution, or reorganization. The amendments provided for rights, preferences and privileges for the Series B-2 convertible preferred stock similar to those of the Series A-1, A-2 and B-1 convertible preferred stock described in Note 9, Convertible Preferred Stock and Stockholders' Deficit.

Denali Therapeutics Inc.

Condensed Consolidated Balance Sheets
(In thousands, except share and per share amounts)

	December 31, 2016	September 30, 2017 (Unaudited)	Pro Forma Stockholders' Equity as of September 30, 2017 (Unaudited)
Assets			
Current assets:			
Cash and cash equivalents	$ 39,853	$ 36,269	
Short-term marketable securities	138,478	149,532	
Prepaid expenses and other current assets	3,624	2,442	
Total current assets	181,955	188,243	
Long-term marketable securities	72,580	4,975	
Property and equipment, net	15,262	14,635	
Other non-current assets	1,270	2,456	
Total assets	$ 271,067	$ 210,309	
Liabilities, convertible preferred stock and stockholders' equity (deficit)			
Current liabilities:			
Accounts payable	$ 1,963	$ 2,270	
Accrued liabilities	3,850	4,116	
Accrued compensation	2,592	2,865	
Deferred rent and other current liabilities	701	903	
Total current liabilities	9,106	10,154	
Deferred rent	7,045	6,519	
Other non-current liabilities	397	499	
Total liabilities	16,548	17,172	
Commitments and contingencies (Note 6)			
Convertible preferred stock, $0.01 par value; 63,288,466 shares authorized as of December 31, 2016 and September 30, 2017 (unaudited); 58,600,315 shares issued and outstanding as of December 31, 2016 and September 30, 2017 (unaudited); aggregate liquidation preference of $390,974 as of September 30, 2017 (unaudited); no shares issued and outstanding, pro forma (unaudited)	348,673	348,673	$ —
Stockholders' equity (deficit):			
Common stock, $0.01 par value; 83,587,362 shares authorized as of December 31, 2016 and September 30, 2017 (unaudited); 8,597,316 and 10,607,828 shares issued and outstanding as of December 31, 2016 and September 30, 2017 (unaudited), respectively; 69,208,143 shares issued and outstanding, pro forma (unaudited)	344	424	2,768
Additional paid-in capital	9,387	13,087	359,416
Accumulated other comprehensive loss	(373)	(237)	(237)
Accumulated deficit	(103,512)	(168,810)	(168,810)
Total stockholders' equity (deficit)	(94,154)	(155,536)	193,137
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	$ 271,067	$ 210,309	$ 210,309

See accompanying notes to condensed consolidated financial statements.

Denali Therapeutics Inc.

Condensed Consolidated Statements of Operations and Comprehensive Loss
(Unaudited)
(In thousands, except share and per share amounts)

	Nine Months Ended September 30,	
	2016	2017
Operating expenses:		
Research and development	$ 58,972	$ 55,989
General and administrative	8,685	10,611
Total operating expenses	67,567	66,600
Loss from operations	(67,567)	(66,600)
Interest income, net	359	1,302
Net loss	(67,298)	(65,298)
Other comprehensive income (loss):		
Net unrealized gain (loss) on marketable securities, net of tax	(131)	136
Comprehensive loss	$ (67,429)	$ (65,162)
Net loss per share, basic and diluted	$ (11.43)	$ (6.77)
Weighted average number of shares outstanding, basic and diluted	5,888,385	9,643,686
Pro forma net loss per share, basic and diluted		$ (0.96)
Weighted-average number of shares used in computing pro forma net loss per share, basic and diluted		68,244,028

See accompanying notes to condensed consolidated financial statements.

Denali Therapeutics Inc.

Condensed Consolidated Statements of Cash Flows
(Unaudited)
(In thousands)

	Nine Months Ended September 30,	
	2016	2017
Operating activities		
Net loss	$ (67,298)	$ (65,298)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	783	2,275
Stock-based compensation expense	2,260	2,952
Net amortization of premiums and discounts on marketable securities	144	899
Loss on disposal of property and equipment	—	1
Fair value of common stock issued in connection with asset acquisition	5,280	—
Changes in operating assets and liabilities:		
Restricted cash	(451)	—
Prepaid expenses and other assets	769	(3)
Accounts payable	1,592	318
Accrued and other current liabilities	3,077	884
Other non-current liabilities	(149)	(327)
Net cash used in operating activities	(53,993)	(58,299)
Investing activities		
Purchase of marketable securities	(195,736)	(46,651)
Purchase of property and equipment	(3,821)	(1,804)
Purchase of other investments	(500)	—
Maturities and sales of marketable securities	—	102,438
Net cash provided by (used in) investing activities	(200,057)	53,983
Financing activities		
Proceeds from exercise of common stock options	114	732
Proceeds from issuance of convertible preferred stock, net of issuance costs	300,366	—
Net cash provided by financing activities	300,480	732
Net increase (decrease) in cash and cash equivalents	46,430	(3,584)
Cash and cash equivalents at beginning of period	30,740	39,853
Cash and cash equivalents at end of period	$ 77,170	$ 36,269
Supplemental disclosures of cash flow information		
Convertible preferred stock issuance costs incurred but not yet paid	$ 27	$ —
Property and equipment purchases accrued but not yet paid	$ 1,938	$ 78
Deferred IPO costs accrued but not yet paid	$ —	$ 1,136

See accompanying notes to condensed consolidated financial statements.

Denali Therapeutics Inc.
Notes to Unaudited Interim Condensed Consolidated Financial Statements

1. Significant Accounting Policies

Organization and Description of Business

Denali Therapeutics Inc. (the "Company") is a biopharmaceutical company, incorporated in Delaware, that discovers and develops therapeutics to defeat neurodegenerative diseases. The Company was incorporated in October 2013 as SPR Pharma Inc. The Company's name was changed to Denali Therapeutics Inc. in March 2015. The Company is headquartered in South San Francisco, California.

Basis of Presentation

These consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP"). All share and per share information included in the accompanying consolidated financial statements has been adjusted to reflect a 4-for-1 reverse stock split to be effected prior to the completion of this offering.

Principles of Consolidation

These consolidated financial statements include the accounts of the Company and its wholly-owned subsidiary. This subsidiary was dissolved in September 2016. All intercompany balances and transactions have been eliminated on consolidation.

The Company assesses whether it is the primary beneficiary of any variable interest entity ("VIE") in which it has a variable interest at the inception of the arrangement and at each reporting date. This assessment is based on the Company's power to direct the activities of the VIE that most significantly impact the VIE's economic performance and the Company's obligation to absorb losses or the right to receive benefits from the VIE that could potentially be significant to the VIE.

Unaudited Interim Consolidated Financial Statements

The interim condensed consolidated balance sheet as of September 30, 2017, and the statements of operations and comprehensive loss, and cash flows for the nine months ended September 30, 2016 and 2017 are unaudited. The unaudited interim consolidated financial statements have been prepared on the same basis as the annual consolidated financial statements and reflect, in the opinion of management, all adjustments of a normal and recurring nature that are necessary for the fair presentation of the Company's financial position as of September 30, 2017 and its results of operations and cash flows for the nine months ended September 30, 2016 and 2017. The financial data and the other financial information disclosed in these notes to the consolidated financial statements related to the nine-month periods are also unaudited. The consolidated results of operations for the nine months ended September 30, 2017 are not necessarily indicative of the results to be expected for the year ended December 31, 2017 or for any other future annual or interim period. The consolidated balance sheet as of December 31, 2016 included herein was derived from the audited consolidated financial statements as of that date. These interim condensed consolidated financial statements should be read in conjunction with the Company's audited consolidated financial statements included elsewhere in this prospectus.

Unaudited Pro Forma Information

Immediately prior to the completion of this offering, all outstanding shares of convertible preferred stock will convert into common stock. Unaudited pro forma balance sheet information as of

Denali Therapeutics Inc.
Notes to Unaudited Interim Condensed Consolidated Financial Statements

September 30, 2017 assumes the conversion of all outstanding convertible preferred stock into shares of common stock. The shares of common stock issuable and the proceeds expected to be received in the initial public offering are excluded from such pro forma financial information.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires the Company to make certain estimates, judgments and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the reported amounts of expenses during the reporting period. Actual results could differ from those estimates, and such differences could be material to the consolidated financial position and results of operations.

Need for Additional Capital

Since inception, the Company has incurred net losses and negative cash flows from operations. During the nine months ended September 30, 2017, the Company incurred a net loss of $65.3 million and used $58.3 million of cash in operations. At September 30, 2017, the Company had an accumulated deficit of $168.8 million and does not expect to experience positive cash flows in the near future. The Company has financed operations to date primarily through the sale and issuance of convertible preferred stock. Management expects to incur additional operating losses in the future as the Company continues the development of, and seeks regulatory approvals for, its product candidates, and begins to commercialize any approved products and recognizes the need to raise additional capital to fully implement its business plan. The Company intends to raise such capital through public and private equity offerings, debt financings, strategic partnerships and alliances and licensing arrangements. The Company had $190.8 million of cash, cash equivalents and marketable securities at September 30, 2017. Based on the Company's business plans, management believes that this is sufficient to meet its obligations for at least the next twelve months from the issuance date of these condensed consolidated financial statements.

Segments

The Company has one operating segment. The Company's chief operating decision maker, its Chief Executive Officer, manages the Company's operations on a consolidated basis for the purposes of allocating resources.

Fair Value of Financial Instruments

ASC Topic 820, Fair Value Measurement ("ASC 820"), establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability, and are developed based on the best information available in the circumstances.

ASC 820 identifies fair value as the exchange price, or exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market

participants. As a basis for considering market participant assumptions in fair value measurements, ASC 820 establishes a three-tier fair value hierarchy that distinguishes between the following:

Level 1 – inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities.

Level 2 – inputs are inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly.

Level 3 – inputs are unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability. Financial assets and liabilities are classified in their entirety based on the lowest level of input that is significant to the fair value measurement.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The carrying amounts reflected in the consolidated balance sheets for cash and cash equivalents, prepaid expenses and other current assets, accounts payable and accrued liabilities approximate their fair values, due to their short-term nature.

Cash and Cash Equivalents

The Company considers all highly liquid investments with original maturities of 90 days or less at the date of purchase to be cash and cash equivalents. Cash equivalents, which consist primarily of highly liquid investments with maturities of three months or less when purchased, are stated at fair value.

Marketable Securities

The Company generally invests its excess cash in money market funds and investment grade short to intermediate-term fixed income securities. Such investments are included in cash and cash equivalents, short-term marketable securities, or long-term marketable securities on the balance sheets, are considered available-for-sale, and reported at fair value with unrealized gains and losses included as a component of stockholders' deficit. The amortized cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity, which is included in interest income, net on the consolidated statements of operations. Realized gains and losses and declines in value judged to be other-than-temporary, if any, on marketable securities are included in interest income, net. The cost of securities sold is determined using specific identification.

The Company periodically evaluates whether declines in fair values of its marketable securities below their book value are other-than-temporary. This evaluation consists of several qualitative and quantitative factors regarding the severity and duration of the unrealized loss as well as the Company's ability and intent to hold the marketable security until a forecasted recovery occurs. Additionally, the Company assesses whether it has plans to sell the security or it is more likely than not it will be required to sell any marketable securities before recovery of its amortized cost basis. Factors considered include quoted market prices, recent financial results and operating trends, implied values from any recent transactions or offers of investee securities, credit quality of debt instrument issuers, other publicly available information that may affect the value of the marketable security, duration and severity of the decline in value, and our strategy and intentions for holding the marketable security.

Denali Therapeutics Inc.
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Restricted Cash

The Company's restricted cash consists of restricted cash in connection with the building leases for the Company's former and current headquarters. The current portion is classified within prepaid expenses and other current assets and the non-current portion within other non-current assets on the accompanying consolidated balance sheets.

Deferred IPO Costs

Deferred IPO costs of $1.2 million are capitalized and included within other non-current assets on the condensed consolidated balance sheet as of September 30, 2017. There were no deferred IPO costs as of December 31, 2016. The deferred IPO costs will be offset against proceeds from the IPO upon the consummation of the IPO. In the event the IPO is terminated, all capitalized deferred IPO costs will be expensed.

Research and Development Expenses

Research and development costs are expensed as incurred. Research and development costs consist of salaries and other personnel related expenses, including associated stock–based compensation, consulting fees, lab supplies, and facility costs, as well as fees paid to other entities that conduct certain research, development and manufacturing activities on behalf of the Company.

Nonrefundable advance payments for goods and services that will be used or rendered in future research and development activities are deferred and recognized as expense in the period in which the related goods are delivered or services are performed.

The Company has acquired and may continue to acquire the rights to develop and commercialize new product candidates from third parties. The upfront payments to acquire license, product or rights, as well as any future milestone payments, are immediately recognized as research and development expense provided that there is no alternative future use of the rights in other research and development projects.

Stock-Based Compensation

The Company measures employee and director stock-based compensation expense for all stock-based awards at the grant date based on the fair value measurement of the award. The expense is recorded on a straight-line basis over the requisite service period, which is generally the vesting period, for the entire award. Expense is adjusted for actual forfeitures of unvested awards as they occur. The Company calculates the fair value measurement of stock options using the Black-Scholes valuation model.

The Company granted restricted stock awards that vest in conjunction with certain performance conditions to certain key employees and directors. At each reporting date, the Company is required to evaluate whether achievement of the performance conditions is probable. Compensation expense is recorded over the appropriate service period based upon the Company's assessment of accomplishing each performance provision.

The Company accounts for stock options issued to non-employees in accordance with the provisions of ASC 505-50, Equity-Based Payments to Non-employees, which requires valuing the stock options on their grant date and remeasuring such stock options at the current fair value at the end of each reporting period until they vest.

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Notes to Unaudited Interim Condensed Consolidated Financial Statements

Comprehensive Loss

Comprehensive loss includes net loss and certain changes in stockholders' deficit that are excluded from net loss, primarily unrealized losses on the Company's marketable securities.

Net Loss per Share

Basic net loss per share is calculated by dividing the net loss by the weighted-average number of shares of common stock outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is the same as basic net loss per share, since the effects of potentially dilutive securities are antidilutive given the net loss for each period presented.

Unaudited Pro Forma Net Loss per Share

Pro forma basic and diluted net loss per share has been computed to give effect to the conversion of all outstanding convertible preferred stock into shares of common stock. Pro forma basic and diluted net loss per share has been computed to give effect to the conversion of all outstanding convertible preferred stock into shares of common stock. The unaudited pro forma net loss per share does not include the shares expected to be sold and related proceeds to be received from the initial public offering. The unaudited pro forma net loss per share for the nine months ended September 30, 2017 was computed using the weighted-average number of shares of common stock outstanding, including the pro forma effect of the conversion of all outstanding shares of convertible preferred stock into shares of common stock, as if such conversion had occurred at the beginning of the period, or their issuance dates if later.

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2014–09 ("ASU 2014-09"), Revenue from Contracts with Customers (Topic 606), and further updated through ASU 2016-12 ("ASU 2016-12"), which amends the existing accounting standards for revenue recognition. ASU 2014–09 is based on principles that govern the recognition of revenue at an amount to which an entity expects to be entitled when products are transferred to customers. This guidance is effective for annual reporting periods, and interim periods within those years, beginning after December 15, 2017, for public entities and no later than for annual reporting periods beginning after December 15, 2018, for non–public entities. Early adoption is not permitted. The new revenue standard may be applied retrospectively to each prior period presented or retrospectively with the cumulative effect recognized as of the date of adoption. While the Company continues to assess all potential impacts under ASU 2014-09, it does not believe adopting the new revenue standard will have a material impact on its consolidated financial statements as the Company is not yet generating revenues.

In February 2016, the FASB issued ASU No. 2016-02 ("ASU 2016-02"), Leases (Topic 842), which supersedes the guidance in former ASC 840, Leases. The new standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than 12 months regardless of their classification. Leases with a term of 12 months or less will be accounted for similar to existing guidance for operating

leases today. The standard is effective for interim and annual periods beginning after December 15, 2018, with early adoption permitted. The ASU is expected to impact the Company's consolidated financial statements as the Company has certain operating lease arrangements for which the Company is the lessee. Management is currently evaluating the impact the adoption of ASU 2016-02 will have on the Company's financial position and results of operations. Management expects that the adoption of this standard will result in the recognition of an asset for the right to use the leased facility on the Company's balance sheet, as well as the recognition of a liability for the lease payments remaining on the lease. While the balance sheet presentation is expected to change, management does not expect a material change to the consolidated statement of operations.

In November 2016, the FASB issued ASU 2016-18, Statement of Cash Flows (Topic 230): Restricted Cash. The purpose of Update No. 2016-18 is to clarify guidance and presentation related to restricted cash in the statement of cash flows. The amendment requires beginning-of-period and end-of-period total amounts shown on the statement of cash flows to include cash and cash equivalents as well as restricted cash and restricted cash equivalents. The update is effective for fiscal years beginning after December 15, 2017, including interim reporting periods within those fiscal years. Early adoption is permitted. The Company is currently evaluating the impact of adopting this standard on the consolidated financial statements and disclosures, but does not expect it to be material.

In May 2017, the FASB issued ASU 2017-09, Compensation - Stock Compensation (Topic 718): Scope of Modification Accounting, which clarifies when to account for a change to the terms or conditions of a share-based payment award as a modification. Under the new guidance, modification accounting is required only if the fair value, the vesting conditions, or the classification of the award (as equity or liability) changes as a result of the change in terms or conditions. It is effective for annual and interim periods beginning after December 15, 2017. Early adoption is permitted. The Company is currently evaluating the impact of adopting this standard on the consolidated financial statements and disclosures, but does not expect it to have a significant impact.

Denali Therapeutics Inc.
Notes to Unaudited Interim Condensed Consolidated Financial Statements

2. Fair Value Measurements

Assets measured at fair value at each balance sheet date are as follows (in thousands):

	December 31, 2016			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	$28,705	$ —	$ —	$ 28,705
Short-term:				
U.S. government treasuries	22,268	—	—	22,268
U.S. government agency securities	—	70,787	—	70,787
Corporate debt securities	—	38,941	—	38,941
Commercial paper	—	6,482	—	6,482
Long-term:				
U.S. government treasuries	4,989	—	—	4,989
U.S. government agency securities	—	52,868	—	52,868
Corporate debt securities	—	14,723	—	14,723
Total marketable securities	27,257	183,801	—	211,058
Total fair value measurements	**$55,962**	**$183,801**	**$ —**	**$239,763**

	September 30, 2017			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	$30,399	$ —	$ —	$ 30,399
Short-term:				
U.S. government treasuries	14,710	—	—	14,710
U.S. government agency securities	—	99,972	—	99,972
Corporate debt securities	—	34,850	—	34,850
Long-term:				
U.S. government agency securities	—	4,975	—	4,975
Total marketable securities	14,710	139,797	—	154,507
Total fair value measurements	**$45,109**	**$139,797**	**$ —**	**$184,906**

The carrying amounts of accounts payable and accrued liabilities approximate their fair values due to their short-term maturities.

The Company's Level 2 securities are valued using third-party pricing sources. The pricing services utilize industry standard valuation models, including both income and market-based approaches, for which all significant inputs are observable, either directly or indirectly. There were no transfers of assets or liabilities between the fair value measurement levels during the nine months ended September 30, 2017.

3. Marketable Securities

All marketable securities were considered available-for-sale at December 31, 2016 and September 30, 2017. The amortized cost, gross unrealized holding gains or losses, and fair value of

Denali Therapeutics Inc.
Notes to Unaudited Interim Condensed Consolidated Financial Statements

the Company's marketable securities by major security type at each balance sheet date are summarized in the tables below (in thousands):

	December 31, 2016			
	Amortized Cost	Unrealized Holding Gains	Unrealized Holding Losses	Aggregate Fair Value
Short-term marketable securities:				
U.S. government treasuries	$ 22,277	$ —	$ (9)	$ 22,268
U.S. government agency securities	70,835	—	(48)	70,787
Corporate debt securities	39,037	—	(96)	38,941
Commercial paper	6,482	—	—	6,482
Total short-term marketable securities	138,631	—	(153)	138,478
Long-term marketable securities:				
U.S. government treasuries	4,996	1	(8)	4,989
U.S. government agency securities	53,005	—	(137)	52,868
Corporate debt securities	14,799	—	(76)	14,723
Total long-term marketable securities	72,800	1	(221)	72,580
Total	**$211,431**	**$ 1**	**$ (374)**	**$ 211,058**

	September 30, 2017			
	Amortized Cost	Unrealized Holding Gains	Unrealized Holding Losses	Aggregate Fair Value
Short-term marketable securities:				
U.S. government treasuries	$ 14,726	$ —	$ (16)	$ 14,710
U.S. government agency securities	100,118	—	(146)	99,972
Corporate debt securities	34,900	—	(50)	34,850
Total short-term marketable securities	149,744	—	(212)	149,532
Long-term marketable securities:				
U.S. government agency securities	5,000	—	(25)	4,975
Total long-term marketable securities	5,000	—	(25)	4,975
Total	**$154,744**	**$ —**	**$ (237)**	**$ 154,507**

As of December 31, 2016 and September 30, 2017, some of the Company's marketable securities were in an unrealized loss position. At each date, the Company determined that it did have the ability and intent to hold all marketable securities that have been in a continuous loss position until maturity or recovery, thus there has been no recognition of any other-than-temporary impairment in the year ended December 31, 2016 or the nine months ended September 30, 2017. All marketable securities with unrealized losses as of as of each balance sheet date have been in a loss position for less than twelve months or the loss is not material.

All of the Company's short-term marketable securities have an effective maturity date of less than one year, and all of the Company's long-term marketable securities have an effective maturity of less than two years.

Denali Therapeutics Inc.
Notes to Unaudited Interim Condensed Consolidated Financial Statements

4. Acquisition

In June 2015, the Company acquired Incro Pharmaceuticals Corporation ("Incro"), a preclinical private biotechnology company incorporated in Delaware. The primary asset purchased in the acquisition was an in-process research and development license agreement which would allow the Company to further its RIPK1 research program. The Company concluded that the assets acquired and liabilities assumed did not meet the accounting definition of a business as a limited number of inputs were acquired but no processes were acquired, and the licensed technology had not achieved technological feasibility. As such, the acquisition was accounted for as an asset purchase and the Company recorded the purchase price as $1.5 million in research and development expense in the accompanying statement of operations and comprehensive loss in the year ended December 31, 2015.

As purchase consideration the Company issued an aggregate of 472,942 shares of common stock, valued at $0.6 million on the transaction date, to the former Incro stockholders, and recognized within additional paid-in capital an obligation to issue an additional 27,054 shares of common stock, valued at $32,466 to one former Incro stockholder. The deemed fair value (see Note 8) of the Company's common stock was $1.20 per common share as of the date of the transaction. In addition to the issuance of this equity, the Company assumed liabilities of $0.9 million.

The Company also agreed to issue an additional 945,880 shares of common stock to the former Incro stockholders, and to recognize an obligation to issue 54,110 shares of common stock to one former Incro shareholder ("Milestone Shares"), upon acceptance of an investigational new drug ("IND") application by the U.S. FDA or an equivalent in the EU, Canada, Australia, or New Zealand within six years of the date of the acquisition. Of these shares, 350,000 shares of common stock ("Indemnification Shares") were to be held in escrow by Denali, and would be released to former stockholders of Incro within 30 days of the later of (i) expiration of 18 months after the closing; and (ii) the date the Milestone Shares vest as noted above. The number of Indemnification Shares to be released to Incro's stockholders were to be reduced to the extent of breaches of standard representations by Incro's stockholders. As this transaction was accounted for as an asset purchase rather than a business combination, no amounts were recognized on the acquisition date relating to the contingent consideration.

In August 2016, the Company filed a Clinical Trial Application ("CTA") in Europe to initiate a Phase 1 clinical trial. Upon acceptance of the CTA in September 2016, the issuance of the Milestone Shares was triggered. The Company issued a total of 595,880 shares of common stock, recognized an obligation to issue 54,110 shares of common stock, and recorded a liability of $1.8 million for the 350,000 Indemnification Shares held in escrow. The Company recognized $5.3 million of research and development expense related to the estimated fair value of these shares of $5.28 per share during the nine months ended September 30, 2016. In December 2016, the 350,000 Indemnification Shares were released and issued and the related liability was extinguished upon the expiration of the 18-month period after the closing of the acquisition.

5. License and Collaboration Agreements

F-star

On August 24, 2016, the Company entered into a License and Collaboration Agreement ("Collaboration Agreement") with F-star Gamma Limited ("F-star Gamma"), f-star Biotechnologische Forschungs-und Entwicklungsges m.b.H and F-star Biotechnology Limited (collectively, "F-star"). The goal of the collaboration is the development of certain constant Fc-domains of an antibody with

non-native antigen binding activity (“Fcabs”), to enhance delivery of therapeutics across the blood-brain barrier (“BBB”) into the brain. The collaboration leverages F-star’s modular antibody technology and the Company’s expertise in the development of therapies for neurodegenerative diseases.

Under the terms of the Collaboration Agreement, the Company can nominate up to three Fcab targets (“Accepted Fcab Targets”), within the first three years of the date of the Collaboration Agreement; and the Company has selected transferrin receptor (“TfR”) as the first Accepted Fcab Target. With respect to each Accepted Fcab Target, the Company can nominate up to eight Fab targets (“Accepted Fab Targets”), which are targets bound by the variable domains of an antibody or other therapeutic modalities (“Fabs”). For each accepted Fcab target, the Company is obligated to use commercially reasonable efforts during the research term to perform development activities in accordance with certain specified development plans. Under the terms of the Collaboration Agreement, the Company received non-exclusive licenses under certain intellectual property to conduct technology development to discover and develop Fcabs. The Company is obligated to assign to F-star certain patents and know-how that the Company generates under the Collaboration Agreement related to F-star’s platform technology or certain Fcabs identified solely by F-star and the Company received a non-exclusive license under certain of F-star Biotechnology’s platform patents and know-how to develop and commercialize products in connection with the delivery of therapeutics across the BBB, subject to certain specified restrictions. F-star retains the right to use its intellectual property, including any intellectual property that the Company and F-star jointly own pursuant to the terms of the Collaboration Agreement, outside the scope of the licenses granted to the Company.

Under the terms of the Collaboration Agreement, the Company paid F-star Gamma an upfront fee of $5.5 million, which includes selection of the first Accepted Fcab Target. The Company is obligated to pay a one-time fixed fee in the low single-digit millions for each additional Accepted Fcab Target the Company selects, technical milestone payments for each Accepted Fcab Target, up to a maximum of $15.0 million in the aggregate for all Accepted Fcab Targets, and, at specified times, monthly exclusivity fees for Accepted Fcab Targets and Accepted Fab Targets, which may be eliminated in certain circumstances. The Company is also responsible for certain research costs incurred by F-star in conducting activities under each agreed development plan, for up to 24 months. These research costs for the agreed TfR development plan will be up to $2.1 million.

Either party may terminate the agreement if the other party materially breaches the agreement, subject to specified notice and cure provisions, or for the other party’s bankruptcy or insolvency. In addition, F-star Gamma may terminate the agreement if the Company challenges any of the patent rights licensed to it by F-star. The Company is able to terminate the agreement for convenience, either in its entirety or on an Accepted Fcab Target-by-Accepted Fcab Target basis or an Accepted Fab Target-by-Accepted Fab Target basis, on 90 days’ prior written notice to F-star. Unless earlier terminated, the agreement with F-star will remain in effect until all royalty and milestone payment obligations to F-star Gamma expire.

In connection with the entry into the Collaboration Agreement, the Company also purchased an option for an upfront option fee of $0.5 million (the “buy-out-option”), to acquire all of the outstanding shares of F-star Gamma pursuant to a pre-negotiated buy-out option agreement (the “Option Agreement”). The Company must elect whether to exercise its buy-out option before the earlier of (i) dosing of the fifth patient dosed in the first Phase 1 trial of an antibody that binds to an Accepted Fab Target and an Accepted Fcab Target, (ii) the fourth anniversary of the first delivery by F-star of an Fcab meeting certain delivery criteria, and (iii) five and one half years after the delivery by the Company of a notice that it is progressing an Fcab identified from the Company’s library that binds to

an Accepted Fcab Target. If the Company exercises this buy-out option, it will be obligated to make initial exercise payments ranging from $18.0 million to $50.0 million in the aggregate, plus the estimated net cash held by F-star Gamma at the time of such exercise. In addition, it will be required to make certain contingent payments upon the achievement of certain preclinical, clinical, regulatory and commercial milestones, up to a maximum amount of $447.0 million in the aggregate. The amount of the initial exercise and contingent payments varies based on whether F-star delivers an Fcab that meets pre-defined criteria, whether the Fcab has been identified solely by the Company or solely by F-star or jointly by the Company and F-star and the timing of the Company's exercise of the buy-out option. Following exercise of the buy-out option, the Company will not be required to make any further milestone or royalty payments under the Collaboration Agreement. If the Company exercises the buy-out option, then f-star Biotechnologische Forschungs-und Entwicklungsges m.b.H and F-star Biotechnology continue to be prohibited from developing, commercializing and manufacturing any antibody or other molecule that incorporates any Selected Fcab, or any Selected Fcab as a standalone product, and from authorizing any third party to take any such action. If the Company does not exercise its option to acquire F-star Gamma prior to the expiration of the buy-out option period, then, from the lapse of the buy-out option period until the Company's rights with respect to an Accepted Fab Target expire or terminate, F-star is prohibited from developing, commercializing and manufacturing any antibody or other molecule that contains both a Selected Fcab and a Fab that specifically binds to the relevant Accepted Fab Target.

If the Company does not exercise the buy-out option, then with respect to each Accepted Fab Target, the Company has the right to obtain from F-star an exclusive, worldwide license to certain intellectual property to develop and commercialize licensed products that contain (i) a Fab that specifically binds to such Accepted Fab Target and (ii) an Fcab that the Company or F-star identifies, either solely or jointly, and that specifically binds to an Accepted Fcab Target, for up to eight Accepted Fab Targets per each Accepted Fcab Target. Each time the Company exercises such license option, it will be obligated to pay F-star Gamma (i) a one-time fixed fee in the low single-digit millions, (ii) milestone payments upon the achievement of certain clinical development and commercial milestones, up to a maximum of $362.5 million in the aggregate; (iii) additional sales-based milestones if net sales of licensed products achieve certain specified levels, up to a maximum amount payable to F-star of $650.0 million in the aggregate and (iv) low-to-mid single-digit percentage royalties on net sales of licensed products. Such amounts may be reduced by a specified percentage depending on the origin of the Fcab incorporated in the applicable licensed product and whether F-star delivers to the Company an Fcab that meets pre-defined criteria. The Company has the right to credit a certain amount of royalty payments that it pays to third parties with respect to certain licensed products against the Company's royalty obligation to F-star Gamma, up to a maximum reduction of fifty percent. The Company's royalty payment obligations will expire on a country-by-country and licensed product-by-licensed product basis upon the later of (a) the expiration of the last valid claim of a licensed patent covering such licensed product in such country, (b) the expiration of regulatory exclusivity for such licensed product in such country and (c) the twelfth anniversary of the first commercial sale of such licensed product in such country.

The Company recognized the upfront option fee of $0.5 million within other non-current assets recorded at cost. This asset will be assessed for potential impairment on an ongoing basis. No impairment charge was recognized during the nine months ended September 30, 2016 or 2017.

The Company determined that F-star Gamma is and continues to be a variable interest entity and that the Company holds a variable interest in F-star Gamma's intellectual property assets and the related potential future product candidates these assets may produce through the Collaboration

Agreement and the Option Agreement. However, the Company concluded that its governance role in the collaboration, which is specified by the terms of a joint steering committee, does not provide the Company the power to direct the activities of F-star Gamma that most significantly impact F-star Gamma's economic performance. Based on this conclusion, the Company is not considered to be the primary beneficiary of F-star Gamma; and therefore F-star Gamma is not subject to consolidation by the Company.

The Company recognized $0.8 million of research and development expense related to the funding of F-star Gamma research costs during the nine months ended September 30, 2017. No such expense was recognized in the nine months ended September 30, 2016.

The $0.5 million other non-current asset is the only asset or liability recorded in the Company's interim condensed consolidated balance sheets that relates to the Company's variable interest in F-star Gamma at December 30, 2016 and September 30, 2017. The upfront payments of $0.5 million and $5.5 million, along with 1) the obligation to fund certain future research costs, 2) any future Fcab selection fee, technical milestone payments or monthly exclusivity fees and 3) any future license fees or pre-commercial milestone payments represent the Company's maximum exposure to loss under the arrangements with F-star. The ultimate expense that the Company incurs under the arrangements with F-Star cannot be quantified at this time as the amount will vary based on the timing and outcome of future research activities.

Genentech

On June 17, 2016, the Company entered into an Exclusive License Agreement with Genentech, Inc. ("Genentech"). The agreement gives the Company access to Genentech's preclinical stage LRRK2 small molecule program, which can be used to enhance and further progress the Company's in-house LRRK2 program for Parkinson's disease. Under the agreement, Genentech granted the Company (i) an exclusive, worldwide, sublicenseable license under Genentech's rights to certain patents and patent applications directed to small molecule compounds which bind to and inhibit LRRK2 and (ii) a non-exclusive, worldwide, sublicenseable license to certain related know-how, in each case, to develop and commercialize certain compounds and licensed products incorporating any such compound. The Company is obligated to use commercially reasonable efforts during the first three years of the agreement to research, develop and commercialize at least one licensed product.

As consideration, the Company paid an upfront fee of $8.5 million and a technology transfer fee of $1.5 million, both of which are included within research and development expense for the nine months ended September 30, 2016.

The Company may owe Genentech milestone payments upon the achievement of certain development, regulatory, and commercial milestones, up to a maximum of $315.0 million in the aggregate, as well as royalties on net sales of licensed products ranging from low to high single-digit percentages, with the exact royalty rate dependent on various factors, including (i) whether the compound incorporated in the relevant licensed product is a Genentech-provided compound or a compound acquired or developed by the Company, (ii) the date a compound was first discovered, derived or optimized by the Company, (iii) the existence of patent rights covering the relevant licensed product in the relevant country, (iv) the existence of orphan drug exclusivity covering a licensed product that is a Genentech-provided compound and (v) the level of annual net sales of the relevant licensed product. The Company also has the right to credit a certain amount of third-party royalty and milestone payments against royalty and milestone payments owed to Genentech, up to a maximum

reduction of fifty percent. The Company's royalty payment obligations will expire on a country-by-country and licensed product-by-licensed product basis upon the later of (a) ten years after the first commercial sale of such licensed product in such country and (b) the expiration of the last valid claim of a licensed patent covering such licensed product in such country.

Genentech may terminate the agreement if the Company challenges any of the patent rights licensed to the Company by Genentech, or if the Company materially breaches the agreement, subject to specified notice and cure provisions, or enters into bankruptcy or insolvency proceedings. If Genentech terminates the agreement for the Company's material breach, bankruptcy or insolvency after the Company has made a milestone payment to Genentech, then the Company is obligated to grant to Genentech an exclusive right of first negotiation with respect to certain of the Company's patents, know-how and regulatory filings directed to Genentech-provided compounds. The Company does not have the right to terminate the agreement without cause, but may terminate the agreement for Genentech's material breach, subject to specified notice and cure provisions.

Unless earlier terminated, the agreement with Genentech will continue in effect until all of the Company's royalty and milestone payment obligations to Genentech expire. Following expiration of the agreement, the Company will retain the licenses under the intellectual property Genentech licensed to the Company on a non-exclusive, royalty-free basis.

The first clinical milestone payment of $2.5 million became due in June 2017 upon first patient dosing in the Phase 1 clinical trial for DNL201. The full amount was included in research and development expense in the nine months ended September 30, 2017.

6. Commitments and Contingencies

Lease Obligations

In September 2015, the Company entered into a non-cancelable operating lease for its corporate headquarters comprising 38,109 of rentable square feet in a building in South San Francisco ("Headquarters Lease"). The Headquarters Lease commenced on August 1, 2016 with a lease term of eight years. The Company has an option to extend the lease term for a period of five years by giving the landlord written notice of the election to exercise the option at least nine months, but not more than twelve months, prior to the original expiration of the lease term. The Headquarters Lease provides for monthly base rent amounts escalating over the term of the lease. In addition, the Headquarters Lease provides both a tenant improvement allowance ("TIA") of up to $7.4 million, of which $1.9 million will be repaid to the landlord in the form of additional monthly rent with interest applied. This additional monthly rent commenced in November 2016 when the entire TIA was utilized, and results in an increase of base rent of $0.4 million per year.

The total $7.4 million TIA has been recorded as leasehold improvements and deferred rent liability on the consolidated balance sheet. The Company is amortizing the deferred rent liability as a reduction of rent expense and the leasehold improvement through an increase of depreciation expense of leasehold improvements ratably over the lease term. Under the terms of the Headquarters Lease, the Company was required to pay a security deposit of $0.5 million, which is recorded as other non-current assets in the accompanying consolidated balance sheets.

In May 2015, the Company entered into a non-cancelable operating lease for office and research and development space in South San Francisco that expires in December 2017 (the "First Lease"). The

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First Lease provides for 9,855 of rentable square feet at a base rent that increases annually. Under the terms of the First Lease, the Company was required to pay a security deposit of $0.1 million, which is recorded as prepaid expenses other current assets in the accompanying consolidated balance sheets.

On July 22, 2016, the Company entered into a sublease agreement with a third party for the entirety of the remaining term of the First Lease. The sublease commenced on August 22, 2016. The Company received sublease payments totaling $42,000 and $0.3 million in the nine months ended September 30, 2016 and 2017, respectively. The Company expects to receive future minimum payments from this sublease of $0.1 million in the remainder of 2017, which will be recognized as an offset to rent expense.

The Company recognizes rent expense on a straight-line basis over the non-cancelable lease term and records the difference between cash rent payments and the recognition of rent expense as a deferred rent liability. Where leases contain escalation clauses, rent abatements, and/or concessions such as rent holidays and landlord or tenant incentives or allowances, the Company applies them in the determination of straight-line rent expense over the lease term. The Company records tenant improvement allowances as deferred rent and associated expenditures as leasehold improvements that are being amortized over the shorter of their estimated useful life or the term of the lease. The Company does not assume renewals in its determination of the lease term unless the renewals are deemed by management to be reasonably assured at lease inception.

As of September 30, 2017, the future minimum lease payments under non-cancelable operating leases are as follows (in thousands):

Year Ended December 31:	
2017 (three months)	$ 729
2018	2,586
2019	2,664
2020	2,745
2021	2,829
2022 and later	7,704
	$19,257

Rent expense for the nine months ended September 30, 2016 and 2017 was $0.5 million and $1.6 million, respectively.

Commitments

Effective September 2017, the Company entered into a Development and Manufacturing Services Agreement as amended (“DMSA”) with Lonza Sales AG (“Lonza”) for the development and manufacture of biologic products. Under the DMSA, the Company will execute purchase orders based on project plans authorizing Lonza to provide development and manufacturing services with respect to certain of our antibody and enzyme products, and will pay for the services provided and batches delivered in accordance with the DMSA and project plan. Unless earlier terminated, the DMSA will expire on September 6, 2022. As of September 30, 2017, the Company had not incurred any amounts or made any purchase commitments under the DMSA. In October 2017, the Company executed the first purchase order of up to $0.7 million, the activities under which will commence prior to the end of 2017.

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7. Convertible Preferred Stock and Stockholders' Deficit

Convertible Preferred Stock

At December 31, 2016, convertible preferred stock consisted of the following (in thousands, except share and per share amounts):

	Shares Authorized	Shares Issued and Outstanding	Issuance Price per Share	Carrying Value	Liquidation Preference
Series A-1	46,114,433	46,114,423	$ 4.00	$183,951	$198,264
Series A-2	4,361,533	4,361,527	8.00	34,885	36,483
Series B-1	8,125,000	8,124,365	16.00	129,837	135,324
Series B-2	4,687,500	—	—	—	—
	63,288,466	58,600,315		$348,673	$370,071

At September 30, 2017, convertible preferred stock consisted of the following (in thousands, except share and per share amounts):

	Shares Authorized	Shares Issued and Outstanding	Issuance Price per Share	Carrying Value	Liquidation Preference
Series A-1	46,114,433	46,114,423	$ 4.00	$183,951	$209,301
Series A-2	4,361,533	4,361,527	8.00	34,885	38,571
Series B-1	8,125,000	8,124,365	16.00	129,837	143,102
Series B-2	4,687,500	—	—	—	—
	63,288,466	58,600,315		$348,673	$390,974

Common Stock

As of September 30, 2017, the Company had reserved shares of common stock for issuance as follows:

Series A-1 convertible preferred stock outstanding	46,114,433
Series A-2 convertible preferred stock outstanding	4,361,533
Series B-1 convertible preferred stock outstanding	8,125,000
Series B-2 convertible preferred stock outstanding	4,687,500
Options issued and outstanding	6,179,687
Restricted shares subject to future vesting	2,701,059
Early exercised common stock subject to future vesting	416,669
Options available for future grant	312,456
Shares to be issued under Incro acquisition agreement	81,164
Total	72,979,501

8. Stock Incentive Plan

2015 Stock Incentive Plan

As of September 30, 2017, there were 312,456 shares available for the Company to grant under the 2015 Stock Incentive Plan (the "2015 Plan").

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Stock Option Activity

The following table summarizes option award activity under the 2015 plan:

	Number of Options	Weighted-Average Exercise Price	Weighted-Average remaining contractual life (years)	Aggregate Intrinsic Value (in thousands)
Balance at December 31, 2016	5,374,014	$ 1.77	9.03	$ 18,873
Options granted	1,622,629	6.48		
Options exercised	(695,192)	1.41		
Options forfeited	(121,764)	0.95		
Balance at September 30, 2017	6,179,687	$ 3.06	8.61	$ 53,006
Options vested and expected to vest at September 30, 2017	4,434,941	$ 4.00	8.89	$ 33,884
Options exercisable at September 30, 2017	854,786	$ 3.12	8.71	$ 7,282

The aggregate intrinsic values of options outstanding, exercisable, vested and expected to vest were calculated as the difference between the exercise price of the options and the estimated fair value of the Company's common stock, as determined by the Board of Directors, as of September 30, 2017.

During the nine months ended September 30, 2016 and 2017, the estimated weighted-average grant-date fair value of the options vested was $0.99 and $2.08 per share, respectively, and the estimated weighted-average grant-date fair value of common stock underlying options granted was $2.12 and $4.84 per share, respectively.

Stock Options Granted to Employees with Service-Based Vesting Valuation Assumptions

The estimated fair value of stock options granted to employees were calculated using the Black-Scholes option-pricing model using the following assumptions:

	Nine Months Ended September 30,	
	2016	2017
Expected term (in years)	6.00-6.08	6.08
Volatility	91.2%-92.2%	86.8%-91.3%
Risk-free interest rate	1.2%-1.5%	1.8%-2.3%
Dividend yield	—	—

Denali Therapeutics Inc.
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Stock Options Granted to Non-Employees with Service-Based Vesting Valuation Assumptions

Stock-based compensation related to stock options granted to non-employees is recognized as the stock options are earned. The estimated fair value of the stock options granted is calculated at each reporting date using the Black-Scholes option-pricing model with the following assumptions:

	Nine Months Ended September 30,	
	2016	2017
Expected term (in years)	8.75-9.90	7.75-9.45
Volatility	93.9%-98.3%	86.8%-98.0%
Risk-free interest rate	1.5%-1.6%	2.2%-2.4%
Dividend yield	—	—

Restricted Stock Activity

The following table summarizes restricted stock activity:

	Shares	Weighted-Average Fair Value at Date of Grant per Share
Unvested at December 31, 2016	3,922,638	$ 0.18
Granted	—	—
Vested	(1,221,579)	0.18
Forfeited	—	—
Unvested at September 30, 2017	2,701,059	$ 0.18
Vested and expected to vest – September 30, 2017	2,701,059	$ 0.18

At September 30, 2017, there was $0.4 million of total unrecognized compensation cost related to non-vested restricted stock, all which is expected to be recognized over a remaining weighted-average period of 1.3 years.

Stock-Based Compensation Expense

The Company's results of operations include expenses relating to employee and non-employee stock-based awards and restricted stock awards, as follows (in thousands):

	Nine Months Ended September 30,	
	2016	2017
Research and development	$ 1,600	$ 1,947
General and administrative	660	1,005
Total	$ 2,260	$ 2,952

As of September 30, 2017, total unamortized stock-based compensation expense related to unvested employee and non-employee awards that are expected to vest was $12.5 million and $0.5 million respectively. The weighted-average period over which such stock-based compensation expense will be recognized is approximately 3.1 years.

Denali Therapeutics Inc.
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The Company recorded stock-based compensation expense for options issued to non-employees under the 2015 Plan of $1.0 million and $0.5 million for the nine months ended September 30, 2016 and 2017, respectively.

9. Net Loss and Unaudited Pro Forma Net Loss Per Share

The following table sets forth the computation of the basic and diluted net loss per share (in thousands, except share and per share data):

	Nine Months Ended September 30,	
	2016	2017
Numerator:		
Net loss	$ (67,298)	$ (65,298)
Denominator:		
Weighted average common shares outstanding	5,888,385	9,643,686
Net loss per share, basic and diluted	$ (11.43)	$ (6.77)

Since the Company was in a loss position for all periods presented, basic net loss per share is the same as diluted net loss per share for all periods as the inclusion of all potential shares of common stock outstanding would have been anti-dilutive. Potentially dilutive securities that were not included in the diluted per share calculations because they would be anti-dilutive were as follows:

	September 30,	
	2016	2017
Series A-1 convertible preferred stock	46,114,423	46,114,423
Series A-2 convertible preferred stock	4,361,527	4,361,527
Series B-1 convertible preferred stock	8,124,365	8,124,365
Options issued and outstanding	4,920,232	6,179,687
Restricted shares subject to future vesting	4,414,322	2,701,059
Early exercised common stock subject to future vesting	671,875	416,669
Shares to be issued under Incro acquisition agreement	81,164	81,164
Total	68,687,908	67,978,894

Pro Forma Net Loss Per Share

The following table sets forth the computation of the Company's unaudited pro forma basic and diluted net loss per share (in thousands, except for share and per share amounts):

	Nine Months Ended September 30, 2017
Net loss	$ (65,298)
Shares used in computing net loss per share, basic and diluted	9,643,686
Pro forma adjustment to reflect assumed conversion of preferred stock	58,600,342
Shares used to compute pro forma net loss per share, basic and diluted	68,244,028
Pro forma net loss per share, basic and diluted	$ (0.96)

Denali Therapeutics Inc.
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10. Subsequent event

In November 2017, the Company sold 1,764,705 shares of Series B-2 convertible preferred stock at a price of $17.00 per share for net proceeds of $29.9 million. In connection with this financing, the Company amended and restated its certificate of incorporation to reflect that the holders of preferred stock are entitled to receive dividends, if and when declared by the Board of Directors, at the rate of $0.34 per share per annum, and to establish the Series B-2 original issuance price at $4.25 per share, both subject to adjustment in the event of a stock split, combination, common stock dividend or distribution, reclassification, exchange, substitution, or reorganization. The amendments provided for rights, preferences and privileges for the Series B-2 convertible preferred stock similar to those of the Series A-1, A-2 and B-1 convertible preferred stock.

8,333,333 Shares

Denali Therapeutics Inc.

Common Stock

Goldman Sachs & Co. LLC **Morgan Stanley** **J.P. Morgan**

Evercore ISI

PART II

INFORMATION NOT REQUIRED IN THE PROSPECTUS

Item 13. *Other Expenses of Issuance and Distribution*

The following table sets forth the expenses to be incurred in connection with the offering described in this Registration Statement, other than underwriting discounts and commissions, all of which will be paid by us. All amounts are estimates except the SEC's registration fee, the Financial Industry Regulatory Authority, Inc.'s filing fee and the NASDAQ listing fee.

	Amount to be Paid
SEC Registration Fee	$ 22,670
FINRA filing fee	27,813
NASDAQ listing fee	225,000
Printing and engraving expenses	425,000
Legal fees and expenses	1,500,000
Accounting fees and expenses	915,000
Transfer agent and registrar fees	6,500
Miscellaneous expenses	378,017
Total	$ 3,500,000

Item 14. *Indemnification of Directors and Officers*

Section 145 of the Delaware General Corporation Law empowers a corporation to indemnify its directors and officers and to purchase insurance with respect to liability arising out of their capacity or status as directors and officers, provided that the person acted in good faith and in a manner the person reasonably believed to be in our best interests, and, with respect to any criminal action, had no reasonable cause to believe the person's actions were unlawful. The Delaware General Corporation Law further provides that the indemnification permitted thereunder shall not be deemed exclusive of any other rights to which the directors and officers may be entitled under the corporation's bylaws, any agreement, a vote of stockholders or otherwise. The certificate of incorporation of the registrant to be in effect upon the completion of this offering provides for the indemnification of the registrant's directors and officers to the fullest extent permitted under the Delaware General Corporation Law. In addition, the bylaws of the registrant to be in effect upon the completion of this offering require the registrant to fully indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding (whether civil, criminal, administrative or investigative) by reason of the fact that such person is or was a director or officer of the registrant, or is or was a director or officer of the registrant serving at the registrant's request as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorney's fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by such person in connection with such action, suit or proceeding, to the fullest extent permitted by applicable law.

Section 102(b)(7) of the Delaware General Corporation Law permits a corporation to provide in its certificate of incorporation that a director of the corporation shall not be personally liable to the corporation or its stockholders for monetary damages for breach of fiduciary duty as a director, except (1) for any breach of the director's duty of loyalty to the corporation or its stockholders, (2) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (3) for payments of unlawful dividends or unlawful stock repurchases or redemptions or (4) for any transaction from which the director derived an improper personal benefit. The registrant's certificate of

incorporation to be in effect upon the completion of this offering provides that the registrant's directors shall not be personally liable to it or its stockholders for monetary damages for breach of fiduciary duty as a director and that if the Delaware General Corporation Law is amended to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of the registrant's directors shall be eliminated or limited to the fullest extent permitted by the Delaware General Corporation Law, as so amended.

Section 174 of the Delaware General Corporation Law provides, among other things, that a director who willfully or negligently approves of an unlawful payment of dividends or an unlawful stock purchase or redemption may be held liable for such actions. A director who was either absent when the unlawful actions were approved, or dissented at the time, may avoid liability by causing his or her dissent to such actions to be entered in the books containing minutes of the meetings of the board of directors at the time such action occurred or immediately after such absent director receives notice of the unlawful acts.

As permitted by the Delaware General Corporation Law, the registrant has entered into separate indemnification agreements with each of the registrant's directors and certain of the registrant's officers which require the registrant, among other things, to indemnify them against certain liabilities which may arise by reason of their status as directors, officers or certain other employees.

The registrant expects to obtain and maintain insurance policies under which its directors and officers are insured, within the limits and subject to the limitations of those policies, against certain expenses in connection with the defense of, and certain liabilities which might be imposed as a result of, actions, suits or proceedings to which they are parties by reason of being or having been directors or officers. The coverage provided by these policies may apply whether or not the registrant would have the power to indemnify such person against such liability under the provisions of the Delaware General Corporation Law.

These indemnification provisions and the indemnification agreements entered into between the registrant and the registrant's officers and directors may be sufficiently broad to permit indemnification of the registrant's officers and directors for liabilities (including reimbursement of expenses incurred) arising under the Securities Act of 1933, as amended.

The underwriting agreement between the registrant and the underwriters to be filed as Exhibit 1.1 to this registration statement provides for the indemnification by the underwriters of the registrant's directors and officers and certain controlling persons against specified liabilities, including liabilities under the Securities Act with respect to information provided by the underwriters specifically for inclusion in the registration statement.

Item 15. *Recent Sales of Unregistered Securities*

The following list sets forth information regarding all unregistered securities sold by us in the past three years. No underwriters were involved in the sales and the certificates representing the securities sold and issued contain legends restricting transfer of the securities without registration under the Securities Act or an applicable exemption from registration.

(a) In March 2015, we issued 5,796,874 restricted shares of our common stock outside of the 2015 Stock Incentive Plan, or 2015 Plan, to Drs. Watts, Schuth and Tessier-Lavigne.

(b) In April 2015, we issued 225,000 restricted shares of our common stock under the 2015 Plan to Drs. Sato and Schenkein and Mr. Flatley.

(c) In May 2015, we issued 9,777,055 shares of our Series A-1 convertible preferred stock at $4.00 per share, for aggregate proceeds of $39.1 million, to a total of 30 accredited investors.

(d) In May 2015, we issued and sold 2,815,787 shares of our common stock to six accredited investors at $0.04 per share.

(e) In June 2015, we issued an aggregate of 1,418,828 shares of our common stock in connection with the closing of the acquisition of Incro Pharmaceuticals Corporation, of which 945,886 shares were held in escrow by us until such shares vested and were released in September 2016.

(f) In July 2015, we issued 2,420,825 shares of our Series A-1 convertible preferred stock at $4.00 per share, for aggregate proceeds of $9.7 million, to a total of 11 accredited investors.

(g) In August 2015, we issued 804,896 restricted shares of our common stock outside of the 2015 Stock Incentive Plan, as amended, or 2015 Plan, to Ryan J. Watts, Ph.D., Alexander O. Schuth, M.D. and Marc Tessier-Lavigne, Ph.D.

(h) In January 2016, we issued 11,749,997 shares of our Series A-1 convertible preferred stock at $4.00 per share, for aggregate proceeds of $47.0 million, to a total of nine accredited investors.

(i) In June 2016, we issued 22,166,546 shares of our Series A-1 convertible preferred stock at $4.00 per share, for aggregate proceeds of $88.7 million, to a total of eight accredited investors.

(j) In June 2016, we issued 4,361,527 shares of our Series A-2 convertible preferred stock at $8.00 per share, for aggregate proceeds of $34.9 million, to a total of 15 accredited investors.

(k) In June 2016, we issued 7,646,241 shares of our Series B-1 convertible preferred stock at $16.00 per share, for aggregate proceeds of $122.3 million, to a total of 17 accredited investors.

(l) In August 2016, we issued 478,124 shares of our Series B-1 convertible preferred stock at $16.00 per share, for aggregate proceeds of $7.7 million, to a total of 10 accredited investors.

(m) In November 2017, we issued 1,764,705 shares of our Series B-2 convertible preferred stock at $17.00 per share, for aggregate proceeds of $30.0 million, to a total of three accredited investors.

(n) From August 2015 through November 2017, we granted stock options to purchase an aggregate of 8,110,812 shares of common stock to certain employees, directors and consultants under our 2015 Plan at exercise prices per share ranging from $0.68 to $11.64, for an aggregate exercise price of approximately $23.0 million.

(o) From October 2015 through November 2017, we issued and sold an aggregate of 1,607,857 shares of common stock upon the exercise of options under our 2015 Plan to our directors, employees, consultants and other service providers at exercise prices per share ranging from $0.68 to $5.28, for an aggregate exercise price of approximately $1.6 million.

The offers, sales and issuances of the securities described in Items 15(a) through 15(m) were exempt from registration under the Securities Act under Section 4(a)(2) of the Securities Act as transactions by an issuer not involving a public offering. The recipients of securities in each of these transactions acquired the securities for investment only and not with a view to or for sale in connection with any distribution thereof and appropriate legends were affixed to the securities issued in these transactions. Each of the recipients of securities in these transactions was an accredited person and had adequate access, through employment, business or other relationships, to information about the registrant.

The offers, sales and issuances of the securities described in Items 15(n) and 15(o) were exempt from registration under the Securities Act under either (1) Rule 701 in that the transactions were under compensatory benefit plans and contracts relating to compensation as provided under Rule 701 or (2) Section 4(a)(2) of the Securities Act as transactions by an issuer not involving any public offering. The recipients of such securities were the registrant's employees, consultants or directors and received the securities under the registrant's 2015 Plan. The recipients of securities in each of these transactions represented their intention to acquire the securities for investment only and not with view to or for sale in connection with any distribution thereof and appropriate legends were affixed to the securities issued in these transactions.

Item 16. *Exhibit and Financial Statement Schedules*

(a) Exhibits.

The following exhibits are filed as part of this Registration Statement:

Exhibit Number	Description of Exhibit
1.1	Form of Underwriting Agreement, including Form of Lock-up Agreement.
3.1	Amended and Restated Certificate of Incorporation of the Registrant, as currently in effect.
3.1.1	Form of Certificate of Amendment to the Amended and Restated Certificate of Incorporation of Registrant, to be in effect prior to the completion of this offering.
3.2	Form of Amended and Restated Certificate of Incorporation of the Registrant, to be in effect upon the completion of this offering.
3.3^	Amended and Restated Bylaws of the Registrant, as currently in effect.
3.4	Form of Amended and Restated Bylaws of the Registrant, to be in effect upon the completion of this offering.
4.1^	Investors' Rights Agreement among the Registrant and certain of its stockholders, dated May 8, 2015, as amended on June 4, 2015, July 22, 2015 and June 22, 2016.
4.2	Specimen common stock certificate of the Registrant.
5.1	Opinion of Wilson Sonsini Goodrich & Rosati, Professional Corporation.
10.1+	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers.
10.2+^	2015 Stock Incentive Plan, as amended, and forms of agreement thereunder.
10.3+	2017 Equity Incentive Plan and forms of agreements thereunder, to be in effect upon the completion of this offering.
10.4+	2017 Employee Stock Purchase Plan and form of agreement thereunder, to be in effect upon the completion of this offering.
10.5+^	Offer Letter between the Registrant and Ryan J. Watts, Ph.D., dated November 10, 2017.
10.6+^	Offer Letter between the Registrant and Alexander O. Schuth, M.D., dated November 10, 2017.
10.7+^	Offer Letter between the Registrant and Steve E. Krognes, dated November 10, 2017.
10.8+^	Offer Letter between the Registrant and Carole Ho, M.D., dated November 10, 2017.

Exhibit Number	Description of Exhibit
10.9^	Lease Agreement between the Registrant and HCP Oyster Point III LLC, dated September 24, 2015.
10.10#^	Exclusive License Agreement between the Registrant and Genentech, Inc., dated June 17, 2016.
10.11#^	License and Collaboration Agreement between the Registrant, F-star Gamma Limited, f-star Biotechnologische Forschungs- und Entwicklungsges m.b.H. and F-star Biotechnology Limited, dated August 24, 2016.
10.12#^	Development and Manufacturing Services Agreement between the Registrant and Lonza Sales AG, dated September 6, 2017, as amended on October 18, 2017.
10.13+^	Key Executive Change in Control and Severance Plan.
10.14+^	Executive Incentive Compensation Plan.
10.15+^	Outside Director Compensation Policy.
23.1	Consent of Independent Registered Public Accounting Firm.
23.2	Consent of Wilson Sonsini Goodrich & Rosati, Professional Corporation (included in Exhibit 5.1).
24.1^	Power of Attorney (see page II-6 to Form S-1 filed with the SEC on November 13, 2017).

^ Previously filed.
+ Indicated management contract or compensatory plan.
# Portions of this exhibit have been omitted pursuant to a request for confidential treatment and this exhibit has been filed separately with the SEC.

(b) Financial Statement Schedules.

Schedules have been omitted because the information required to be set forth therein is not applicable or is shown in the financial statements or notes thereto.

Item 17. *Undertakings*

The undersigned registrant hereby undertakes to provide to the underwriters at the closing specified in the underwriting agreements, certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

The undersigned hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and

contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act of 1933 shall be deemed to be part of this registration statement as of the time it was declared effective.

(2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the registrant has duly caused this registration statement on Form S-1 to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of South San Francisco, State of California, on the 27th day of November, 2017.

DENALI THERAPEUTICS INC.

By: /s/ Ryan J. Watts
Ryan J. Watts, Ph.D.
President and Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1933, as amended, this registration statement on Form S-1 has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Ryan J. Watts Ryan J. Watts, Ph.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	November 27, 2017
/s/ Steve E. Krognes Steve E. Krognes	Chief Financial Officer and Treasurer (Principal Financial and Accounting Officer)	November 27, 2017
* Vicki Sato, Ph.D.	Chairperson of our Board of Directors	November 27, 2017
* Marc Tessier-Lavigne, Ph.D.	Director	November 27, 2017
* Douglas Cole, M.D.	Director	November 27, 2017
* Jay Flatley	Director	November 27, 2017
* Robert Nelsen	Director	November 27, 2017
* David Schenkein, M.D.	Director	November 27, 2017

*By: /s/ Steve E. Krognes
Steve E. Krognes
Attorney-in-Fact

Exhibit 1.1

Denali Therapeutics Inc.

Common Stock, par value $0.01 per share

Underwriting Agreement

[•], 2017

Goldman Sachs & Co. LLC,
Morgan Stanley & Co. LLC, and
J.P. Morgan Securities LLC
As representatives (the "Representatives") of the several Underwriters
named in Schedule I hereto,

c/o Goldman Sachs & Co. LLC
200 West Street,
New York, New York 10282-2198

c/o Morgan Stanley & Co. LLC
1585 Broadway
New York, NY 10036

c/o J.P. Morgan Securities LLC
383 Madison Avenue
New York, NY 10179

Ladies and Gentlemen:

Denali Therapeutics Inc., a Delaware corporation (the "Company"), proposes, subject to the terms and conditions stated in this agreement (this "Agreement"), to issue and sell to the Underwriters named in Schedule I hereto (the "Underwriters") an aggregate of [•] shares (the "Firm Shares") and, at the election of the Underwriters, up to [•] additional shares (the "Optional Shares") of the Common Stock, par value $0.01 per share ("Stock") of the Company (the Firm Shares and the Optional Shares that the Underwriters elect to purchase pursuant to Section 2 hereof being collectively called the "Shares").

1. The Company represents and warrants to, and agrees with, each of the Underwriters that:

(a) A registration statement on Form S-1 (File No. 333-221522) (the "Initial Registration Statement") in respect of the Shares has been filed with the Securities and Exchange Commission (the "Commission"); the Initial Registration Statement and any post-effective amendment thereto, each in the form heretofore delivered to you, have been declared effective by the Commission in such form;

other than a registration statement, if any, increasing the size of the offering (a "Rule 462(b) Registration Statement"), filed pursuant to Rule 462(b) under the Securities Act of 1933, as amended (the "Act"), which became effective upon filing, no other document with respect to the Initial Registration Statement has been filed with the Commission; and no stop order suspending the effectiveness of the Initial Registration Statement, any post-effective amendment thereto or the Rule 462(b) Registration Statement, if any, has been issued and no proceeding for that purpose has been initiated or, to the Company's knowledge, threatened by the Commission (any preliminary prospectus included in the Initial Registration Statement or filed with the Commission pursuant to Rule 424(a) of the rules and regulations of the Commission under the Act is hereinafter called a "Preliminary Prospectus"; the various parts of the Initial Registration Statement and the Rule 462(b) Registration Statement, if any, including all exhibits thereto and including the information contained in the form of final prospectus filed with the Commission pursuant to Rule 424(b) under the Act in accordance with Section 5(a) hereof and deemed by virtue of Rule 430A under the Act to be part of the Initial Registration Statement at the time it was declared effective, each as amended at the time such part of the Initial Registration Statement became effective or such part of the Rule 462(b) Registration Statement, if any, became or hereafter becomes effective, are hereinafter collectively called the "Registration Statement"; the Preliminary Prospectus relating to the Shares that was included in the Registration Statement immediately prior to the Applicable Time (as defined in Section 1(c) hereof) is hereinafter called the "Pricing Prospectus"; and such final prospectus, in the form first filed pursuant to Rule 424(b) under the Act, is hereinafter called the "Prospectus"; any oral or written communication with potential investors undertaken in reliance on Section 5(d) of the Act is hereinafter called a "Section 5(d) Communication"; and any Section 5(d) Communication that is a written communication within the meaning of Rule 405 under the Act is hereinafter called a "Section 5(d) Writing"; and any "issuer free writing prospectus" as defined in Rule 433 under the Act relating to the Shares is hereinafter called an "Issuer Free Writing Prospectus");

(b) (A) No order preventing or suspending the use of any Preliminary Prospectus or any Issuer Free Writing Prospectus has been issued by the Commission, and (B) each Preliminary Prospectus, at the time of filing thereof, conformed in all material respects to the requirements of the Act and the rules and regulations of the Commission thereunder, and did not contain an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading; *provided*, *however*, that this representation and warranty shall not apply to any statements or omissions made in reliance upon and in conformity with the Underwriter Information (as defined in Section 9(b) of this Agreement);

(c) For the purposes of this Agreement, the "Applicable Time" is [___:___ __m] (Eastern time) on the date of this Agreement. The Pricing Prospectus, as supplemented by the information listed on Schedule II(c) hereto, taken together (collectively, the "Pricing Disclosure Package"), as of the

Applicable Time, did not include any untrue statement of a material fact or omit to state any material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading; and each Issuer Free Writing Prospectus and each Section 5(d) Writing does not conflict with the information contained in the Registration Statement, the Pricing Prospectus or the Prospectus and each Issuer Free Writing Prospectus and each Section 5(d) Writing, as supplemented by and taken together with the Pricing Disclosure Package, as of the Applicable Time, did not include any untrue statement of a material fact or omit to state any material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading; *provided*, *however*, that this representation and warranty shall not apply to statements or omissions made in reliance upon and in conformity with the Underwriter Information;

(d) The Registration Statement, at the time it was declared effective, conforms, and the Prospectus and any further amendments or supplements to the Registration Statement and the Prospectus, on the date when such Prospectus, amendment or supplement is filed, will conform, in all material respects to the requirements of the Act and the rules and regulations of the Commission thereunder and do not and will not, as of the applicable effective date as to each part of the Registration Statement, as of the applicable filing date as to the Prospectus and any amendment or supplement thereto, and as of each Time of Delivery, contain an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading; *provided*, *however*, that this representation and warranty shall not apply to any statements or omissions made in reliance upon and in conformity with the Underwriter Information;

(e) The Company has not, since the date of the latest audited financial statements included in the Pricing Prospectus, (i) sustained any material loss or interference with its business from fire, explosion, flood or other calamity, whether or not covered by insurance, or from any labor dispute or court or governmental action, order or decree or (ii) entered into any transaction or agreement (whether or not in the ordinary course of business) that is material to the Company or incurred any liability or obligation, direct or contingent, that is material to the Company, in each case otherwise than as set forth or contemplated in the Pricing Prospectus; and, since the respective dates as of which information is given in the Registration Statement and the Pricing Prospectus, there has not been (x) any change in the capital stock (other than as a result of (i) the exercise, if any, of stock options or the award, if any, of stock options or restricted stock in the ordinary course of business pursuant to the Company's equity plans that are described in the Pricing Prospectus and the Prospectus or (ii) the issuance, if any, of stock upon conversion of Company securities as described in the Pricing Prospectus and the Prospectus) or long-term debt of the Company or (y) any Material Adverse Effect (as defined below); as used in this Agreement, "Material Adverse Effect" shall mean any material adverse change or effect, or any development involving a prospective material adverse change or effect, in or affecting (i) the business, properties, general affairs, management, financial

position, stockholders' equity or results of operations of the Company, except as set forth or contemplated in the Pricing Prospectus, or (ii) the ability of the Company to perform its obligations under this Agreement, including the issuance and sale of the Shares, or to consummate the transactions contemplated in the Pricing Prospectus and the Prospectus;

(f) Nothing has come to the attention of the Company that has caused the Company to believe that the statistical and market-related data included in the Registration Statement, the Pricing Disclosure Package and the Prospectus is not based on or derived from sources that are reliable and accurate in all material respects;

(g) The Company has good and marketable title to all personal property (other than with respect to Intellectual Property (as defined below), which is addressed exclusively in subsection (h) below) owned by it, in each case free and clear of all liens, encumbrances and defects except such as are described in the Pricing Prospectus or such as do not materially affect the value of such property and do not interfere with the use made and proposed to be made of such property by the Company; and any real property and buildings held under lease by the Company are held by it under, to the Company's knowledge, valid, subsisting and enforceable leases (subject to the effects of (i) bankruptcy, insolvency, fraudulent conveyance, fraudulent transfer, reorganization, moratorium or other similar laws relating to or affecting the rights or remedies of creditors generally; (ii) the application of general principles of equity; and (iii) applicable law and public policy with respect to rights to indemnity and contribution) with such exceptions as are not material and do not materially interfere with the use made and proposed to be made of such property and buildings by the Company;

(h) The Company owns or possesses sufficient rights to use all owned or in-licensed patents, patent applications, trademarks, service marks, trade names, trademark registrations, service mark registrations, domain names and other source indicators, copyrights and copyrightable works, know-how, trade secrets, systems, procedures, proprietary or confidential information and all other worldwide intellectual property, industrial property and proprietary rights (including all goodwill associated with the foregoing) (collectively, "Intellectual Property") material to the conduct of its business as presently conducted or currently proposed to be conducted in the Registration Statement, the Pricing Disclosure Package and the Prospectus. Except as described in the Registration Statement, the Pricing Disclosure Package and the Prospectus, to the knowledge of the Company, the Company has not materially infringed, misappropriated or otherwise violated any Intellectual Property of any person and the conduct of its business as presently conducted or as proposed to be conducted in the Registration Statement, the Pricing Disclosure Package and the Prospectus does not and will not infringe, misappropriate or otherwise violate any Intellectual Property of any person. Except as would not reasonably be expected to have a Material Adverse Effect, or except as described in the Registration Statement, the Pricing Disclosure Package and the Prospectus, there is no pending or, to the knowledge of the Company, threatened action, suit, proceeding or

claim (i) challenging the Company's rights in or to, or alleging the violation of any of the terms of, any of its Intellectual Property; (ii) alleging that the Company has infringed, misappropriated or otherwise violated or conflicted with any Intellectual Property of any third party; or (iii) challenging the validity, scope or enforceability of any Intellectual Property owned by or exclusively licensed to the Company. Except as would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect, or except as described in the Registration Statement, the Pricing Disclosure Package and the Prospectus, (w) all Intellectual Property owned by or licensed to the Company (1) is, to the knowledge of the Company, valid and enforceable, (2) is solely owned by or, licensed or co-licensed by the Company, and (3) is owned free and clear of all liens, encumbrances, defects and other restrictions, and (x) to the knowledge of the Company, no third party has infringed, misappropriated or otherwise violated any Intellectual Property owned by or exclusively licensed to the Company. The Company has at all times taken reasonable steps in accordance with normal industry practice to maintain the confidentiality of all material Intellectual Property the value of which to the Company is contingent upon maintaining the confidentiality thereof. All founders, current and former employees, contractors, consultants and other parties involved in the development of material Intellectual Property for the Company have signed confidentiality and invention assignment agreements with the Company, pursuant to which the Company either (y) has obtained ownership of and is the exclusive owner of such material Intellectual Property, or (z) has obtained a valid right to exploit such material Intellectual Property, sufficient for the conduct of its business as currently conducted and as proposed in the Registration Statement, the Pricing Disclosure Package and the Prospectus to be conducted;

(i) The Company possesses all licenses, sub-licenses, certificates, permits and other authorizations issued by, and have made all declarations and filings with, the appropriate federal, state, local or foreign governmental or regulatory authorities that are required for the ownership or lease of its property or the conduct of its businesses as currently conducted and described in the Registration Statement, the Pricing Disclosure Package and the Prospectus, including, without limitation, from the U.S. Food and Drug Administration ("FDA") except where the failure to possess or make the same would not, individually or in the aggregate, have a Material Adverse Effect; and except as described in the Registration Statement, the Pricing Disclosure Package and the Prospectus, the Company has not received notice of any revocation of any such license, sub-license, certificate, permit or authorization or has any reason to believe that any such license, sub-license, certificate, permit or authorization will not be renewed in the ordinary course;

(j) The Company has operated and currently is in compliance with all applicable rules and regulations of the FDA, except where the failure to so operate or be in compliance would not reasonably be expected to have a Material Adverse Effect;

(k) Any studies, tests and preclinical and clinical trials conducted by the Company and, to the knowledge of the Company, any studies, tests and preclinical and clinical trials conducted on behalf of the Company or in which the Company has participated, were, and if still pending are, being conducted in accordance with experimental protocols, procedures and controls pursuant to accepted professional scientific standards and all applicable rules and regulations, including those of the FDA and comparable regulatory agencies outside of the United States, to which the Company is subject and, for studies submitted to regulatory authorities as a basis for regulatory approval and preclinical and clinical trials, current Good Clinical Practices and Good Laboratory Practices, except where the failure to be so conducted would not reasonably be expected to have a Material Adverse Effect; the descriptions of the results of such studies, tests and trials contained in the Registration Statement, the Pricing Prospectus and the Prospectus are, to the Company's knowledge, accurate and complete in all material respects and fairly present the data derived from such studies, tests and trials; except to the extent disclosed in the Registration Statement, the Pricing Prospectus and the Prospectus, the Company is not aware of any studies, tests or trials, the results of which the Company believes reasonably call into question the study, test, or trial results described or referred to in the Registration Statement, the Pricing Prospectus and the Prospectus when viewed in the context in which such results are described and the clinical state of development; and, except to the extent disclosed in the Registration Statement, the Pricing Prospectus or the Prospectus, the Company has not received any notices or correspondence from the FDA or any other comparable federal, state, local or foreign governmental or regulatory authority requiring the termination or suspension of any studies, tests or preclinical or clinical trials conducted by or on behalf of the Company;

(l) No material labor disturbance by or dispute with employees of the Company exists or, to the knowledge of the Company, is contemplated or threatened, and the Company is not aware of any existing or imminent labor disturbance by, or dispute with, the employees of any of its principal suppliers or contractors, except as would not have a Material Adverse Effect. The Company has not received any notice of cancellation or termination with respect to any collective bargaining agreement material to the Company;

(m) (i) Each employee benefit plan, within the meaning of Section 3(3) of the Employee Retirement Income Security Act of 1974, as amended ("ERISA"), for which the Company or any member of its "Controlled Group" (defined as any entity, whether or not incorporated, that is under common control with the Company within the meaning of Section 4001(a)(14) of ERISA or any entity that would be regarded as a single employer with the Company under Section 414(b),(c),(m) or (o) of the Internal Revenue Code of 1986, as amended (the "Code")) would have any liability (each, a "Plan") has been maintained in compliance with its terms and the requirements of any applicable statutes, orders, rules and regulations, including but not limited to ERISA and the Code, except for noncompliance that would not reasonably be expected to result in material liability to the Company; (ii) no prohibited transaction, within the meaning of Section 406 of ERISA or Section 4975 of the Code, has occurred with respect to any Plan, excluding transactions effected pursuant to a statutory or administrative exemption; (iii) for each Plan that is subject to the funding rules of Section 412 of

the Code or Section 302 of ERISA, no Plan has failed (whether or not waived), or is reasonably expected to fail, to satisfy the minimum funding standards (within the meaning of Section 302 of ERISA or Section 412 of the Code) applicable to such Plan; (iv) no Plan is, or is reasonably expected to be, in "at risk status" (within the meaning of Section 303(i) of ERISA) and no Plan that is a "multiemployer plan" within the meaning of Section 4001(a)(3) of ERISA is in "endangered status" or "critical status" (within the meaning of Sections 304 and 305 of ERISA) (v) for each Plan that is subject to the funding rules of Section 412 of the Code or Section 302 of ERISA, the fair market value of the assets of each such Plan exceeds the present value of all benefits accrued under such Plan (determined based on those assumptions used to fund such Plan); (vi) no "reportable event" (within the meaning of Section 4043(c) of ERISA and the regulations promulgated thereunder) has occurred or is reasonably expected to occur; (vii) each Plan that is intended to be qualified under Section 401(a) of the Code is so qualified, and to the knowledge of the Company, nothing has occurred, whether by action or by failure to act, which would cause the loss of such qualification; (viii) neither the Company nor any member of the Controlled Group has incurred, nor reasonably expects to incur, any liability under Title IV of ERISA (other than contributions to the Plan or premiums to the Pension Benefit Guarantee Corporation, in the ordinary course and without default) in respect of a Plan (including a "multiemployer plan" within the meaning of Section 4001(a)(3) of ERISA); and (ix) none of the following events has occurred or is reasonably likely to occur: (A) a material increase in the aggregate amount of contributions required to be made to all Plans by the Company or its Controlled Group affiliates in the current fiscal year of the Company and its Controlled Group affiliates compared to the amount of such contributions made in the Company's and its Controlled Group affiliates' most recently completed fiscal year; or (B) a material increase in the Company's "accumulated post-retirement benefit obligations" (within the meaning of Accounting Standards Codification Topic 715-60) compared to the amount of such obligations in the Company's most recently completed fiscal year, except in each case with respect to the events or conditions set forth in (i) through (ix) hereof, as would not, individually or in the aggregate, have a Material Adverse Effect;

(n) (i) Except in each case as otherwise disclosed in the Pricing Prospectus and the Prospectus, the Company (x) has complied and is in compliance with all applicable federal, state, local and foreign laws, rules, regulations, requirements, decisions, judgments, decrees and orders relating to pollution, hazardous or toxic substances, wastes, pollutants, contaminants or the protection of human health or safety, the environment or natural resources (collectively, "Environmental Laws"); (y) has received and is in compliance with all permits, licenses, certificates or other authorizations or approvals required of it under any Environmental Laws to conduct its business; and (z) has not received notice of any actual or potential liability of the Company, or obligation of the Company under or relating to, or any actual or potential violation of, any Environmental Laws by the Company, including for the investigation or remediation of any disposal or release of hazardous or toxic substances or wastes, pollutants or contaminants, and has no knowledge of any event or

condition that would reasonably be expected to result in any such notice, and (ii) there are no costs or liabilities associated with Environmental Laws of or relating to the Company, except in the case of each of (i) and (ii) above, for any such matter as would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect; and (iii) except as described in each of the Pricing Disclosure Package and the Prospectus, (x) there is no proceeding that is pending, or that is known by the Company to be contemplated, against the Company under any Environmental Laws in which a governmental entity is also a party, other than such proceeding regarding which the Company reasonably believes no monetary sanctions of $100,000 or more will be imposed, (y) the Company is not aware of any facts regarding compliance with Environmental Laws, or liabilities or other obligations under Environmental Laws or concerning hazardous or toxic substances or wastes, pollutants or contaminants, that individually or in the aggregate, would reasonably be expected to have a Material Adverse Effect, and (z) the Company does not anticipate material capital expenditures relating to any Environmental Laws;

(o) The Company has no subsidiaries;

(p) The Company has been (i) duly organized and is validly existing and in good standing under the laws of its jurisdiction of organization, with power and authority (corporate and other) to own its properties and conduct its business as described in the Pricing Prospectus, and (ii) duly qualified as a foreign corporation for the transaction of business and is in good standing under the laws of each other jurisdiction in which it owns or leases properties or conducts any business so as to require such qualification, except, in the case of this clause (ii), where the failure to be so qualified or in good standing would not, individually or in the aggregate, have a Material Adverse Effect;

(q) The Company has an authorized capitalization as set forth in the Pricing Prospectus and all of the issued shares of capital stock of the Company have been duly and validly authorized and issued and are fully paid and non-assessable and conform in all material respects to the description of the Stock contained in the Pricing Disclosure Package and Prospectus;

(r) The unissued Shares to be issued and sold by the Company to the Underwriters hereunder have been duly and validly authorized and, when issued and delivered against payment therefor as provided herein, will be duly and validly issued and fully paid and non-assessable and will conform in all material respects to the description of Stock contained in the Pricing Disclosure Package and the Prospectus; and the issuance of the Shares is not subject to any preemptive or similar rights that have not been duly waived;

(s) The issue and sale of the Shares and the compliance by the Company with this Agreement and the consummation by the Company of the transactions contemplated in this Agreement and the Pricing Prospectus will not conflict with or result in a breach or violation of any of the terms or provisions of, or constitute a default under, (A) any indenture, mortgage, deed of trust, loan agreement or other agreement or instrument to which the Company is a party or

by which the Company is bound or to which any of the property or assets of the Company is subject, except, in the case of this clause (A) for such defaults, breaches, or violations that would not, individually or in the aggregate, have a Material Adverse Effect, (B) the certificate of incorporation or by-laws (or other applicable organizational document) of the Company, or (C) any statute or any judgment, order, rule or regulation of any court or governmental agency or body having jurisdiction over the Company or any of its property, except, in the case of this clause (C) for such violations that would not, individually or in the aggregate, have a Material Adverse Effect; and no consent, approval, authorization, order, registration or qualification of or with any such court or governmental agency or body is required for the issue and sale of the Shares or the consummation by the Company of the transactions contemplated by this Agreement, except such as have been obtained under the Act, the approval by the Financial Industry Regulatory Authority ("FINRA") of the underwriting terms and arrangements, the approval for listing on the NASDAQ Global Select Market (the "Exchange"), and such consents, approvals, authorizations, registrations or qualifications as may be required under state securities or Blue Sky laws in connection with the purchase and distribution of the Shares by the Underwriters;

(t) The Company is not (i) in violation of its certificate of incorporation or by-laws (or other applicable organizational document), (ii) in violation of any statute or any judgment, order, rule or regulation of any court or governmental agency or body having jurisdiction over the Company or any of its property, or (iii) in default in the performance or observance of any obligation, agreement, covenant or condition contained in any indenture, mortgage, deed of trust, loan agreement, lease or other agreement or instrument to which it is a party or by which it or any of its property may be bound, except, in the case of the foregoing clauses (ii) and (iii), for such violations or defaults as would not, individually or in the aggregate, have a Material Adverse Effect;

(u) The statements set forth in the Pricing Prospectus and Prospectus under the caption ["Description of Capital Stock"], insofar as they purport to constitute a summary of the terms of the Stock[, under the caption ["Material U.S. Federal Income and Estate Tax Considerations for Non-U.S. Holders of our Common Stock"],] and under the caption ["Underwriting"], insofar as they purport to describe the provisions of the laws and documents referred to therein, are accurate, complete and fair in all material respects;

(v) Other than as set forth in the Pricing Prospectus, there are no legal or governmental proceedings pending to which the Company is a party or of which any property of the Company is the subject which, if determined adversely to the Company (or such officer or director), would individually or in the aggregate have a Material Adverse Effect; and, to the Company's knowledge, no such proceedings are threatened or contemplated by governmental authorities or threatened by others;

(w) No relationship, direct or indirect, exists between the Company, on the one hand, and the directors, officers, or stockholders of the Company, on the other, that is required by the Act to be described in the Registration Statement and the Prospectus and that is not so described in such documents and in the Pricing Disclosure Package;

(x) The Company is not and, after giving effect to the offering and sale of the Shares and the application of the proceeds thereof, will not be an "investment company", as such term is defined in the Investment Company Act of 1940, as amended;

(y) At the time of filing the Initial Registration Statement and any post-effective amendment thereto, at the earliest time thereafter that the Company or any offering participant made a *bona fide* offer (within the meaning of Rule 164(h)(2) under the Act) of the Shares, and at the date hereof, the Company was not and is not an "ineligible issuer", as defined under Rule 405 under the Act;

(z) There are (and prior to the Time of Delivery, will be) no debt securities or preferred stock issued or guaranteed by the Company that are rated by a "nationally recognized statistical rating organization", as such term is defined under Section 3(a)(62) under the Exchange Act.

(aa) Except as described in the Pricing Prospectus, the Company has not sold, issued or distributed any shares of Stock during the six-month period preceding the date hereof, including any sales pursuant to Rule 144A under, or Regulation D or S of, the Act, other than shares issued pursuant to employee benefit plans or other employee compensation plans or pursuant to outstanding options, rights or warrants;

(bb) Ernst & Young LLP, who have certified certain financial statements of the Company, are independent public accountants as required by the Act and the rules and regulations of the Commission thereunder;

(cc) The Company maintains a system of internal control over financial reporting (as such term is defined in Rule 13a-15(f) under the Securities Exchange Act of 1934, as amended (the "Exchange Act")) that (i) complies with the requirements of the Exchange Act applicable to the Company and (ii) has been designed by the Company's principal executive officer and principal financial officer, or under their supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and (iii) is sufficient to provide reasonable assurance that (A) transactions are executed in accordance with management's general or specific authorization, (B) transactions are recorded as necessary to permit preparation of financial statements in conformity with generally accepted accounting principles and to maintain accountability for assets, (C) access to assets is permitted only in accordance with management's general or specific authorization and (D) the recorded accountability for assets is compared with the existing assets at reasonable intervals and appropriate action is taken with respect to any differences; and the Company is not aware of any material weaknesses in its internal control over financial reporting (it being understood that this subsection shall not require the Company to comply with Section 404 of the Sarbanes-Oxley Act of 2002 as of an earlier date than it would otherwise be required to so comply under applicable law);

(dd) Since the date of the latest audited financial statements included in the Pricing Prospectus, there has been no change in the Company's internal control over financial reporting that has materially and adversely affected, or is reasonably likely to materially and adversely affect, the Company's internal control over financial reporting;

(ee) The Company maintains disclosure controls and procedures (as such term is defined in Rule 13a-15(e) under the Exchange Act) that comply with the requirements of the Exchange Act applicable to the Company; such disclosure controls and procedures have been designed to ensure that material information relating to the Company is made known to the Company's principal executive officer and principal financial officer by others within those entities; and such disclosure controls and procedures are effective;

(ff) The Company has taken all necessary steps to ensure that, upon the effectiveness of the Registration Statement, it shall be in compliance with any applicable provision of the Sarbanes-Oxley Act of 2002 and the rules and regulations promulgated in connection therewith that the Company is required to be in compliance with upon the effectiveness of the Registration Statement, including Section 402 related to loans;

(gg) Except as described in or expressly contemplated by the Registration Statement, the Pricing Disclosure Package and the Prospectus, the Company has insurance covering its property, operations, personnel and businesses, including clinical trial insurance and business interruption insurance, which insurance is, in the Company's reasonable judgment, in amounts and insures against such losses and risks as are generally maintained by similarly situated companies and which the Company believes are reasonably adequate to protect the Company and its business; and the Company has not (i) received notice from any insurer or agent of such insurer that capital improvements or other expenditures are required or necessary to be made in order to continue such insurance or (ii) any reason to believe that it will not be able to renew its existing insurance coverage as and when such coverage expires or to obtain similar coverage at reasonable cost from similar insurers as may be necessary to continue its business;

(hh) The Company has all requisite rights, power and authority to execute and delivery this Agreement and to perform its obligations hereunder; and all action required to be taken for the due and proper authorization, execution and delivery by it of this Agreement and the consummation by it of the transactions contemplated hereby has been duly and validly taken;

(ii) This Agreement has been duly authorized, executed and delivered by the Company;

(jj) Neither the Company nor its directors, officers, employees and affiliates, nor, to the knowledge of the Company, any agent or other person associated with or acting on behalf of the Company, (i) has made, offered, promised or authorized or will make, offer, promise or authorize any unlawful contribution, gift, entertainment or other unlawful expense; (ii) has made, offered, promised or authorized or will make, offer, promise or authorize any direct or indirect unlawful payment; or (iii) has violated or is in violation of any provision of the Foreign Corrupt Practices Act of 1977, the Bribery Act 2010 of the United Kingdom or any other applicable anti-bribery or anti-corruption law; the Company and its affiliates have conducted their businesses in compliance with applicable anti-bribery and anti-corruption laws and have instituted and maintain policies and procedures designed to promote and achieve compliance with such laws and with the representation and warranty contained herein; and the Company will not use, directly or indirectly, the proceeds of the offering and sale of the Shares in furtherance of an offer, payment, promise to pay or authorization of the payment or giving of money, or anything else of value, to any person in violation of any applicable anti-bribery or anti-corruption laws;

(kk) Except as described in the Pricing Prospectus and the Prospectus, Company is not a party to any contract, agreement or understanding with any person (other than this Agreement) that would give rise to a valid claim against the Company or any Underwriter for a brokerage commission, finder's fee or like payment in connection with the offering and sale of the Shares;

(ll) No person has the right to require the Company to register any securities for sale under the Act by reason of the filing of the Registration Statement with the Commission or the issuance and sale of the Shares, except such rights that have been waived or complied with;

(mm) The Company has not taken, directly or indirectly, without giving effect to activities by the Underwriters or affiliate or agent of any Underwriter acting on behalf of such Underwriter, any action designed to or that would reasonably be expected to cause or result in any stabilization or manipulation of the price of the Shares;

(nn) The operations of the Company are and have been conducted at all times in compliance with the requirements of applicable anti-money laundering laws, including, but not limited to, the Bank Secrecy Act of 1970, as amended by the USA PATRIOT ACT of 2001, and the rules and regulations promulgated thereunder, and the applicable anti-money laundering laws of the various jurisdictions in which the Company conducts business (collectively, the "Money Laundering Laws") and no action, suit or proceeding by or before any court or governmental agency, authority or body or any arbitrator involving the Company with respect to the Money Laundering Laws is pending or, to the knowledge of the Company, threatened;

(oo) Neither the Company nor, to the knowledge of the Company, its directors or officers, or any agent, employee or affiliate of the Company, is, or is owned or controlled by one or more individuals or entities that is, currently the subject or the target of any sanctions administered or enforced by the U.S. Government, including, without limitation, the Office of Foreign Assets Control of the U.S. Department of the Treasury ("OFAC"), or the U.S. Department of State and including, without limitation, the designation as a "specially designated national" or "blocked person", the European Union, Her Majesty's Treasury, the United Nations Security Council, or other relevant sanctions authority (collectively, "Sanctions"), nor located, organized or resident in a country or territory that is the subject of Sanctions (including, without limitation, Crimea, Cuba, Iran, North Korean, Sudan and Syria); the Company will not directly or indirectly use the proceeds of the offering of the Shares hereunder, or lend, contribute or otherwise make available such proceeds to any joint venture partner or other person or entity (i) to fund or facilitate any activities of or business with any person, or in any country or territory, that, at the time of such funding, is the subject or the target of Sanctions or (ii) in any other manner that will result in a violation by any person (including any person participating in the transaction, whether as underwriter, advisor, investor or otherwise) of Sanctions; and for the past five years, the Company has not knowingly engaged in and is not now knowingly engaged in any dealings or transactions with any person that at the time of the dealing or transaction is or was the subject or target of Sanctions or with any Sanctioned country;

(pp) The Company has paid all federal, state, local and foreign taxes and filed all tax returns required to be paid or filed through the date hereof (after giving effect to any valid extensions with respect to the filing of tax returns), except where the failure to pay or file would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect, or except as described in the Registration Statement, the Pricing Disclosure Package and the Prospectus; and except as otherwise disclosed in the Registration Statement, the Pricing Disclosure Package and the Prospectus, there are no tax deficiencies that have been, or would reasonably be expected to be, asserted against the Company or any of its property or assets and which would, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect;

(qq) The financial statements included in the Registration Statement, the Pricing Prospectus and the Prospectus, together with the related schedules and notes, present fairly, in all material respects, the financial position of the Company at the dates indicated and the statement of operations, stockholders' equity and cash flows of the Company for the periods specified; said financial statements have been prepared in conformity with U.S. generally accepted accounting principles ("GAAP") applied on a consistent basis throughout the periods involved. The supporting schedules, if any, present fairly in all material respects in accordance with GAAP the information required to be stated therein. The selected financial data and the summary financial information included in the Registration Statement, the Pricing Prospectus and the Prospectus present fairly in all material respects the information shown therein and have been compiled on a basis consistent with that of the audited financial statements included therein. Except as included therein, no historical or pro forma financial statements or supporting schedules are required to be included in the Registration Statement,

the Pricing Prospectus or the Prospectus under the Act or the rules and regulations promulgated thereunder. All disclosures contained in the Registration Statement, the Pricing Prospectus and the Prospectus regarding "non-GAAP financial measures" (as such term is defined by the rules and regulations of the Commission) comply with Regulation G of the Exchange Act and Item 10 of Regulation S-K of the Act, to the extent applicable; and

(rr) From the time of initial confidential submission of a registration statement relating to the Shares with the Commission (or, if earlier, the first date on which a Section 5(d) Communication was made) through the date hereof, the Company has been and is an "emerging growth company" as defined in Section 2(a)(19) of the Act (an "Emerging Growth Company").

2. Subject to the terms and conditions herein set forth, (a) the Company agrees to issue and sell to each of the Underwriters, and each of the Underwriters agrees, severally and not jointly, to purchase from the Company, at a purchase price per share of $[•], the number of Firm Shares set forth opposite the name of such Underwriter in Schedule I hereto and (b) in the event and to the extent that the Underwriters shall exercise the election to purchase Optional Shares as provided below, the Company agrees to issue and sell to each of the Underwriters, and each of the Underwriters agrees, severally and not jointly, to purchase from the Company, at the purchase price per share set forth in clause (a) of this Section 2, that portion of the number of Optional Shares as to which such election shall have been exercised (to be adjusted by you so as to eliminate fractional shares) determined by multiplying such number of Optional Shares by a fraction, the numerator of which is the maximum number of Optional Shares which such Underwriter is entitled to purchase as set forth opposite the name of such Underwriter in Schedule I hereto and the denominator of which is the maximum number of Optional Shares that all of the Underwriters are entitled to purchase hereunder.

The Company hereby grants to the Underwriters the right to purchase at their election up to [•] Optional Shares, at the purchase price per share set forth in the paragraph above, for the sole purpose of covering sales of shares in excess of the number of Firm Shares, provided that the purchase price per Optional Share shall be reduced by an amount per share equal to any dividends or distributions declared by the Company and payable on the Firm Shares but not payable on the Optional Shares. Any such election to purchase Optional Shares may be exercised only by written notice from you to the Company, given within a period of 30 calendar days after the date of this Agreement, setting forth the aggregate number of Optional Shares to be purchased and the date on which such Optional Shares are to be delivered, as determined by you but in no event earlier than the First Time of Delivery (as defined in Section 4 hereof) or, unless you and the Company otherwise agree in writing, earlier than two or later than ten business days after the date of such notice.

3. Upon the authorization by you of the release of the Firm Shares, the several Underwriters propose to offer the Firm Shares for sale upon the terms and conditions set forth in the Pricing Prospectus and the Prospectus.

4. (a) The Shares to be purchased by each Underwriter hereunder, in definitive or book-entry form, and in such authorized denominations and registered in such names as the Representatives may request upon at least forty-eight hours' prior notice to the Company shall be delivered by or on behalf of the Company to the Representatives, through the facilities of the Depository Trust Company ("DTC"), for the account of such Underwriter, against payment by or on behalf of such Underwriter of the purchase price therefor by wire transfer of Federal (same-day) funds to the account specified by the Company to the Representatives at least forty-eight hours in advance. The Company will cause the certificates, if any, representing the Shares to be made available for checking and packaging at least twenty-four hours prior to the Time of Delivery (as defined below) with respect thereto at the office of DTC or its designated custodian (the "Designated Office"). The time and date of such delivery and payment shall be, with respect to the Firm Shares, 9:30 a.m., New York City time, on [•], 20[•] or such other time and date as the Representatives and the Company may agree upon in writing, and, with respect to the Optional Shares, 9:30 a.m., New York time, on the date specified by the Representatives in the written notice given by the Representatives of the Underwriters' election to purchase such Optional Shares, or such other time and date as the Representatives and the Company may agree upon in writing. Such time and date for delivery of the Firm Shares is herein called the "First Time of Delivery", such time and date for delivery of the Optional Shares, if not the First Time of Delivery, is herein called the "Second Time of Delivery", and each such time and date for delivery is herein called a "Time of Delivery".

(b) The documents to be delivered at each Time of Delivery by or on behalf of the parties hereto pursuant to Section 8 hereof, including the cross receipt for the Shares and any additional documents requested by the Underwriters pursuant to Section 8(j) hereof, will be delivered at the offices of Davis Polk & Wardwell LLP, 1600 El Camino Real, Menlo Park, CA 94025 (the "Closing Location"), and the Shares will be delivered at the Designated Office, all at such Time of Delivery. A meeting will be held at the Closing Location at [•] p.m., New York City time, on the New York Business Day next preceding such Time of Delivery, at which meeting the final drafts of the documents to be delivered pursuant to the preceding sentence will be available for review by the parties hereto. For the purposes of this Section 4, "New York Business Day" shall mean each Monday, Tuesday, Wednesday, Thursday and Friday which is not a day on which banking institutions in New York City are generally authorized or obligated by law or executive order to close.

5. The Company agrees with each of the Underwriters:

(a) To prepare the Prospectus in a form approved by you and to file such Prospectus pursuant to Rule 424(b) under the Act not later than the Commission's close of business on the second business day following the execution and delivery of this Agreement, or, if applicable, such earlier time as may be required by Rule 430A(a)(3) under the Act; to make no further amendment or any supplement to the Registration Statement or the Prospectus prior to the last Time of Delivery which shall be disapproved by you promptly after reasonable notice thereof; to advise you, promptly after it receives notice thereof, of the time when any amendment to the Registration Statement has been filed or becomes effective or any amendment or supplement to the Prospectus has been filed and

to furnish you with copies thereof; to file promptly all material required to be filed by the Company with the Commission pursuant to Rule 433(d) under the Act; to advise you, promptly after it receives notice thereof, of the issuance by the Commission of any stop order or of any order preventing or suspending the use of any Preliminary Prospectus or other prospectus in respect of the Shares, of the suspension of the qualification of the Shares for offering or sale in any jurisdiction, of the initiation or threatening of any proceeding for any such purpose, or of any request by the Commission for the amending or supplementing of the Registration Statement or the Prospectus or for additional information; and, in the event of the issuance of any stop order or of any order preventing or suspending the use of any Preliminary Prospectus or other prospectus or suspending any such qualification, to promptly use its best efforts to obtain the withdrawal of such order;

(b) Promptly from time to time to take such action as you may reasonably request to qualify the Shares for offering and sale under the securities laws of such jurisdictions as you may reasonably request and to comply with such laws so as to permit the continuance of sales and dealings therein in such jurisdictions for as long as may be necessary to complete the distribution of the Shares; *provided* that in connection therewith the Company shall not be required to qualify as a foreign corporation or to file a general consent to service of process in any jurisdiction or subject itself to taxation in any such jurisdiction in which it was not otherwise subject to taxation;

(c) Prior to 10:00 a.m., New York City time, on the New York Business Day next succeeding the date of this Agreement (or such later time as may be agreed by the Company and the Representatives) and from time to time, to furnish the Underwriters with written and electronic copies of the Prospectus in New York City in such quantities as you may reasonably request, and, if the delivery of a prospectus (or in lieu thereof, the notice referred to in Rule 173(a) under the Act) is required at any time prior to the expiration of nine months after the time of issue of the Prospectus in connection with the offering or sale of the Shares and if at such time any event shall have occurred as a result of which the Prospectus as then amended or supplemented would include an untrue statement of a material fact or omit to state any material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made when such Prospectus (or in lieu thereof, the notice referred to in Rule 173(a) under the Act) is delivered, not misleading, or, if for any other reason it shall be necessary during such same period to amend or supplement the Prospectus in order to comply with the Act, to notify you and upon your request to prepare and furnish without charge to each Underwriter and to any dealer (whose name and address the Underwriters shall furnish to the Company) in securities as many written and electronic copies as you may from time to time reasonably request of an amended Prospectus or a supplement to the Prospectus which will correct such statement or omission or effect such compliance; and in case any Underwriter is required to deliver a prospectus (or in lieu thereof, the notice referred to in Rule 173(a) under the Act) in connection with sales of any of the Shares at any time nine months or more after the time of issue of the Prospectus, upon your request but at the expense of such Underwriter, to prepare and deliver to such Underwriter as many written and electronic copies as you may request of an amended or supplemented Prospectus complying with Section 10(a)(3) of the Act;

(d) To make generally available to its securityholders as soon as practicable (which may be satisfied by filing with the Commission's Electronic Data Gathering Analysis and Retrieval System ("EDGAR")), but in any event not later than sixteen months after the effective date of the Registration Statement (as defined in Rule 158(c) under the Act), an earnings statement of the Company (which need not be audited) complying with Section 11(a) of the Act and the rules and regulations of the Commission thereunder (including, at the option of the Company, Rule 158);

(e) (1) During the period beginning from the date hereof and continuing to and including the date 180 days after the date of the Prospectus (the "Lock-Up Period"), not to (i) offer, sell, contract to sell, pledge, grant any option to purchase, make any short sale or otherwise transfer or dispose of, directly or indirectly, or file with or confidentially submit to the Commission a registration statement under the Act relating to, any securities of the Company that are substantially similar to the Shares, including but not limited to any options or warrants to purchase shares of Stock or any securities that are convertible into or exchangeable for, or that represent the right to receive, Stock or any such substantially similar securities, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing or (ii) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the Stock or any such other securities, whether any such transaction described in clause (i) or (ii) above is to be settled by delivery of Stock or such other securities, in cash or otherwise, without the Representatives' written consent; provided, however, that the foregoing restrictions shall not apply to (a) the Shares to be sold hereunder, (b) the issuance by the Company of shares of Common Stock upon the exercise or settlement of options pursuant to the Company's equity plans that are described in the Pricing Prospectus, or upon the conversion of convertible securities outstanding as of the date of this Agreement and as described in the Pricing Prospectus, (c) the issuance by the Company of shares of Common Stock or securities convertible into, exchangeable for or that represent the right to receive shares of Common Stock, in each case pursuant to the Company's stock plans that are described in the Pricing Prospectus, (d) the issuance by the Company of shares of Common Stock or securities convertible into, exchangeable for or that represent the right to receive shares of Common Stock in connection with (1) the acquisition by the Company of the business, technology, not less than a majority or controlling portion of the securities, property or other assets of another person or entity or pursuant to an employee benefit plan assumed by the Company in connection with such acquisition and the issuance of any such securities pursuant to any such agreement, or (2) the Company's bona fide commercial transactions (including joint ventures, commercial relationships or other strategic transactions) or (e) the filing of any registration statement on Form S-8 relating to securities granted or to be granted pursuant to the Company's stock plans that are described in the Pricing Prospectus or any assumed

employee benefit plan contemplated by clause (d); provided that the aggregate number of shares of Common Stock that the Company may sell or issue or agree to sell or issue pursuant to clause (d) and, with respect to securities to be granted pursuant to any assumed employee benefit plan, pursuant to clause (e), shall not exceed 7.5 of the total number of shares of Common Stock outstanding immediately following the offering of the Shares contemplated by this Agreement; and provided, further, that in the case of clauses (c) through (e), each recipient of such securities shall execute and deliver to the Representatives, on or prior to the issuance of such securities, a lock-up agreement substantially to the effect set forth in Section 8(i) hereto.

(2) To enforce the terms of all existing agreements, plan and arrangements restricting the transfer by any holder of such holder's Common Stock or other securities convertible into or exercisable or exchangeable for Common Stock (the "Securities") following the public offering and sale of the Shares contemplated hereby, including, without limitation, Section 2.11 of the Investors' Rights Agreement, dated as of May 8, 2015, as amended as of the date hereof, and all other "market standoff," "holdback," or similar agreements, transfer restrictions or provisions, applicable to the Common Stock or other Securities (the "Company Transfer Restrictions"), the Company shall issue stop-transfer instructions to the transfer agent with respect to any transaction that would constitute a breach of, or default under, the Company Transfer Restrictions. During the Lock-Up Period, the Company shall enforce and not waive or amend, such Company Transfer Restrictions and stop transfer instructions unless the Company shall have obtained the prior written consent of the Representatives; provided that this Section 5(e)(2) shall not prohibit the Company from effecting a waiver or amendment to permit a transfer of securities which is permissible under the terms of the lock-up letters described in Section 8(i) hereof.

(3) If the Representatives, in their sole discretion, agree to release or waive the restrictions set forth in a lock-up letter described in Section 8(i) hereof for an officer or director of the Company or a holder of the Company's Registrable Securities, as such term is defined pursuant to that certain Investors' Rights Agreement, dated May 8, 2015, as amended as of June 22, 2016, the Representatives agree to use their commercially reasonable efforts to provide the Company with notice of the impending release or waiver at least three business days before the effective date of the release or waiver, and the Company agrees to announce the impending release or waiver by a press release substantially in the form of Annex I hereto through a major news service at least two business days before the effective date of the release or waiver, if required by FINRA Rule 5131 (or any successor provision thereto);

(f) During a period of three years from the effective date of the Registration Statement, so long as the Company is subject to the reporting requirements of either Section 13 or Section 15(d) of the Exchange Act, to furnish to its stockholders as soon as practicable after the end of each fiscal year an annual report (including a balance sheet and statements of income, stockholders' equity and cash flows of the Company and any consolidated subsidiaries certified by independent public accountants) and, as soon as practicable after the end of each of the first three quarters of each fiscal year (beginning with the fiscal quarter ending after the effective date of the Registration Statement), to make available to its stockholders consolidated summary financial information of the Company and any subsidiaries for such quarter in reasonable detail, provided that no reports, documents or other information needs to be furnished pursuant to this Section 5(f) to the extent they are available on EDGAR;

(g) During a period of three years from the effective date of the Registration Statement, so long as the Company is subject to the reporting requirements of either Section 13 or Section 15(d) of the Exchange Act, to furnish to you copies of all reports or other communications (financial or other) furnished to stockholders, and to deliver to you, as soon as they are available, copies of any reports and financial statements furnished to or filed with the Commission or any national securities exchange on which any class of securities of the Company is listed, provided that no reports, documents or other information needs to be furnished pursuant to this Section 5(g) to the extent they are available on EDGAR;

(h) To use the net proceeds received by it from the sale of the Shares pursuant to this Agreement in the manner specified in the Pricing Prospectus under the caption "Use of Proceeds";

(i) To use its best efforts to list, subject to notice of issuance, the Shares on the Exchange;

(j) To file with the Commission such information on Form 10-Q or Form 10-K as may be required by Rule 463 under the Act;

(k) If the Company elects to rely upon Rule 462(b), the Company shall file a Rule 462(b) Registration Statement with the Commission in compliance with Rule 462(b) by 10:00 P.M., Washington, D.C. time, on the date of this Agreement, and the Company shall at the time of filing either pay to the Commission the filing fee for the Rule 462(b) Registration Statement or give irrevocable instructions for the payment of such fee pursuant to Rule 111(b) under the Act;

(l) Upon request of any Underwriter, to furnish, or cause to be furnished, to such Underwriter an electronic version of the Company's trademarks, servicemarks and corporate logo for use on the website, if any, operated by such Underwriter for the purpose of facilitating the on-line offering of the Shares (the "License"); *provided*, *however*, that the License shall be used solely for the purpose described above, is granted without any fee and may not be assigned or transferred; and

(m) To promptly notify you if the Company ceases to be an Emerging Growth Company at any time prior to the later of (i) completion of the distribution of the Shares within the meaning of the Act and (ii) the last Time of Delivery.

6. (a) The Company represents and agrees that, without the prior consent of the Representatives, it has not made and will not make any offer relating to the Shares that would constitute a "free writing prospectus" as defined in Rule 405 under the Act; each Underwriter represents and agrees that, without the prior consent of the Company and the Representatives, it has not made and will not make any offer relating to the Shares that would constitute a free writing prospectus required to be filed with the Commission; any such free writing prospectus the use of which has been consented to by the Company and the Representatives is listed on Schedule II(a) or Schedule II(c) hereto;

(b) The Company has complied and will comply with the requirements of Rule 433 under the Act applicable to any Issuer Free Writing Prospectus, including timely filing with the Commission or retention where required and legending; and the Company represents that it has satisfied and agrees that it will satisfy the conditions under Rule 433 under the Act to avoid a requirement to file with the Commission any electronic road show;

(c) The Company agrees that if at any time following issuance of an Issuer Free Writing Prospectus or Section 5(d) Writing any event occurred or occurs as a result of which such Issuer Free Writing Prospectus or Section 5(d) Writing would conflict with the information in the Registration Statement, the Pricing Prospectus or the Prospectus or would include an untrue statement of a material fact or omit to state any material fact necessary in order to make the statements therein, in the light of the circumstances then prevailing, not misleading, the Company will give prompt notice thereof to the Representatives and, if requested by the Representatives, will prepare and furnish without charge to each Underwriter an Issuer Free Writing Prospectus, Section 5(d) Writing or other document which will correct such conflict, statement or omission; *provided*, *however*, that this representation and warranty shall not apply to any statements or omissions in an Issuer Free Writing Prospectus made in reliance upon and in conformity with the Underwriter Information**;**

(d) The Company represents and agrees that (i) it has not engaged in, or authorized any other person to engage in, any Section 5(d) Communications, other than Section 5(d) Communications with the prior consent of the Representatives with entities that are qualified institutional buyers as defined in Rule 144A under the Act or institutions that are accredited investors as defined in Rule 501(a) under the Act; and (ii) it has not distributed, or authorized any other person to distribute, any Section 5(d) Writings, other than those distributed with the prior consent of the Representatives that are listed on Schedule II(d) hereto; and the Company reconfirms that the Underwriters have been authorized to act on its behalf in engaging in Section 5(d) Communications;

(e) Each Underwriter represents and agrees that (i) any Section 5(d) Communications undertaken by it were with entities that are qualified institutional buyers as defined in Rule 144A under the Act or institutions that are accredited investors as defined in Rule 501(a) under the Act and (ii) it will not distribute, or authorize any other person to distribute, any Section 5(d) Writing, other than those distributed with the prior consent of the Company;

7. The Company covenants and agrees with the several Underwriters that the Company will pay or cause to be paid the following: (i) the fees, disbursements and expenses of the Company's counsel and accountants in connection with the registration of the Shares under the Act and all other expenses in connection with the preparation, printing, reproduction and filing of the Registration Statement, any Preliminary Prospectus, any Section 5(d) Writing, any Issuer Free Writing Prospectus and the Prospectus and amendments and supplements thereto and the mailing and delivering of copies thereof to the Underwriters and dealers; (ii) the cost of printing or producing any Agreement among Underwriters, this Agreement, any Blue Sky Memorandum, closing documents (including any compilations thereof) and any other documents in connection with the offering, purchase, sale and delivery of the Shares; (iii) all expenses in connection with the qualification of the Shares for offering and sale under state securities laws as provided in Section 5(b) hereof, including the fees and disbursements of counsel for the Underwriters in connection with such qualification and in connection with any Blue Sky survey, if any (iv) all fees and expenses in connection with listing the Shares on the Exchange; (v) the filing fees incident to, and the fees and disbursements of counsel for the Underwriters in connection with, any required review by FINRA of the terms of the sale of the Shares; (vi) the cost of preparing stock certificates; (vii) the cost and charges

of any transfer agent or registrar; and (viii) all other costs and expenses incident to the performance of its obligations hereunder which are not otherwise specifically provided for in this Section 7; provided, however, that the amount payable by the Company pursuant to subsection (iii) and the reasonable fees and disbursements of counsel to the Underwriters described in subsection (v) of this Section 7 shall not exceed $35,000 in the aggregate. It is understood, however, that, except as provided in this Section, and Sections 9 and 12 hereof, the Underwriters will pay all of their own costs and expenses, including the fees of their counsel, stock transfer taxes on resale of any of the Shares by them, and any advertising expenses connected with any offers they may make.

8. The obligations of the Underwriters hereunder, as to the Shares to be delivered at each Time of Delivery, shall be subject, in their discretion, to the condition that all representations and warranties and other statements of the Company herein are, at and as of the Applicable Time and such Time of Delivery, true and correct, the condition that the Company shall have performed all of its obligations hereunder theretofore to be performed, and the following additional conditions:

(a) The Prospectus shall have been filed with the Commission pursuant to Rule 424(b) under the Act within the applicable time period prescribed for such filing by the rules and regulations under the Act and in accordance with Section 5(a) hereof; all material required to be filed by the Company pursuant to Rule 433(d) under the Act shall have been filed with the Commission within the applicable time period prescribed for such filing by Rule 433; if the Company has elected to rely upon Rule 462(b) under the Act, the Rule 462(b) Registration Statement shall have become effective by 10:00 P.M., Washington, D.C. time, on the date of this Agreement; no stop order suspending the effectiveness of the Registration Statement or any part thereof shall have been issued and no proceeding for that purpose shall have been initiated or threatened by the Commission; no stop order suspending or preventing the use of the Pricing Prospectus, Prospectus or any Issuer Free Writing Prospectus shall have been initiated or threatened by the Commission; and all requests for additional information on the part of the Commission shall have been complied with to your reasonable satisfaction;

(b) Davis Polk & Wardwell LLP, counsel for the Underwriters, shall have furnished to you their written opinion and 10b-5 statement, dated such Time of Delivery, in form and substance satisfactory to you, and such counsel shall have received such papers and information as they may reasonably request to enable them to pass upon such matters;

(c) Wilson Sonsini Goodrich & Rosati, Professional Corporation, counsel for the Company, shall have furnished to you their written opinion and 10b-5 statement, dated such Time of Delivery, in form and substance satisfactory to you;

(d) Wilson Sonsini Goodrich & Rosati, Professional Corporation, intellectual property counsel for the Company, shall have furnished to you their written opinion, dated such Time of Delivery, in form and substance satisfactory to you;

(e) On the date of the Prospectus at a time prior to the execution of this Agreement, at 9:30 a.m., New York City time, on the effective date of any post-effective amendment to the Registration Statement filed subsequent to the date of this Agreement and also at each Time of Delivery, Ernst & Young LLP shall have furnished to you a letter or letters, dated the respective dates of delivery thereof, in form and substance satisfactory to you;

(f) (i) The Company shall not have sustained since the date of the latest audited financial statements included in the Pricing Prospectus any loss or interference with its business from fire, explosion, flood or other calamity, whether or not covered by insurance, or from any labor dispute or court or governmental action, order or decree, otherwise than as set forth or contemplated in the Pricing Prospectus, and (ii) since the respective dates as of which information is given in the Pricing Prospectus there shall not have been any change in the capital stock or long-term debt of the Company or any change or effect, or any development involving a prospective change or effect, in or affecting (x) the business, properties, general affairs, management, financial position, stockholders' equity or results of operations of the Company, except as set forth or contemplated in the Pricing Prospectus and the Prospectus, or (y) the ability of the Company to perform its obligations under this Agreement, including the issuance and sale of the Shares, or to consummate the transactions contemplated in the Pricing Prospectus and the Prospectus, the effect of which, in any such case described in clause (i) or (ii), is in your judgment so material and adverse as to make it impracticable or inadvisable to proceed with the public offering or the delivery of the Shares being delivered at such Time of Delivery on the terms and in the manner contemplated in the Pricing Prospectus and the Prospectus;

(g) On or after the Applicable Time there shall not have occurred any of the following: (i) a suspension or material limitation in trading in securities generally on the Exchange; (ii) a suspension or material limitation in trading in the Company's securities on the Exchange; (iii) a general moratorium on commercial banking activities declared by either Federal or New York State authorities or a material disruption in commercial banking or securities settlement or clearance services in the United States; (iv) the outbreak or escalation of hostilities involving the United States or the declaration by the United States of a national emergency or war or (v) the occurrence of any other calamity or crisis or any change in financial, political or economic conditions in the United States or elsewhere, if the effect of any such event specified in clause (iv) or (v) in your judgment makes it impracticable or inadvisable to proceed with the public offering or the delivery of the Shares being delivered at such Time of Delivery on the terms and in the manner contemplated in the Pricing Prospectus and the Prospectus;

(h) The Shares to be sold at such Time of Delivery shall have been duly listed, subject to notice of issuance, on the Exchange;

(i) The Company shall have obtained and delivered to the Underwriters executed copies of an agreement from each member of the Company's board of directors, each executive officer of the Company and holders representing substantially all of the outstanding Common Stock on an as converted basis, substantially to the effect set forth in Annex II hereto;

(j) The Company shall have complied with the provisions of Section 5(c) hereof with respect to the furnishing of prospectuses on the New York Business Day next succeeding the date of this Agreement;

(k) You shall have received at each Time of Delivery satisfactory evidence of the good standing of the Company in its jurisdiction of organization and its good standing in such other jurisdictions as you may reasonably request, in each case in writing or any standard form of telecommunication from the appropriate governmental authorities of such jurisdictions; and

(l) The Company shall have furnished or caused to be furnished to you at such Time of Delivery certificates of officers of the Company satisfactory to you as to the accuracy of the representations and warranties of the Company herein at and as of such Time of Delivery, as to the performance by the Company of all of its obligations hereunder to be performed at or prior to such Time of Delivery and as to such other matters as you may reasonably request;

All opinions, letters, certificates and evidence mentioned above or elsewhere in this Agreement shall be deemed to be in compliance with the provisions hereof only if they are in form and substance reasonably satisfactory to counsel for the Underwriters.

9. (a) The Company will indemnify and hold harmless each Underwriter against any losses, claims, damages or liabilities, joint or several, to which such Underwriter may become subject, under the Act or otherwise, insofar as such losses, claims, damages or liabilities (or actions in respect thereof) arise out of or are based upon an untrue statement or alleged untrue statement of a material fact contained in the Registration Statement, any Preliminary Prospectus, the Pricing Prospectus or the Prospectus, or any amendment or supplement thereto, any Issuer Free Writing Prospectus, any "roadshow" as defined in Rule 433(h) under the Act (a "roadshow"), any "issuer information" filed or required to be filed pursuant to Rule 433(d) under the Act or any Section 5(d) Writing prepared or authorized by the Company, or arise out of or are based upon the omission or alleged omission to state therein a material fact required to be stated therein or necessary to make the statements therein not misleading, and will reimburse each Underwriter for any legal or other expenses reasonably incurred by such Underwriter in connection with investigating or defending any such action or claim as such expenses are incurred; *provided*, *however*, that the Company shall not be liable in any such case to the extent that any such loss, claim, damage or liability arises out of or is based upon an untrue statement or alleged untrue statement or omission or alleged omission made in the Registration Statement, any Preliminary Prospectus, the Pricing Prospectus or the Prospectus, or any amendment or supplement thereto, or any Issuer Free Writing Prospectus or any Section 5(d) Writing, in reliance upon and in conformity with the Underwriter Information.

(b) Each Underwriter will indemnify and hold harmless the Company against any losses, claims, damages or liabilities to which the Company may become subject, under the Act or otherwise, insofar as such losses, claims, damages or liabilities (or actions in respect thereof) arise out of or are based upon an untrue statement or alleged untrue statement of a material fact contained in the Registration Statement, any Preliminary Prospectus, the Pricing Prospectus or the Prospectus, or any amendment or supplement thereto, or any Issuer Free Writing Prospectus, or any roadshow or any Section 5(d) Writing, or arise out of or are based upon the omission or alleged omission to state therein a material fact required to be stated therein or necessary to make the statements therein not misleading, in each case to the extent, but only to the extent, that such untrue statement or alleged untrue statement or omission or alleged omission was made in the Registration Statement, any Preliminary Prospectus, the Pricing Prospectus or the Prospectus, or any amendment or supplement thereto, or any Issuer Free Writing Prospectus, or any roadshow or any Section 5(d) Writing, in reliance upon and in conformity with the Underwriter Information; and will reimburse the Company for any legal or other expenses reasonably incurred by the Company in connection with investigating or defending any such action or claim as such expenses are incurred. As used in this Agreement with respect to an Underwriter and an applicable document, "Underwriter Information" shall mean the written information furnished to the Company by such Underwriter through the Representatives expressly for use therein; it being understood and agreed upon that the only such information furnished by any Underwriter consists of the following information in the Prospectus furnished on behalf of each Underwriter: the concession and reallowance figures appearing in the [__] paragraph under the caption "Underwriting", and the information contained in the [__] paragraph under the caption "Underwriting".

(c) Promptly after receipt by an indemnified party under subsection (a) or (b) above of notice of the commencement of any action, such indemnified party shall, if a claim in respect thereof is to be made against the indemnifying party under such subsection, notify the indemnifying party in writing of the commencement thereof; *provided* that the failure to notify the indemnifying party shall not relieve it from any liability that it may have under the preceding paragraphs of this Section 9 except to the extent that it has been materially prejudiced (through the forfeiture of substantive rights or defenses) by such failure; and provided further that the failure to notify the indemnifying party shall not relieve it from any liability that it may have to an indemnified party otherwise than under the preceding paragraphs of this Section 9. In case any such action shall be brought against any indemnified party and it shall notify the indemnifying party of the commencement thereof, the indemnifying party shall be entitled to participate therein and, to the extent that it shall wish, jointly with any other indemnifying party similarly notified, to assume the defense thereof, with counsel reasonably satisfactory to such indemnified party (who shall not, except with the consent of the indemnified party, be counsel to the indemnifying party), and, after notice from the indemnifying party to such indemnified party of its election so to assume the defense thereof, the indemnifying party shall not be liable to such indemnified party under such subsection for any legal expenses of other counsel

or any other expenses, in each case subsequently incurred by such indemnified party, in connection with the defense thereof other than reasonable costs of investigation. No indemnifying party shall, without the written consent of the indemnified party, effect the settlement or compromise of, or consent to the entry of any judgment with respect to, any pending or threatened action or claim in respect of which indemnification or contribution may be sought hereunder (whether or not the indemnified party is an actual or potential party to such action or claim) unless such settlement, compromise or judgment (i) includes an unconditional release of the indemnified party from all liability arising out of such action or claim and (ii) does not include a statement as to or an admission of fault, culpability or a failure to act, by or on behalf of any indemnified party.

(d) If the indemnification provided for in this Section 9 is unavailable to or insufficient to hold harmless an indemnified party under subsection (a) or (b) above in respect of any losses, claims, damages or liabilities (or actions in respect thereof) referred to therein, then each indemnifying party shall contribute to the amount paid or payable by such indemnified party as a result of such losses, claims, damages or liabilities (or actions in respect thereof) in such proportion as is appropriate to reflect the relative benefits received by the Company on the one hand and the Underwriters on the other from the offering of the Shares. If, however, the allocation provided by the immediately preceding sentence is not permitted by applicable law, then each indemnifying party shall contribute to such amount paid or payable by such indemnified party in such proportion as is appropriate to reflect not only such relative benefits but also the relative fault of the Company on the one hand and the Underwriters on the other in connection with the statements or omissions which resulted in such losses, claims, damages or liabilities (or actions in respect thereof), as well as any other relevant equitable considerations. The relative benefits received by the Company on the one hand and the Underwriters on the other shall be deemed to be in the same proportion as the total net proceeds from the offering (before deducting expenses) received by the Company bear to the total underwriting discounts and commissions received by the Underwriters, in each case as set forth in the table on the cover page of the Prospectus. The relative fault shall be determined by reference to, among other things, whether the untrue or alleged untrue statement of a material fact or the omission or alleged omission to state a material fact relates to information supplied by the Company on the one hand or the Underwriters on the other and the parties' relative intent, knowledge, access to information and opportunity to correct or prevent such statement or omission. The Company and the Underwriters agree that it would not be just and equitable if contribution pursuant to this subsection (d) were determined by *pro rata* allocation (even if the Underwriters were treated as one entity for such purpose) or by any other method of allocation which does not take account of the equitable considerations referred to above in this subsection (d). The amount paid or payable by an indemnified party as a result of the losses, claims, damages or liabilities (or actions in respect thereof) referred to above in this subsection (d) shall be deemed to include any legal or other expenses reasonably incurred by such indemnified party in connection with investigating or defending any such action or claim. Notwithstanding the provisions of this subsection (d), no Underwriter shall be

required to contribute any amount in excess of the amount by which the total price at which the Shares underwritten by it and distributed to the public were offered to the public exceeds the amount of any damages which such Underwriter has otherwise been required to pay by reason of such untrue or alleged untrue statement or omission or alleged omission. No person guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Act) shall be entitled to contribution from any person who was not guilty of such fraudulent misrepresentation. The Underwriters' obligations in this subsection (d) to contribute are several in proportion to their respective underwriting obligations and not joint.

(e) The obligations of the Company under this Section 9 shall be in addition to any liability which the Company may otherwise have and shall extend, upon the same terms and conditions, to each person, if any, who controls any Underwriter within the meaning of the Act and each affiliate of any Underwriter; and the obligations of the Underwriters under this Section 9 shall be in addition to any liability which the respective Underwriters may otherwise have and shall extend, upon the same terms and conditions, to each officer and director of the Company (including any person who, with his or her consent, is named in the Registration Statement as about to become a director of the Company) and to each person, if any, who controls the Company within the meaning of the Act.

10. (a) If any Underwriter shall default in its obligation to purchase the Shares which it has agreed to purchase hereunder at a Time of Delivery, you may in your discretion arrange for you or another party or other parties to purchase such Shares on the terms contained herein. If within thirty-six hours after such default by any Underwriter you do not arrange for the purchase of such Shares, then the Company shall be entitled to a further period of thirty-six hours within which to procure another party or other parties satisfactory to you to purchase such Shares on such terms. In the event that, within the respective prescribed periods, you notify the Company that you have so arranged for the purchase of such Shares, or the Company notifies you that it has so arranged for the purchase of such Shares, you or the Company shall have the right to postpone such Time of Delivery for a period of not more than seven days, in order to effect whatever changes may thereby be made necessary in the Registration Statement or the Prospectus, or in any other documents or arrangements, and the Company agrees to file promptly any amendments or supplements to the Registration Statement or the Prospectus which in your opinion may thereby be made necessary. The term "Underwriter" as used in this Agreement shall include any person substituted under this Section with like effect as if such person had originally been a party to this Agreement with respect to such Shares.

(b) If, after giving effect to any arrangements for the purchase of the Shares of a defaulting Underwriter or Underwriters by you and the Company as provided in subsection (a) above, the aggregate number of such Shares which remains unpurchased does not exceed one-eleventh of the aggregate number of all the Shares to be purchased at such Time of Delivery, then the Company shall have the right to require each non-defaulting Underwriter to purchase the number of shares which such Underwriter agreed to purchase hereunder at such Time of

Delivery and, in addition, to require each non-defaulting Underwriter to purchase its pro rata share (based on the number of Shares which such Underwriter agreed to purchase hereunder) of the Shares of such defaulting Underwriter or Underwriters for which such arrangements have not been made; but nothing herein shall relieve a defaulting Underwriter from liability for its default.

(c) If, after giving effect to any arrangements for the purchase of the Shares of a defaulting Underwriter or Underwriters by you and the Company as provided in subsection (a) above, the aggregate number of such Shares which remains unpurchased exceeds one-eleventh of the aggregate number of all the Shares to be purchased at such Time of Delivery, or if the Company shall not exercise the right described in subsection (b) above to require non-defaulting Underwriters to purchase Shares of a defaulting Underwriter or Underwriters, then this Agreement (or, with respect to the Second Time of Delivery, the obligations of the Underwriters to purchase and of the Company to sell the Optional Shares) shall thereupon terminate, without liability on the part of any non-defaulting Underwriter or the Company, except for the expenses to be borne by the Company and the Underwriters as provided in Section 7 hereof and the indemnity and contribution agreements in Section 9 hereof; but nothing herein shall relieve a defaulting Underwriter from liability for its default.

11. If this Agreement shall be terminated pursuant to Section 10 hereof, the Company shall not then be under any liability to any Underwriter except as provided in Sections 7 and 9 hereof; but, if for any other reason, any Shares are not delivered by or on behalf of the Company as provided herein, the Company will reimburse the Underwriters through you for all out-of-pocket expenses approved in writing by you, including fees and disbursements of counsel, reasonably incurred by the Underwriters in making preparations for the purchase, sale and delivery of the Shares not so delivered, but the Company shall then be under no further liability to any Underwriter except as provided in Sections 7 and 9 hereof.

12. In all dealings hereunder, the Representatives shall act on behalf of each of the Underwriters, and the parties hereto shall be entitled to act and rely upon any statement, request, notice or agreement on behalf of any Underwriter made or given by you jointly.

All statements, requests, notices and agreements hereunder shall be in writing, and if to the Underwriters shall be delivered or sent by mail, telex or facsimile transmission to you as the representatives at: (a) Goldman Sachs & Co. LLC, 200 West Street, New York, New York 10282-2198, Attention: Registration Department; (b) Morgan Stanley & Co. LLC, 1585 Broadway, New York, NY 10036, Attention: Equity Syndicate Desk and (c) J.P. Morgan Securities LLC, 383 Madison Avenue, New York, NY 10179, Attention: Equity Syndicate Desk, Fax: (212) 622-8358; and if to the Company shall be delivered or sent by mail, telex or facsimile transmission to the address of the Company set forth in the Registration Statement, Attention: Secretary; *provided, however,* that any notice to an Underwriter pursuant to Section 9(c) hereof shall be delivered or sent by mail, telex or facsimile transmission to such Underwriter at its address set forth in its Underwriters' Questionnaire, or telex constituting such

Questionnaire, which address will be supplied to the Company by you upon request; *provided*, *however*, that notices under subsection 5(e) shall be in writing, and if to the Underwriters shall be delivered or sent by mail, telex or facsimile transmission to you as the representatives at Goldman Sachs & Co. LLC, 200 West Street, New York, New York 10282-2198, Attention: Control Room. Any such statements, requests, notices or agreements shall take effect upon receipt thereof.

In accordance with the requirements of the USA Patriot Act (Title III of Pub. L. 107-56 (signed into law October 26, 2001)), the underwriters are required to obtain, verify and record information that identifies their respective clients, including the Company, which information may include the name and address of their respective clients, as well as other information that will allow the underwriters to properly identify their respective clients.

13. This Agreement shall be binding upon, and inure solely to the benefit of, the Underwriters, the Company and, to the extent provided in Sections 9 and 11 hereof, the officers and directors of the Company and each person who controls the Company or any Underwriter, and their respective heirs, executors, administrators, successors and assigns, and no other person shall acquire or have any right under or by virtue of this Agreement. No purchaser of any of the Shares from any Underwriter shall be deemed a successor or assign by reason merely of such purchase.

14. Time shall be of the essence of this Agreement. As used herein, the term "business day" shall mean any day when the Commission's office in Washington, D.C. is open for business.

15. The Company acknowledges and agrees that (i) the purchase and sale of the Shares pursuant to this Agreement is an arm's-length commercial transaction between the Company, on the one hand, and the several Underwriters, on the other, (ii) in connection therewith and with the process leading to such transaction each Underwriter is acting solely as a principal and not the agent or fiduciary of the Company, (iii) no Underwriter has assumed an advisory or fiduciary responsibility in favor of the Company with respect to the offering contemplated hereby or the process leading thereto (irrespective of whether such Underwriter has advised or is currently advising the Company on other matters) or any other obligation to the Company except the obligations expressly set forth in this Agreement and (iv) the Company has consulted its own legal and financial advisors to the extent it deemed appropriate. The Company agrees that it will not claim that the Underwriters, or any of them, has rendered advisory services of any nature or respect, or owes a fiduciary or similar duty to the Company, in connection with such transaction or the process leading thereto.

16. This Agreement supersedes all prior agreements and understandings (whether written or oral) between the Company and the Underwriters, or any of them, with respect to the subject matter hereof.

17. **This Agreement and any transaction contemplated by this Agreement shall be governed by and construed in accordance with the laws of the State of New York without regard to principles of conflict of laws that would results in the application of any other law than the laws of the State of New York. The Company**

agrees that any suit or proceeding arising in respect of this Agreement or any transaction contemplated by this Agreement will be tried exclusively in the U.S. District Court for the Southern District of New York or, if that court does not have subject matter jurisdiction, in any state court located in The City and County of New York and the Company agrees to submit to the jurisdiction of, and to venue in, such courts.

18. The Company and each of the Underwriters hereby irrevocably waives, to the fullest extent permitted by applicable law, any and all right to trial by jury in any legal proceeding arising out of or relating to this Agreement or the transactions contemplated hereby.

19. This Agreement may be executed by any one or more of the parties hereto in any number of counterparts, each of which shall be deemed to be an original, but all such counterparts shall together constitute one and the same instrument.

20. Notwithstanding anything herein to the contrary, the Company is authorized to disclose to any persons the U.S. federal and state income tax treatment and tax structure of the potential transaction and all materials of any kind (including tax opinions and other tax analyses) provided to the Company relating to that treatment and structure, without the Underwriters imposing any limitation of any kind. However, any information relating to the tax treatment and tax structure shall remain confidential (and the foregoing sentence shall not apply) to the extent necessary to enable any person to comply with securities laws. For this purpose, “tax structure” is limited to any facts that may be relevant to that treatment.

If the foregoing is in accordance with your understanding, please sign and return to us six counterparts hereof, and upon the acceptance hereof by you, on behalf of each of the Underwriters, this letter and such acceptance hereof shall constitute a binding agreement between each of the Underwriters and the Company. It is understood that your acceptance of this letter on behalf of each of the Underwriters is pursuant to the authority set forth in a form of Agreement among Underwriters, the form of which shall be submitted to the Company for examination upon request, but without warranty on your part as to the authority of the signers thereof.

Very truly yours,

DENALI THERAPEUTICS INC.

By: _____
Name:
Title:

Accepted as of the date hereof:

Goldman Sachs & Co. LLC

By: _____
Name:
Title:

Morgan Stanley & Co. LLC

By: _____
Name:
Title:

J.P. Morgan Securities LLC

By: _____
Name:
Title:

On behalf of each of the Underwriters

SCHEDULE I

Underwriter	Firm Shares to be Purchased	Optional Shares to be Purchased if Maximum Option is Exercised
Goldman Sachs & Co. LLC		
Morgan Stanley & Co. LLC		
J.P. Morgan Securities LLC		
Evercore Group L.L.C.		
Total		

SCHEDULE II

(a) Issuer Free Writing Prospectuses not included in the Pricing Disclosure Package:

Electronic roadshow dated [●]

(b) Additional Documents Incorporated by Reference:

None

(c) [Information other than the Pricing Prospectus that comprise the Pricing Disclosure Package:

The initial public offering price per share for the Shares is $_____
The number of Shares purchased by the Underwriters is [_____].
[Any other pricing disclosures]]

(d) Section 5(d) Writings:

Investor Presentation dated [●]

Annex I

[Form of press release]

Annex II

Denali Therapeutics Inc.

Lock-Up Agreement

_____, 2017

Goldman Sachs & Co. LLC
Morgan Stanley & Co. LLC
J.P. Morgan Securities LLC

c/o Goldman Sachs & Co. LLC
200 West Street
New York, NY 10282

c/o Morgan Stanley & Co. LLC
1585 Broadway
New York, NY 10036

c/o J.P. Morgan Securities LLC
383 Madison Avenue
New York, NY 10179

Re: Denali Therapeutics Inc. - Lock-Up Agreement

Ladies and Gentlemen:

The undersigned understands that you, as representatives (the "Representatives"), propose to enter into an Underwriting Agreement on behalf of the several Underwriters named in Schedule I to such agreement (collectively, the "Underwriters"), with Denali Therapeutics Inc., a Delaware corporation (the "Company"), providing for a public offering (the "Public Offering") of shares of the Common Stock of the Company, par value $0.01 per share, (the "Shares") pursuant to a Registration Statement on Form S-1 (the "Registration Statement") to be filed with the Securities and Exchange Commission (the "SEC").

In consideration of the agreement by the Underwriters to offer and sell the Shares, and of other good and valuable consideration the receipt and sufficiency of which is hereby acknowledged, the undersigned agrees that, during the period beginning from the date of this Lock-Up Agreement and continuing to and including the date 180 days after the date set forth on the final prospectus (the "Prospectus") used to sell the Shares (the "Public Offering Date") pursuant to the Underwriting Agreement (the "Lock-Up Period"), the undersigned will not offer, sell, contract to sell, pledge, grant any option to purchase, make any short sale or otherwise dispose of ("Transfer") any shares of Common Stock of the Company, or any options or warrants to purchase any shares of Common Stock of the Company, or any securities convertible into, exchangeable for or that represent the right to receive shares of Common Stock of the Company (collectively, the "Equity Securities"), whether now owned or hereinafter acquired, owned directly by the undersigned (including holding as a custodian) or with respect to which the undersigned has beneficial ownership within the rules and regulations of the SEC (collectively the "Undersigned's Shares") or make any public announcement or SEC filing relating to any proposed Transfer or intent to engage in such a Transfer, other than any Shares sold to the Underwriters

pursuant to the Underwriting Agreement or as otherwise provided herein. In addition, the undersigned also agrees that it will not, during the Lock-Up Period, without the prior written consent of the Representatives on behalf of the Underwriters, make any demand for or exercise any right with respect to, the registration of any of the Undersigned's Shares. Notwithstanding the foregoing or any other agreement or waiver to which the undersigned is a party, the undersigned may make a demand under any registration rights agreement with the Company described in the Prospectus for, and exercise its rights under any such registration rights agreement with respect to, the registration after the expiration of the Lock-Up Period of Equity Securities that does not require the filing of a registration statement or any public announcement or activity regarding the registration by the undersigned, the Company or any third party during the Lock-Up Period (and no such public announcement or activity shall be voluntarily made or taken during the Lock-Up Period). The foregoing restrictions are expressly agreed to preclude the undersigned from engaging in any hedging or other transaction which is designed to or which reasonably could be expected to lead to or result in a sale or disposition of the Undersigned's Shares even if such Shares would be disposed of by someone other than the undersigned. Such prohibited hedging or other transactions would include without limitation any short sale or any purchase, sale or grant of any right (including without limitation any put or call option) with respect to any of the Undersigned's Shares or with respect to any security that includes, relates to, or derives any significant part of its value from such Shares. If the undersigned is an officer or director of the Company, the undersigned further agrees that the foregoing provisions shall be equally applicable to any issuer-directed Shares the undersigned may purchase in the Public Offering.

Notwithstanding the foregoing, the undersigned may:

(a) Transfer the Undersigned's Shares or make an SEC filing related to any such Transfer:

(i) as a *bona fide* gift or gifts, including without limitation to a charitable organization or educational institution, or for *bona fide* estate planning purposes;

(ii) to any member of the undersigned's immediate family or to any trust or other legal entity for the direct or indirect benefit of the undersigned or the immediate family of the undersigned, or if the undersigned is a trust, to a trustor or beneficiary of the trust or to the estate of a beneficiary of such trust, provided that any such transfer shall not involve a disposition for value;

(iii) by will, other testamentary document or the laws of intestate succession;

(iv) in connection with a sale of the Undersigned's Shares acquired in the Public Offering (other than any issuer-directed shares of Common Stock purchased in the Public Offering by an officer or director of the Company) or in open market transactions on or after the Public Offering Date;

(v) if the undersigned is a corporation, partnership, limited liability company, trust or other business entity, (A) to another corporation, member, partner, partnership, limited liability company, trust or other business entity that is an affiliate (as defined in Rule 405 as promulgated by the SEC under the Securities Act of 1933, as amended) of the undersigned, or to any investment fund or other entity controlling, controlled by, managing or managed by or under common control with the undersigned or affiliates of the undersigned (including, for the avoidance of doubt, where the undersigned is a partnership, to its general partner or a successor partnership or fund, or any other funds managed by such partnership), or (B) as

part of a distribution, transfer or disposition by the undersigned to its or its affiliates' directors, officers, employees, managers, managing members, members, stockholders, partners, beneficiaries (or the estates thereof) or other equity holders;

(vi) (a) surrender or forfeiture to the Company of shares of Common Stock of the Company in connection with the "net" or "cashless" exercise or settlement of stock options, other rights to purchase shares of Common Stock or other awards expiring during the Lock-Up Period (collectively, the "Expiring Awards") or for the payment of tax withholdings or remittance payments due as a result of the vesting, settlement, or exercise of such Expiring Awards, in all such cases, pursuant to an equity incentive plan, stock purchase plan or other employee benefit plan described in the Registration Statement and the Prospectus, or (b) surrender or forfeiture to the Company of shares of Common Stock of the Company upon the conversion of a convertible security of the Company described in the Registration Statement and the Prospectus in order to cover withholding tax obligations in connection with such conversion;

(vii) to the Company in connection with any contractual arrangement in effect on the date of the Prospectus that provides for the repurchase of the undersigned's Equity Securities by the Company in connection with the termination of the undersigned's service with the Company;

(viii) in connection with the conversion of any convertible security into shares of Common Stock in a manner consistent with the description of such securities contained in the Prospectus, provided that for the avoidance of doubt such shares of Common Stock shall remain subject to the provisions of this Lock-Up Agreement;

(ix) to a nominee or custodian of a person or entity to whom a Transfer would be permissible under (i), (ii), (iii) or (v) above;

(x) pursuant to a bona fide third-party tender offer, merger, consolidation or other similar transaction that is approved by the board of directors of the Company and made to all holders of the Company's capital stock involving a Change of Control of the Company, provided that in the event that such tender offer, merger, consolidation or other similar transaction is not completed, the Undersigned's Shares shall remain subject to the provisions of this Lock-Up Agreement;

(xi) in connection with the conversion or reclassification of the outstanding preferred stock or other classes of common stock of the Company into shares of Common Stock, provided that any such shares of Common Stock received upon such conversion or reclassification shall be subject to the terms of this Lock-Up Agreement;

(xii) by operation of law, including pursuant to orders of a court, a qualified domestic order or in connection with a divorce settlement; or

(xiii) with the prior written consent of the Representatives on behalf of the Underwriters;

provided that (A) in the case of (i), (ii), (iii), (v), (ix) and (xii) above, it shall be a condition to the transfer or distribution that the donee, transferee or distributee, as

the case may be, agrees in writing to be bound by the restrictions set forth herein, (B) in the case of (i), (ii), (iii), (iv) and (v) above, no filing under Section 16 of the Securities Exchange Act of 1934, as amended (the "Exchange Act") or other public filing, report or announcement reporting a reduction in beneficial ownership of shares of Common Stock shall be required or shall be voluntarily made during the Lock-Up Period (other than a required filing on Form 5, Schedule 13G (or Schedule 13G/A) or Schedule 13F), (C) in the case of (vi) above, if the undersigned is required to file a report under Section 16 of the Exchange Act during the Lock-Up Period, the undersigned shall include a statement in any such report to the effect that such report relates to the circumstances described in (vi) above, (D) in the case of (i), (ii), (iii) and (v) above, it shall be a condition to the transfer or distribution that such transfer or distribution does not involve a disposition for value and (E) in the case of (vii) above, no filing under Section 16 of the Exchange Act, or other public filing, report or announcement reporting a reduction in beneficial ownership of shares of Common Stock shall be voluntarily made during the Lock-Up Period and, if the undersigned is required to file a report under Section 16 of the Exchange Act during the Lock-Up Period, the undersigned shall include a statement in such report to the effect that such transfer is to the Company in connection with the repurchase of shares of Common Stock, as the case may be.

(b) receive from the Company shares of Common Stock in connection with the exercise of options or other rights granted under a stock incentive plan or other equity award plan, which plan is described in the Registration Statement; or

(c) enter into a written plan meeting the requirements of Rule 10b5-1 under the Exchange Act after the date of this Lock-Up Agreement relating to the sale of the Undersigned's Shares, provided that (i) the securities subject to such plan may not be transferred until after the expiration of the Lock-Up Period and (ii) no public announcement or filing under the Exchange Act shall be voluntarily made regarding the establishment of such plan during the Lock-Up Period and any required report under Section 16 of the Exchange Act shall clearly indicate in the footnotes thereto that the filing relates to the circumstances described in this clause (c).

For purposes of this Lock-Up Agreement, "immediate family" shall mean any relationship by blood, current or former marriage, domestic partnership or adoption, not more remote than first cousin. For purposes of this Lock-Up Agreement, "Change of Control" shall mean the transfer (whether by tender offer, merger, consolidation or other similar transaction) in one transaction or a series of related transactions, to a person or group of affiliated persons (other than an Underwriter pursuant to the Public Offering), of the Company's voting securities if, after such transfer, such person or group of affiliated persons would hold a majority of the outstanding voting securities of the Company (or the surviving entity).

The undersigned also agrees and consents to the entry of stop transfer instructions with the Company's transfer agent and registrar against the transfer of the Undersigned's Shares except in compliance with the foregoing restrictions.

In addition, the Representatives agree that should a discretionary release or waiver be granted to a holder of Equity Securities, then the undersigned will be released on the same terms on a pro rata basis, based on the number of Equity Securities held by the undersigned on the date hereof on an as-converted basis, from the restrictions set forth in this Lock-Up Agreement (such

release, a "Pro-rata Release"); provided, however, that such Pro-rata Release shall not be applied in the event of (a) releases granted from such lockup restrictions to all parties by the Representatives constitute in the aggregate an amount less than or equal to 1% of the Company's total outstanding stock (determined as of the closing date of the Public Offering for, and giving effect to, the Public Offering) and no releases are granted to any officer or director of the Company, or (b) any primary or secondary public offering or sale that is underwritten (the "Underwritten Sale") of the Company's Common Stock during the Lock-Up Period; provided further, that the undersigned is offered the opportunity to participate on a pro rata basis with and otherwise on the same terms as any other equity holders in such Underwritten Sale and, if the undersigned so elects to participate in such Underwritten Sale, the undersigned is hereby released from the restrictions herein with respect to the Undersigned's Shares included in such Underwritten Sale; provided further, that any of the Undersigned's Shares that are released for such Underwritten Sale but not sold in such Underwritten Sale shall be subject to this Lock-Up Agreement immediately following such Underwritten Sale. The Representatives shall use their commercially reasonable efforts to provide at least three business days' notice to the Chief Financial Officer of the Company prior to the effective date of such release or waiver (the effective date of such release or waiver, the "Release Date"), stating the percentage of shares held by such person or entity to be released, and the Company shall use commercially reasonable efforts to send notice within two business days thereafter to the undersigned stating the same percentage of shares of Common Stock held by the undersigned as is held by the release on an as-converted basis shall be released from the restrictions set forth herein on the Release Date; provided that the failure to provide such notices shall not give rise to any claim or liability against the Representatives or the Underwriters. The Company has agreed or will agree in the Underwriting Agreement to announce the impending release or waiver by press release through a major news service at least two business days before the Release Date, if required by FINRA Rule 5131 (or any successor provision thereto). The provisions of this paragraph will not apply if (1) the release or waiver is effected solely to permit a transfer not for consideration and (2) the transferee agrees to be bound in writing by the restrictions set forth herein.

Notwithstanding anything to the contrary contained herein, this Lock-Up Agreement will automatically terminate and the undersigned shall automatically, and without any action on the part of any other party, be released from all obligations hereunder upon the earliest to occur, if any, of (i) the Company advises the Representatives in writing prior to the execution of the Underwriting Agreement that it has determined not to proceed with the Public Offering, (ii) the withdrawal of the Registration Statement prior to the execution of the Underwriting Agreement, (iii) the Underwriting Agreement is executed but is terminated (other than the provisions thereof which survive termination) prior to payment for and delivery of the Shares to be sold thereunder, or (iv) March 31, 2018, in the event that the Underwriting Agreement has not been executed by such date.

In the event that any Representative withdraws from or declines to participate in the Public Offering, all references to the Representatives contained in this Lock-Up Agreement shall be deemed to refer to the remaining Representatives that continue to participate in the Public Offering (the "Remaining Representatives"), and, in such event, any written consent, waiver or notice given or delivered in connection with this Lock-Up Agreement by the Remaining Representatives shall be deemed to be sufficient and effective for all purposes under this Lock-Up Agreement.

The undersigned hereby consents to receipt of this Lock-Up Agreement in electronic form and understands and agrees that execution and delivery of this Lock-Up Agreement by facsimile transmission, electronic mail or other electronic transmission is legal, valid and binding for all purposes.

The undersigned understands that the Company and the Underwriters are relying upon this Lock-Up Agreement in proceeding toward consummation of the offering. The undersigned further understands that this Lock-Up Agreement is irrevocable and shall be binding upon the undersigned's heirs, legal representatives, successors, and assigns.

Very truly yours,

_____

Exact Name of Shareholder

_____

Authorized Signature

_____

Title

AMENDED AND RESTATED CERTIFICATE OF INCORPORATION OF DENALI THERAPEUTICS INC.

(Pursuant to Sections 242 and 245 of the
General Corporation Law of the State of Delaware)

Denali Therapeutics Inc., a corporation organized and existing under and by virtue of the provisions of the General Corporation Law of the State of Delaware (the "**General Corporation Law**"),

DOES HEREBY CERTIFY:

1. That the name of this corporation is Denali Therapeutics Inc., and that this corporation was originally incorporated pursuant to the General Corporation Law on October 14, 2013 under the name SPR Pharma Inc. and changed its name to Denali Therapeutics Inc. pursuant to a Certificate of Amendment filed on March 6, 2015.

2. That the Board of Directors duly adopted resolutions proposing to amend and restate the Certificate of Incorporation of this corporation, declaring said amendment and restatement to be advisable and in the best interests of this corporation and its stockholders, and authorizing the appropriate officers of this corporation to solicit the consent of the stockholders therefor, which resolution setting forth the proposed amendment and restatement is as follows:

RESOLVED, that the Certificate of Incorporation of this corporation be amended and restated in its entirety to read as follows:

FIRST: The name of this corporation is Denali Therapeutics Inc. (the "**Corporation**").

SECOND: The address of the registered office of the Corporation in the State of Delaware is 1209 Orange Street, Wilmington, Delaware 19801, County of New Castle. The name of its registered agent at such address is The Corporation Trust Company.

THIRD: The nature of the business or purposes to be conducted or promoted is to engage in any lawful act or activity for which corporations may be organized under the General Corporation Law.

FOURTH: The total number of shares of all classes of stock which the Corporation shall have authority to issue is (i) 334,349,451 shares of Common Stock, $0.01 par value per share ("**Common Stock**") and (ii) 253,153,867 shares of Preferred Stock, $0.01 par value per share ("**Preferred Stock**").

The following is a statement of the designations and the powers, privileges and rights, and the qualifications, limitations or restrictions thereof in respect of each class of capital stock of the Corporation.

A. COMMON STOCK

1. General. The voting, dividend and liquidation rights of the holders of the Common Stock are subject to and qualified by the rights, powers and preferences of the holders of the Preferred Stock set forth herein.

2. Voting. The holders of the Common Stock are entitled to one vote for each share of Common Stock held at all meetings of stockholders (and written actions in lieu of meetings); provided, however, that, except as otherwise required by law, holders of Common Stock, as such, shall not be entitled to vote on any amendment to the Certificate of Incorporation that relates solely to the terms of one or more outstanding series of Preferred Stock if the holders of such affected series are entitled, either separately or together with the holders of one or more other such series, to vote thereon pursuant to the Certificate of Incorporation or pursuant to the General Corporation Law. There shall be no cumulative voting. The number of authorized shares of Common Stock may be increased or decreased (but not below the number of shares thereof then outstanding) by (in addition to any vote of the holders of one or more series of Preferred Stock that may be required by the terms of the Certificate of Incorporation) the affirmative vote of the holders of shares of capital stock of the Corporation representing a majority of the votes represented by all outstanding shares of capital stock of the Corporation entitled to vote, irrespective of the provisions of Section 242(b)(2) of the General Corporation Law.

B. PREFERRED STOCK

184,457,734 shares of the authorized Preferred Stock of the Corporation are hereby designated "**Series A-1 Preferred Stock**," 17,446,133 shares of the authorized Preferred Stock of the Corporation are hereby designated "**Series A-2 Preferred Stock**" (together with the Series A-1 Preferred Stock, the "**Series A Preferred Stock**"), 32,500,000 shares of the authorized Preferred Stock of the Corporation are hereby designated "**Series B-1 Preferred Stock**," and 18,750,000 shares of the authorized Preferred Stock of the Corporation are hereby designated "**Series B-2 Preferred Stock**" (together with the Series B-1 Preferred Stock, the "**Series B Preferred Stock**"), each with the following rights, preferences, powers, privileges and restrictions, qualifications and limitations. Unless otherwise indicated, references to "sections" or "subsections" in this Part B of this Article Fourth refer to sections and subsections of Part B of this Article Fourth.

1. Dividends. From and after the date of the issuance of any shares of Series A-1 Preferred Stock, dividends at the rate per annum of $0.08 per share shall accrue on such shares of Series A-1 Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series A-1 Preferred Stock), from and after the date of issuance of any shares of Series A-2 Preferred Stock, dividends at the rate per annum of $0.16 per share shall accrue on such shares of Series A-2 Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series A-2 Preferred Stock), from and after the date of issuance of any shares of Series B-1 Preferred Stock, dividends at the rate per annum of $0.32 per share shall accrue on such shares of Series B-1 Preferred Stock

(subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series B-1 Preferred Stock) and from and after the date of issuance of any shares of Series B-2 Preferred Stock, dividends at a rate per annum of $0.34 per share shall accrue on such shares of Series B-2 Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series B-2 Preferred Stock) (together, the "**Accruing Dividends**"). Accruing Dividends shall accrue from day to day, whether or not declared, and shall be cumulative; provided, however, that except as set forth in the following sentence of this Section 1 or in Subsection 2.1 and Section 6, such Accruing Dividends shall be payable only when, as, and if declared by the Board of Directors and the Corporation shall be under no obligation to pay such Accruing Dividends. The Corporation shall not declare, pay or set aside any dividends on shares of any other class or series of capital stock of the Corporation (other than dividends on shares of Common Stock payable in shares of Common Stock) unless (in addition to the obtaining of any consents required elsewhere in the Certificate of Incorporation) the holders of the Preferred Stock then outstanding shall first receive, or simultaneously receive, a dividend on each outstanding share of Preferred Stock in an amount at least equal to the sum of (i) the amount of the aggregate Accruing Dividends then accrued on such share of Series A-1, Series A-2, Series B-1 or Series B-2 Preferred Stock, respectively, and not previously paid and (ii) (A) in the case of a dividend on Common Stock or any class or series that is convertible into Common Stock, that dividend per share of Series A-1, Series A-2, Series B-1 or Series B-2 Preferred Stock as would equal the product of (1) the dividend payable on each share of such class or series determined, if applicable, as if all shares of such class or series had been converted into Common Stock and (2) the number of shares of Common Stock issuable upon conversion of a share of Series A-1, Series A-2, Series B-1 or Series B-2 Preferred Stock, respectively, in each case calculated on the record date for determination of holders entitled to receive such dividend or (B) in the case of a dividend on any class or series that is not convertible into Common Stock, at a rate per share of Series A-1, Series A-2, Series B-1 or Series B-2 Preferred Stock, respectively, determined by (1) dividing the amount of the dividend payable on each share of such class or series of capital stock by the original issuance price of such class or series of capital stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to such class or series) and (2) multiplying such fraction by an amount equal to the Series A-1 Original Issue Price, Series A-2 Original Issue Price, Series B-1 Original Issue Price or Series B-2 Original Issue Price, as applicable (each as defined below); provided that if the Corporation declares, pays or sets aside, on the same date, a dividend on shares of more than one class or series of capital stock of the Corporation, the dividend payable to the holders of Series A-1, Series A-2, Series B-1 or Series B-2 Preferred Stock pursuant to this Section 1 shall be calculated based upon the dividend on the class or series of capital stock that would result in the highest dividend to the Series A-1, Series A-2, Series B-1 or Series B-2 Preferred Stock, respectively. The "**Series A-1 Original Issue Price**" shall mean $1.00 per share, the "**Series A-2 Original Issue Price**" shall mean $2.00 per share, the "**Series B-1 Original Issue Price**" shall mean $4.00 per share and the "**Series B-2 Original Issue Price**" shall mean $4.25 per share, in each case subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the applicable series of Preferred Stock.

2. Liquidation, Dissolution or Winding Up; Certain Mergers, Consolidations and Asset Sales.

2.1 Preferential Payments to Holders of Preferred Stock. In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Corporation or Deemed Liquidation Event (as defined below), the holders of shares of Preferred Stock then outstanding shall be entitled to be paid out of the assets of the Corporation available for distribution to its stockholders before any payment shall be made to the holders of Common Stock by reason of their ownership thereof, an amount per share equal to the greater of (i) the Series A-1 Original Issue Price, Series A-2 Original Issue Price, Series B-1 Original Issue Price or Series B-2 Original Issue Price, as applicable, plus any Accruing Dividends accrued but unpaid thereon, whether or not declared, together with any other dividends declared but unpaid thereon, or (ii) such amount per share as would have been payable had all shares of Preferred Stock been converted into Common Stock pursuant to Section 4 immediately prior to such liquidation, dissolution, winding up or Deemed Liquidation Event (the amount payable pursuant to this sentence is hereinafter referred to as the "**Series A-1 Liquidation Amount**," "**Series A-2 Liquidation Amount**," "**Series B-1 Liquidation Amount**" and "**Series B-2 Liquidation Amount**," respectively). If upon any such liquidation, dissolution or winding up of the Corporation or Deemed Liquidation Event, the assets of the Corporation available for distribution to its stockholders shall be insufficient to pay the holders of shares of Preferred Stock the full amount to which they shall be entitled under this Subsection 2.1, the holders of shares of Preferred Stock shall share ratably in any distribution of the assets available for distribution in proportion to the respective amounts which would otherwise be payable in respect of the shares held by them upon such distribution if all amounts payable on or with respect to such shares were paid in full.

2.2 Payments to Holders of Common Stock. In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Corporation or Deemed Liquidation Event, after the payment of all preferential amounts required to be paid to the holders of shares of Preferred Stock, the remaining assets of the Corporation available for distribution to its stockholders shall be distributed among the holders of the shares of Common Stock, pro rata based on the number of shares held by each such holder.

2.3 Deemed Liquidation Events.

2.3.1 Definition. Each of the following events shall be considered a "**Deemed Liquidation Event**" unless the holders of a majority of the outstanding shares of Preferred Stock elect otherwise by written notice sent to the Corporation at least twenty (20) days prior to the effective date of any such event:

(a) a merger or consolidation in which

(i) the Corporation is a constituent party or

(ii) a subsidiary of the Corporation is a constituent party and the Corporation issues shares of its capital stock pursuant to such merger or consolidation,

except any such merger or consolidation involving the Corporation or a subsidiary in which the shares of capital stock of the Corporation outstanding immediately prior to such merger or consolidation continue to represent, or are converted into or exchanged for shares of capital stock that represent, immediately following such merger or consolidation, at least a majority, by voting power, of the capital stock of (1) the surviving or resulting corporation; or (2) if the surviving or resulting corporation is a wholly owned subsidiary of another corporation immediately following such merger or consolidation, the parent corporation of such surviving or resulting corporation; or

(b) the sale, lease, transfer, exclusive license or other disposition, in a single transaction or series of related transactions, by the Corporation or any subsidiary of the Corporation of all or substantially all the assets of the Corporation and its subsidiaries taken as a whole or the sale or disposition (whether by merger, consolidation or otherwise) of one or more subsidiaries of the Corporation if substantially all of the assets of the Corporation and its subsidiaries taken as a whole are held by such subsidiary or subsidiaries, except where such sale, lease, transfer, exclusive license or other disposition is to a wholly owned subsidiary of the Corporation.

2.3.2 Effecting a Deemed Liquidation Event.

(a) The Corporation shall not have the power to effect a Deemed Liquidation Event referred to in Subsection 2.3.1(a)(i) unless the agreement or plan of merger or consolidation for such transaction (the "**Merger Agreement**") provides that the consideration payable to the stockholders of the Corporation shall be allocated among the holders of capital stock of the Corporation in accordance with Subsections 2.1 and 2.2.

(b) In the event of a Deemed Liquidation Event referred to in Subsection 2.3.1(a)(ii) or 2.3.1(b), if the Corporation does not effect a dissolution of the Corporation under the General Corporation Law within ninety (90) days after such Deemed Liquidation Event, then (i) the Corporation shall send a written notice to each holder of Preferred Stock no later than the ninetieth (90th) day after the Deemed Liquidation Event advising such holders of their right (and the requirements to be met to secure such right) pursuant to the terms of the following clause; (ii) to require the redemption of such shares of Preferred Stock, and (iii) if the holders of a majority of the then outstanding shares of Preferred Stock so request in a written instrument delivered to the Corporation not later than one hundred twenty (120) days after such Deemed Liquidation Event, the Corporation shall use the consideration received by the Corporation for such Deemed Liquidation Event (net of any retained liabilities associated with the assets sold or technology licensed, as determined in good faith by the Board of Directors of the Corporation), together with any other assets of the Corporation available for distribution to its stockholders, all to the extent permitted by Delaware law governing distributions to stockholders (the "**Available Proceeds**"), on the one hundred fiftieth (150th) day after such Deemed Liquidation Event, to redeem all outstanding shares of Preferred Stock at a price per

share equal to the Series A-1 Liquidation Amount, Series A-2 Liquidation Amount, Series B-1 Liquidation Amount or Series B-2 Liquidation Amount, as applicable. Notwithstanding the foregoing, in the event of a redemption pursuant to the preceding sentence, if the Available Proceeds are not sufficient to redeem all outstanding shares of Preferred Stock, the Corporation shall ratably redeem each holder's shares of Preferred Stock to the fullest extent of such Available Proceeds, and shall redeem the remaining shares as soon as it may lawfully do so under Delaware law governing distributions to stockholders. The provisions of Section 6 shall apply, with such necessary changes in the details thereof as are necessitated by the context, to the redemption of the Preferred Stock pursuant to this Subsection 2.3.2(b). Prior to the distribution or redemption provided for in this Subsection 2.3.2(b), the Corporation shall not expend or dissipate the consideration received for such Deemed Liquidation Event, except to discharge expenses incurred in connection with such Deemed Liquidation Event or in the ordinary course of business.

2.3.3 Amount Deemed Paid or Distributed. The amount deemed paid or distributed to the holders of capital stock of the Corporation upon any such merger, consolidation, sale, transfer, exclusive license, other disposition or redemption shall be the cash or the value of the property, rights or securities paid or distributed to such holders by the Corporation or the acquiring person, firm or other entity. The value of such property, rights or securities shall be determined in good faith by the Board of Directors of the Corporation.

2.3.4 Allocation of Escrow and Contingent Consideration. In the event of a Deemed Liquidation Event pursuant to Subsection 2.3.1(a)(i), if any portion of the consideration payable to the stockholders of the Corporation is payable only upon satisfaction of contingencies (the "**Additional Consideration**"), the Merger Agreement shall provide that (a) the portion of such consideration that is not Additional Consideration (such portion, the "**Initial Consideration**") shall be allocated among the holders of capital stock of the Corporation in accordance with Subsections 2.1 and 2.2 as if the Initial Consideration were the only consideration payable in connection with such Deemed Liquidation Event; and (b) any Additional Consideration which becomes payable to the stockholders of the Corporation upon satisfaction of such contingencies shall be allocated among the holders of capital stock of the Corporation in accordance with Subsections 2.1 and 2.2 after taking into account the previous payment of the Initial Consideration as part of the same transaction. For the purposes of this Subsection 2.3.4, consideration placed into escrow or retained as holdback to be available for satisfaction of indemnification or similar obligations in connection with such Deemed Liquidation Event shall be deemed to be Additional Consideration.

3. Voting.

3.1 General. On any matter presented to the stockholders of the Corporation for their action or consideration at any meeting of stockholders of the Corporation (or by written consent of stockholders in lieu of meeting), each holder of outstanding shares of Preferred Stock shall be entitled to cast the number of votes equal to the number of whole shares of Common Stock into which the shares of Preferred Stock held by such holder are convertible as of the record date for determining stockholders entitled to vote on such matter. Except as provided by law or by the other provisions of the Certificate of Incorporation, holders of Preferred Stock shall vote together with the holders of Common Stock as a single class.

3.2 Election of Directors. The holders of record of the shares of Series A Preferred Stock, exclusively and as a separate class, shall be entitled to elect four (4) Series A Directors (as such term is defined in that certain Amended and Restated Voting Agreement dated on or about June 22, 2016 by and between the Corporation and the other parties named therein (as it may be amended from time to time, the "**Voting Agreement**")). Any Series A Director may be removed without cause by, and only by, the affirmative vote of the holders of a majority of the shares of Series A Preferred Stock, given either at a special meeting of such stockholders duly called for that purpose or pursuant to a written consent of stockholders. If the holders of shares of Series A Preferred Stock fail to elect a sufficient number of directors to fill all directorships for which they are entitled to elect directors, voting exclusively and as a separate class, then any directorship not so filled shall remain vacant until such time as the holders of the Series A Preferred Stock elect a person to fill such directorship by vote or written consent in lieu of a meeting; and no such directorship may be filled by stockholders of the Corporation other than by the holders of Series A Preferred Stock, voting exclusively and as a separate class. The holders of record of the shares of Series B Preferred Stock exclusively and as a separate class, shall be entitled to elect one Series B Director (as such term is defined in the Voting Agreement). The Series A Directors and the Series B Director are collectively referred to as the "**Preferred Directors**." The Series B Director may be removed without cause by, and only by, the affirmative vote of the holders of a majority of the shares of Series B Preferred Stock, given either at a special meeting of such stockholders duly called for that purpose or pursuant to a written consent of stockholders. If the holders of shares of Series B Preferred Stock fail to elect a sufficient number of directors to fill all directorships for which they are entitled to elect directors, voting exclusively and as a separate class, then any directorship not so filled shall remain vacant until such time as the holders of the Series B Preferred Stock elect a person to fill such directorship by vote or written consent in lieu of a meeting; and no such directorship may be filled by stockholders of the Corporation other than by the holders of Series B Preferred Stock, voting exclusively and as a separate class. The holders of record of the shares of Common Stock and of any other class or series of voting stock (including the Preferred Stock), exclusively and voting together as a single class, shall be entitled to elect the balance of the total number of directors of the Corporation. At any meeting held for the purpose of electing a director, the presence in person or by proxy of the holders of a majority of the outstanding shares of the class or series entitled to elect such director shall constitute a quorum for the purpose of electing such director. Except as otherwise provided in this Subsection 3.2, a vacancy in any directorship filled by the holders of any class or series shall be filled only by vote or written consent in lieu of a meeting of the holders of such class or series or by any remaining director or directors elected by the holders of such class or series pursuant to this Subsection 3.2. The rights of the holders of the Series A Preferred Stock under this Subsection 3.2 shall terminate on the first date on which there are issued and outstanding less than 100,000 shares of Series A Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination, or other similar recapitalization with respect to the Series A Preferred Stock or any series thereof). The rights of the holders of the Series B Preferred Stock under this Subsection 3.2 shall terminate on the first date following the Series B-1 Original Issue Date (as defined below) on which there are issued and outstanding less than 100,000 shares of Series B Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination, or other similar recapitalization with respect to the Series B Preferred Stock or any series thereof).

3.3 Preferred Stock Protective Provisions. At any time when at least 100,000 shares of Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination, or other similar recapitalization with respect to the Preferred Stock) are outstanding, the Corporation shall not, either directly or indirectly by amendment, merger, consolidation or otherwise, do any of the following without (in addition to any other vote required by law or the Certificate of Incorporation) the written consent or affirmative vote of the holders of a majority of the then outstanding shares of Preferred Stock, given in writing or by vote at a meeting, consenting or voting (as the case may be) separately as a class, and any such act or transaction entered into without such consent or vote shall be null and void *ab initio*, and of no force or effect.

3.3.1 liquidate, dissolve or wind-up the business and affairs of the Corporation, effect any merger or consolidation or any other Deemed Liquidation Event, or consent to any of the foregoing;

3.3.2 amend, alter or repeal any provision of the Certificate of Incorporation or By-laws of the Corporation;

3.3.3 create, or authorize the creation of, or issue or obligate itself to issue shares of, any additional class or series of capital stock unless the same ranks junior to the Preferred Stock with respect to the distribution of assets on the liquidation, dissolution or winding up of the Corporation, the payment of dividends and rights of redemption, or increase the authorized number of shares of Preferred Stock;

3.3.4 create, or authorize the creation of, or issue or obligate itself to issue shares of Common Stock representing more than an aggregate of four percent (4%) of the outstanding shares of Common Stock on a fully diluted basis (assuming the conversion of all outstanding shares of Preferred Stock and the exercise and conversion of all outstanding Convertible Securities) in any single calendar year (the "**4% Annual Cap**") as compensation to officers, directors, employees, consultants and other advisors to the Corporation;

3.3.5 increase or decrease (other than for decreases resulting from conversion of the Preferred Stock) the authorized number of shares of Preferred Stock or any series thereof;

3.3.6 (a) reclassify, alter or amend any existing security of the Corporation that is pari passu with the Preferred Stock in respect of the distribution of assets on the liquidation, dissolution or winding up of the Corporation, the payment of dividends or rights of redemption, if such reclassification, alteration or amendment would render such other security senior to the Preferred Stock in respect of any such right, preference, or privilege or (b) reclassify, alter or amend any existing security of the Corporation that is junior to the Preferred Stock in respect of the distribution of assets on the liquidation, dissolution or winding up of the Corporation, the payment of dividends or rights of redemption, if such reclassification, alteration or amendment would render such other security senior to or pari passu with the Preferred Stock in respect of any such right, preference or privilege;

3.3.7 purchase or redeem (or permit any subsidiary to purchase or redeem) or pay or declare any dividend or make any distribution on, any shares of capital stock of the Corporation other than (a) redemptions of or dividends or distributions on the Preferred Stock as expressly authorized herein, (b) dividends or other distributions payable on the Common Stock solely in the form of additional shares of Common Stock and (c) repurchases of stock from former employees, officers, directors, consultants or other persons who performed services for the Corporation or any subsidiary in connection with the cessation of such employment or service at the lower of the original purchase price or the then-current fair market value thereof;

3.3.8 create, or authorize the creation of, or issue, or authorize the issuance of any debt security, or permit any subsidiary to take any such action with respect to any debt security, unless such debt security has received the prior approval of the Board of Directors, including the approval of a majority of the then-serving Preferred Directors;

3.3.9 create, or hold capital stock in, any subsidiary that is not wholly owned (either directly or through one or more other subsidiaries) by the Corporation, or sell, transfer or otherwise dispose of any capital stock of any direct or indirect subsidiary of the Corporation, or permit any direct or indirect subsidiary to sell, lease, transfer, exclusively license or otherwise dispose (in a single transaction or series of related transactions) of all or substantially all of the assets of such subsidiary;

3.3.10 increase or decrease the authorized number of directors constituting the Board of Directors;

3.3.11 issue shares of capital stock of the Company or any rights, options or warrants to acquire shares of capital stock of the Company representing more than five percent (5%) of the then outstanding shares of Common Stock on a fully diluted basis (assuming the conversion of all outstanding shares of Preferred Stock and the exercise and conversion of all outstanding Convertible Securities) to a third party in connection with any singular sponsored research, collaboration, technology license, development, OEM, manufacturing, marketing, or other similar agreement or strategic partnership in which the Company enters into a simultaneous business relationship with the acquiror of such securities;

3.3.12 change the principal line of business of the Company from the basic discovery, research and commercialization of drugs to treat human disease, with an emphasis on human neurologic diseases;

3.3.13 enter into any transaction or series of related transactions having an aggregate value of $150,000.00 or more with any director or executive officer of the Corporation (other than in connection with their services as a director or employee of the Corporation) or any stockholder owning more than five percent (5%) of the outstanding shares of capital stock of the Corporation; or

3.3.14 amend this Section 3.3.

4. Optional Conversion.

The holders of the Preferred Stock shall have conversion rights as follows (the "**Conversion Rights**"):

4.1 Right to Convert.

4.1.1 Conversion Ratio. Each share of Preferred Stock shall be convertible, at the option of the holder thereof, at any time and from time to time, and without the payment of additional consideration by the holder thereof, into such number of fully paid and non-assessable shares of Common Stock as is determined (w) by dividing the Series A-1 Original Issue Price by the Series A-1 Conversion Price (as defined below) in the case of the Series A-1 Preferred Stock, (x) by dividing the Series A-2 Original Issue Price by the Series A-2 Conversion Price (as defined below), in the case of the Series A-2 Preferred Stock, (y) by dividing the Series B-1 Original Issue Price by the Series B-1 Conversion Price (as defined below), in the case of the Series B-1 Preferred Stock, or (z) by dividing the Series B-2 Original Issue Price by the Series B-2 Conversion Price (as defined below), in the case of the Series B-2 Preferred Stock, in each case in effect at the time of conversion. The "**Series A-1 Conversion Price**" shall initially be equal to $1.00. The "**Series A-2 Conversion Price**" shall initially be equal to $2.00. The "**Series B-1 Conversion Price**" shall initially be equal to $4.00. The "**Series B-2 Conversion Price**" shall initially be equal to $4.25. The Series A-1 Conversion Price, the Series A-2 Conversion Price, the Series B-1 Conversion Price and the Series B-2 Conversion Price shall be known individually or collectively, as applicable, as the "**Conversion Price**." Such initial Conversion Price, and the rate at which shares of Preferred Stock may be converted into shares of Common Stock, shall be subject to adjustment as provided below.

4.1.2 Termination of Conversion Rights. In the event of a notice of redemption of any shares of Preferred Stock pursuant to Section 6, the Conversion Rights of the shares designated for redemption shall terminate at the close of business on the last full day preceding the date fixed for redemption, unless the redemption price is not fully paid on such redemption date, in which case the Conversion Rights for such shares shall continue until such price is paid in full. In the event of liquidation, dissolution or winding up of the Corporation or a Deemed Liquidation Event, the Conversion Rights shall terminate at the close of business on the last full day preceding the date fixed for the payment of any such amounts distributable on such event to the holders of Preferred Stock.

4.2 Fractional Shares. No fractional shares of Common Stock shall be issued upon conversion of the Preferred Stock. In lieu of any fractional shares to which the holder would otherwise be entitled, the Corporation shall pay cash equal to such fraction multiplied by the fair market value of a share of Common Stock as determined in good faith by the Board of Directors of the Corporation. Whether or not fractional shares would be issuable upon such conversion shall be determined on the basis of the total number of shares of Preferred Stock the holder is at the time converting into Common Stock and the aggregate number of shares of Common Stock issuable upon such conversion.

4.3 Mechanics of Conversion.

4.3.1 Notice of Conversion. In order for a holder of Preferred Stock to voluntarily convert shares of Preferred Stock into shares of Common Stock, such holder shall (a) provide written notice to the Corporation's transfer agent at the office of the transfer agent for the Preferred Stock (or at the principal office of the Corporation if the Corporation serves as its own transfer agent) that such holder elects to convert all or any number of such holder's shares of Preferred Stock and, if applicable, any event on which such conversion is contingent and (b), if such holder's shares are certificated, surrender the certificate or certificates for such shares of Preferred Stock (or, if such registered holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate), at the office of the transfer agent for the Preferred Stock (or at the principal office of the Corporation if the Corporation serves as its own transfer agent). Such notice shall state such holder's name or the names of the nominees in which such holder wishes the shares of Common Stock to be issued. If required by the Corporation, any certificates surrendered for conversion shall be endorsed or accompanied by a written instrument or instruments of transfer, in form satisfactory to the Corporation, duly executed by the registered holder or his, her or its attorney duly authorized in writing. The close of business on the date of receipt by the transfer agent (or by the Corporation if the Corporation serves as its own transfer agent) of such notice and, if applicable, certificates (or lost certificate affidavit and agreement) shall be the time of conversion (the "**Conversion Time**"), and the shares of Common Stock issuable upon conversion of the specified shares shall be deemed to be outstanding of record as of such date. The Corporation shall, as soon as practicable after the Conversion Time (i) issue and deliver to such holder of Preferred Stock, or to his, her or its nominees, a certificate or certificates for the number of full shares of Common Stock issuable upon such conversion in accordance with the provisions hereof and a certificate for the number (if any) of the shares of Preferred Stock represented by the surrendered certificate that were not converted into Common Stock, (ii) pay in cash such amount as provided in Subsection 4.2 in lieu of any fraction of a share of Common Stock otherwise issuable upon such conversion and (iii) pay all declared but unpaid dividends on the shares of Preferred Stock converted.

4.3.2 Reservation of Shares. The Corporation shall at all times when the Preferred Stock shall be outstanding, reserve and keep available out of its authorized but unissued capital stock, for the purpose of effecting the conversion of the Preferred Stock, such number of its duly authorized shares of Common Stock as shall from time to time be sufficient to effect the conversion of all outstanding Preferred Stock; and if at any time the number of authorized but unissued shares of Common Stock shall not be sufficient to effect the conversion of all then outstanding shares of the Preferred Stock, the Corporation shall take such corporate action as may be necessary to increase its authorized but unissued shares of Common

Stock to such number of shares as shall be sufficient for such purposes, including, without limitation, engaging in best efforts to obtain the requisite stockholder approval of any necessary amendment to the Certificate of Incorporation. Before taking any action which would cause an adjustment reducing the applicable Conversion Price below the then par value of the shares of Common Stock issuable upon conversion of the Preferred Stock, the Corporation will take any corporate action which may, in the opinion of its counsel, be necessary in order that the Corporation may validly and legally issue fully paid and non-assessable shares of Common Stock at such adjusted applicable Conversion Price.

4.3.3 Effect of Conversion. All shares of Preferred Stock which shall have been surrendered for conversion as herein provided shall no longer be deemed to be outstanding and all rights with respect to such shares shall immediately cease and terminate at the Conversion Time, except only the right of the holders thereof to receive shares of Common Stock in exchange therefor, to receive payment in lieu of any fraction of a share otherwise issuable upon such conversion as provided in Subsection 4.2 and to receive payment of any dividends declared but unpaid thereon. Any shares of Preferred Stock so converted shall be retired and cancelled and may not be reissued as shares of such series, and the Corporation may thereafter take such appropriate action (without the need for stockholder action) as may be necessary to reduce the authorized number of shares of Preferred Stock accordingly.

4.3.4 No Further Adjustment. Upon any such conversion, no adjustment to the applicable Conversion Price shall be made for any declared but unpaid dividends on the Preferred Stock surrendered for conversion or on the Common Stock delivered upon conversion.

4.3.5 Taxes. The Corporation shall pay any and all issue and other similar taxes that may be payable in respect of any issuance or delivery of shares of Common Stock upon conversion of shares of Preferred Stock pursuant to this Section 4. The Corporation shall not, however, be required to pay any tax which may be payable in respect of any transfer involved in the issuance and delivery of shares of Common Stock in a name other than that in which the shares of Preferred Stock so converted were registered, and no such issuance or delivery shall be made unless and until the person or entity requesting such issuance has paid to the Corporation the amount of any such tax or has established, to the satisfaction of the Corporation, that such tax has been paid.

4.4 Adjustments to Applicable Conversion Price for Diluting Issues.

4.4.1 Special Definitions. For purposes of this Article Fourth, the following definitions shall apply:

(a) "**Option**" shall mean rights, options or warrants to subscribe for, purchase or otherwise acquire Common Stock or Convertible Securities.

(b) "**Series B-1 Original Issue Date**" shall mean the date on which the first share of Series B-1 Preferred Stock was issued.

(c) "**Convertible Securities**" shall mean any evidences of indebtedness, shares or other securities directly or indirectly convertible into or exchangeable for Common Stock, but excluding Options.

(d) "**Additional Shares of Common Stock**" shall mean all shares of Common Stock issued (or, pursuant to Subsection 4.4.3 below, deemed to be issued) by the Corporation after the Series B-1 Original Issue Date, other than (1) the following shares of Common Stock and (2) shares of Common Stock deemed issued pursuant to the following Options and Convertible Securities (clauses (1) and (2), collectively, "**Exempted Securities**"):

(i) shares of Common Stock, Options or Convertible Securities issued as a dividend or distribution on Preferred Stock;

(ii) shares of Common Stock, Options or Convertible Securities issued by reason of a dividend, stock split, split-up or other distribution on shares of Common Stock that is covered by Subsection 4.5, 4.6, 4.7 or 4.8;

(iii) shares of Common Stock or Options issued to employees or directors of, or consultants or advisors to, the Corporation or any of its subsidiaries pursuant to a plan, agreement or arrangement approved by the Board of Directors of the Corporation, including the approval of a majority of the then-serving Preferred Directors; provided that such issuance does not exceed the 4% Annual Cap;

(iv) shares of Common Stock or Convertible Securities actually issued upon the exercise of Options or shares of Common Stock actually issued upon the conversion or exchange of Convertible Securities, in each case provided such issuance is pursuant to the terms of such Option or Convertible Security.

(v) shares of Common Stock, Options or Convertible Securities issued to banks, equipment lessors or other financial institutions, or to real property lessors, pursuant to a debt financing, equipment leasing or real property leasing transaction approved by the Board of Directors of the Corporation, including the approval of a majority of the then-serving Preferred Directors;

(vi) shares of Common Stock, Options or Convertible Securities issued to suppliers or third party service providers in connection with the provision of goods or services pursuant to transactions approved by the Board of Directors of the Corporation, including the approval of a majority of the then-serving Preferred Directors;

(vii) shares of Common Stock, Options or Convertible Securities issued to a third party in connection with any singular sponsored research, collaboration, technology license, development, OEM, manufacturing, marketing or other similar agreement or strategic partnership in which the Company enters into a simultaneous business relationship with the acquirer of such securities approved by the Board of Directors of the Corporation, including the approval of a majority of the then-serving Preferred Directors;

provided that such issuance to such third party does not exceed five percent (5%) of the then-outstanding shares of Common Stock on a fully diluted basis (assuming the conversion of all outstanding shares of Preferred Stock and the exercise and conversion of all outstanding Convertible Securities);

(viii) shares of Common Stock Options or Convertible Securities issued pursuant to the acquisition of another corporation by the Corporation by merger, purchase of substantially all of the assets or other reorganization or to a joint venture agreement, provided, that such issuances are approved by the Board of Directors of the Corporation, including the approval of a majority of the then-serving Preferred Directors; and

(ix) shares of Preferred Stock issued pursuant to that certain Preferred Stock Purchase Agreement, dated as of May 8, 2015, among the Corporation and the Investors named therein, as amended from time to time (the "**Purchase Agreement**").

4.4.2 No Adjustment of Conversion Price. No adjustment in the Series A-1 Conversion Price shall be made as the result of the issuance or deemed issuance of Additional Shares of Common Stock if the Corporation receives written notice from the holders of majority of the then outstanding shares of Series A-1 Preferred Stock agreeing that no such adjustment shall be made as the result of the issuance or deemed issuance of such Additional Shares of Common Stock. No adjustment in the Series A-2 Conversion Price shall be made as the result of the issuance or deemed issuance of Additional Shares of Common Stock if the Corporation receives written notice from the holders of a majority of the then outstanding shares of Series A-2 Preferred Stock agreeing that no such adjustment shall be made as the result of the issuance or deemed issuance of such Additional Shares of Common Stock. No adjustment in the Series B-1 Conversion Price shall be made as the result of the issuance or deemed issuance of Additional Shares of Common Stock if the Corporation receives written notice from the holders of a majority of the then outstanding shares of Series B-1 Preferred Stock agreeing that no such adjustment shall be made as the result of the issuance or deemed issuance of such Additional Shares of Common Stock. No adjustment in the Series B-2 Conversion Price shall be made as the result of the issuance or deemed issuance of Additional Shares of Common Stock if the Corporation receives written notice from the holders of a majority of the then outstanding shares of Series B-2 Preferred Stock agreeing that no such adjustment shall be made as the result of the issuance or deemed issuance of such Additional Shares of Common Stock.

4.4.3 Deemed Issue of Additional Shares of Common Stock.

(a) If the Corporation at any time or from time to time after the Series B-1 Original Issue Date shall issue any Options or Convertible Securities (excluding Options or Convertible Securities which are themselves Exempted Securities) or shall fix a record date for the determination of holders of any class of securities entitled to receive any such Options or Convertible Securities, then the maximum number of shares of Common Stock (as set forth in the instrument relating thereto, assuming the satisfaction of any conditions to exercisability, convertibility or exchangeability but without regard to any provision contained therein for a subsequent adjustment of such number) issuable upon the exercise of such Options

or, in the case of Convertible Securities and Options therefor, the conversion or exchange of such Convertible Securities, shall be deemed to be Additional Shares of Common Stock issued as of the time of such issue or, in case such a record date shall have been fixed, as of the close of business on such record date.

(b) If the terms of any Option or Convertible Security, the issuance of which resulted in an adjustment to the applicable Conversion Price pursuant to the terms of Subsection 4.4.4, are revised as a result of an amendment to such terms or any other adjustment pursuant to the provisions of such Option or Convertible Security (but excluding automatic adjustments to such terms pursuant to anti-dilution or similar provisions of such Option or Convertible Security) to provide for either (1) any increase or decrease in the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any such Option or Convertible Security or (2) any increase or decrease in the consideration payable to the Corporation upon such exercise, conversion and/or exchange, then, effective upon such increase or decrease becoming effective, the applicable Conversion Price computed upon the original issue of such Option or Convertible Security (or upon the occurrence of a record date with respect thereto) shall be readjusted to such applicable Conversion Price as would have obtained had such revised terms been in effect upon the original date of issuance of such Option or Convertible Security. Notwithstanding the foregoing, no readjustment pursuant to this clause (b) shall have the effect of increasing the applicable Conversion Price to an amount which exceeds the lower of (i) the applicable Conversion Price in effect immediately prior to the original adjustment made as a result of the issuance of such Option or Convertible Security, or (ii) the applicable Conversion Price that would have resulted from any issuances of Additional Shares of Common Stock (other than deemed issuances of Additional Shares of Common Stock as a result of the issuance of such Option or Convertible Security) between the original adjustment date and such readjustment date.

(c) If the terms of any Option or Convertible Security (excluding Options or Convertible Securities which are themselves Exempted Securities), the issuance of which did not result in an adjustment to the applicable Conversion Price pursuant to the terms of Subsection 4.4.4 (either because the consideration per share (determined pursuant to Subsection 4.4.5) of the Additional Shares of Common Stock subject thereto was equal to or greater than the applicable Conversion Price then in effect, or because such Option or Convertible Security was issued before the Series B-1 Original Issue Date), are revised after the Series B-1 Original Issue Date as a result of an amendment to such terms or any other adjustment pursuant to the provisions of such Option or Convertible Security (but excluding automatic adjustments to such terms pursuant to anti-dilution or similar provisions of such Option or Convertible Security) to provide for either (1) any increase in the number of shares of Common Stock issuable upon the exercise, conversion or exchange of any such Option or Convertible Security or (2) any decrease in the consideration payable to the Corporation upon such exercise, conversion or exchange, then such Option or Convertible Security, as so amended or adjusted, and the Additional Shares of Common Stock subject thereto (determined in the manner provided in Subsection 4.4.3(a) shall be deemed to have been issued effective upon such increase or decrease becoming effective.

(d) Upon the expiration or termination of any unexercised Option or unconverted or unexchanged Convertible Security (or portion thereof) which resulted (either upon its original issuance or upon a revision of its terms) in an adjustment to the Conversion Price pursuant to the terms of Subsection 4.4.4, the applicable Conversion Price shall be readjusted to such applicable Conversion Price as would have obtained had such Option or Convertible Security (or portion thereof) never been issued.

(e) If the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any Option or Convertible Security, or the consideration payable to the Corporation upon such exercise, conversion and/or exchange, is calculable at the time such Option or Convertible Security is issued or amended but is subject to adjustment based upon subsequent events, any adjustment to the applicable Conversion Price provided for in this Subsection 4.4.3 shall be effected at the time of such issuance or amendment based on such number of shares or amount of consideration without regard to any provisions for subsequent adjustments (and any subsequent adjustments shall be treated as provided in clauses (b) and (c) of this Subsection 4.4.3). If the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any Option or Convertible Security, or the consideration payable to the Corporation upon such exercise, conversion and/or exchange, cannot be calculated at all at the time such Option or Convertible Security is issued or amended, any adjustment to the applicable Conversion Price that would result under the terms of this Subsection 4.4.3 at the time of such issuance or amendment shall instead be effected at the time such number of shares and/or amount of consideration is first calculable (even if subject to subsequent adjustments), assuming for purposes of calculating such adjustment to the applicable Conversion Price that such issuance or amendment took place at the time such calculation can first be made.

4.4.4 Adjustment of Conversion Price Upon Issuance of Additional Shares of Common Stock.

(a) In the event the Corporation shall at any time after the Series B-1 Original Issue Date issue Additional Shares of Common Stock (including Additional Shares of Common Stock deemed to be issued pursuant to Subsection 4.4.3), without consideration or for a consideration per share less than the Conversion Price for a series of Preferred Stock in effect immediately prior to such issue, then such Conversion Price shall be reduced, concurrently with such issue, to a price (calculated to the nearest one-hundredth of a cent) determined in accordance with the following formula:

$$CP_2 = CP_1 * (A + B) \div (A + C).$$

For purposes of the foregoing formula, the following definitions shall apply:

(i) "**CP_2**" shall mean the applicable Conversion Price in effect immediately after such issue of Additional Shares of Common Stock

(ii) "**CP_1**" shall mean the applicable Conversion Price in effect immediately prior to such issue of Additional Shares of Common Stock;

(iii) "**A**" shall mean the number of shares of Common Stock outstanding immediately prior to such issue of Additional Shares of Common Stock (treating for this purpose as outstanding all shares of Common Stock issuable upon exercise of Options outstanding immediately prior to such issue or upon conversion or exchange of Convertible Securities (including the Preferred Stock) outstanding (assuming exercise of any outstanding Options therefor) immediately prior to such issue);

(iv) "**B**" shall mean the number of shares of Common Stock that would have been issued if such Additional Shares of Common Stock had been issued at a price per share equal to CP (determined by dividing the aggregate consideration received by the Corporation in respect of such issue by CP_1); and

(v) "**C**" shall mean the number of such Additional Shares of Common Stock issued in such transaction.

Notwithstanding the foregoing, no adjustment shall be made to the Series B-2 Conversion Price with respect to any issuance of Additional Shares of Common Stock issued prior to the first issuance of shares of Series B-2 Preferred Stock.

4.4.5 Determination of Consideration. For purposes of this Subsection 4.4, the consideration received by the Corporation for the issue of any Additional Shares of Common Stock shall be computed as follows:

(a) Cash and Property: Such consideration shall:

(i) insofar as it consists of cash, be computed at the aggregate amount of cash received by the Corporation, excluding amounts paid or payable for accrued interest;

(ii) insofar as it consists of property other than cash, be computed at the fair market value thereof at the time of such issue, as determined in good faith by the Board of Directors of the Corporation; and

(iii) in the event Additional Shares of Common Stock are issued together with other shares or securities or other assets of the Corporation for consideration which covers both, be the proportion of such consideration so received, computed as provided in clauses (i) and (ii) above, as determined in good faith by the Board of Directors of the Corporation.

(b) Options and Convertible Securities. The consideration per share received by the Corporation for Additional Shares of Common Stock deemed to have been issued pursuant to Subsection 4.4.3, relating to Options and Convertible Securities, shall be determined by dividing:

(i) The total amount, if any, received or receivable by the Corporation as consideration for the issue of such Options or Convertible Securities, plus the minimum aggregate amount of additional consideration (as set forth in the instruments relating thereto, without regard to any provision contained therein for a subsequent adjustment of such consideration) payable to the Corporation upon the exercise of such Options or the conversion or exchange of such Convertible Securities, or in the case of Options for Convertible Securities, the exercise of such Options for Convertible Securities and the conversion or exchange of such Convertible Securities, by

(ii) the maximum number of shares of Common Stock (as set forth in the instruments relating thereto, without regard to any provision contained therein for a subsequent adjustment of such number) issuable upon the exercise of such Options or the conversion or exchange of such Convertible Securities, or in the case of Options for Convertible Securities, the exercise of such Options for Convertible Securities and the conversion or exchange of such Convertible Securities.

4.4.6 Multiple Closing Dates. In the event the Corporation shall issue on more than one date Additional Shares of Common Stock that are a part of one transaction or a series of related transactions and that would result in an adjustment to the applicable Conversion Price pursuant to the terms of Subsection 4.4.4, and such issuance dates occur within a period of no more than ninety (90) days from the first such issuance to the final such issuance, then, upon the final such issuance, the applicable Conversion Price shall be readjusted to give effect to all such issuances as if they occurred on the date of the first such issuance (and without giving effect to any additional adjustments as a result of any such subsequent issuances within such period).

4.5 Adjustment for Stock Splits and Combinations. If the Corporation shall at any time or from time to time after the Series B-1 Original Issue Date effect a subdivision of the outstanding Common Stock, the applicable Conversion Price in effect immediately before that subdivision shall be proportionately decreased so that the number of shares of Common Stock issuable on conversion of each share of such series shall be increased in proportion to such increase in the aggregate number of shares of Common Stock outstanding. If the Corporation shall at any time or from time to time after the Series B-1 Original Issue Date combine the outstanding shares of Common Stock, the applicable Conversion Price in effect immediately before the combination shall be proportionately increased so that the number of shares of Common Stock issuable on conversion of each share of such series shall be decreased in proportion to such decrease in the aggregate number of shares of Common Stock outstanding. Any adjustment under this subsection shall become effective at the close of business on the date the subdivision or combination becomes effective.

4.6 Adjustment for Certain Dividends and Distributions. In the event the Corporation at any time or from time to time after the Series B-1 Original Issue Date shall make or issue, or fix a record date for the determination of holders of Common Stock entitled to receive, a dividend or other distribution payable on the Common Stock in additional shares of Common Stock, then and in each such event the applicable Conversion Price in effect immediately before such event shall be decreased as of the time of such issuance or, in the event such a record date shall have been fixed, as of the close of business on such record date, by multiplying the applicable Conversion Price then in effect by a fraction:

(1) the numerator of which shall be the total number of shares of Common Stock issued and outstanding immediately prior to the time of such issuance or the close of business on such record date, and

(2) the denominator of which shall be the total number of shares of Common Stock issued and outstanding immediately prior to the time of such issuance or the close of business on such record date plus the number of shares of Common Stock issuable in payment of such dividend or distribution.

Notwithstanding the foregoing (a) if such record date shall have been fixed and such dividend is not fully paid or if such distribution is not fully made on the date fixed therefor, the applicable Conversion Price shall be recomputed accordingly as of the close of business on such record date and thereafter the applicable Conversion Price shall be adjusted pursuant to this subsection as of the time of actual payment of such dividends or distributions; and (b) that no such adjustment shall be made if the holders of Preferred Stock simultaneously receive a dividend or other distribution of shares of Common Stock in a number equal to the number of shares of Common Stock as they would have received if all outstanding shares of Preferred Stock had been converted into Common Stock on the date of such event.

4.7 Adjustments for Other Dividends and Distributions. In the event the Corporation at any time or from time to time after the Series B-1 Original Issue Date shall make or issue, or fix a record date for the determination of holders of Common Stock entitled to receive, a dividend or other distribution payable in securities of the Corporation (other than a distribution of shares of Common Stock in respect of outstanding shares of Common Stock) or in other property and the provisions of Section 1 do not apply to such dividend or distribution, then and in each such event the holders of Preferred Stock shall receive, simultaneously with the distribution to the holders of Common Stock, a dividend or other distribution of such securities or other property in an amount equal to the amount of such securities or other property as they would have received if all outstanding shares of Preferred Stock had been converted into Common Stock on the date of such event.

4.8 Adjustment for Merger or Reorganization. etc. Subject to the provisions of Subsection 2.3, if there shall occur any reorganization, recapitalization, reclassification, consolidation or merger involving the Corporation in which the Common Stock (but not the Preferred Stock) is converted into or exchanged for securities, cash or other property (other than a transaction covered by Subsections 4.4, 4.6 or 4.7), then, following any such reorganization, recapitalization, reclassification, consolidation or merger, each share of Preferred Stock shall thereafter be convertible in lieu of the Common Stock into which it was convertible prior to such event into the kind and amount of securities, cash or other property which a holder of the number of shares of Common Stock of the Corporation issuable upon conversion of one share of Preferred Stock immediately prior to such reorganization, recapitalization, reclassification, consolidation or merger would have been entitled to receive pursuant to such transaction; and, in such case, appropriate adjustment (as determined in good faith by the Board of Directors of the Corporation) shall be made in the application of the provisions in this Section 4 with respect to the rights and interests thereafter of the holders of the Preferred Stock, to the end that the provisions set forth in this Section 4 (including provisions with respect to changes in

and other adjustments of the applicable Conversion Price) shall thereafter be applicable, as nearly as reasonably may be, in relation to any securities or other property thereafter deliverable upon the conversion of the Preferred Stock. For the avoidance of doubt, nothing in this Subsection 4.8 shall be construed as preventing the holders of Preferred Stock from seeking any appraisal rights to which they are otherwise entitled under the DGCL in connection with a merger triggering an adjustment hereunder, nor shall this Subsection 4.8 be deemed conclusive evidence of the fair value of the shares of Preferred Stock in any such appraisal proceeding.

4.9 Certificate as to Adjustments. Upon the occurrence of each adjustment or readjustment of the applicable Conversion Price pursuant to this Section 4, the Corporation at its expense shall, as promptly as reasonably practicable but in any event not later than ten (10) days thereafter, compute such adjustment or readjustment in accordance with the terms hereof and furnish to each holder of Preferred Stock a certificate setting forth such adjustment or readjustment (including the kind and amount of securities, cash or other property into which the Preferred Stock is convertible) and showing in detail the facts upon which such adjustment or readjustment is based. The Corporation shall, as promptly as reasonably practicable after the written request at any time of any holder of Preferred Stock (but in any event not later than ten (10) days thereafter), furnish or cause to be furnished to such holder a certificate setting forth (i) the applicable Conversion Price then in effect, and (ii) the number of shares of Common Stock and the amount, if any, of other securities, cash or property which then would be received upon the conversion of Preferred Stock.

4.10 Notice of Record Date. In the event:

(a) the Corporation shall take a record of the holders of its Common Stock (or other capital stock or securities at the time issuable upon conversion of the Preferred Stock) for the purpose of entitling or enabling them to receive any dividend or other distribution, or to receive any right to subscribe for or purchase any shares of capital stock of any class or any other securities, or to receive any other security; or

(b) of any capital reorganization of the Corporation, any reclassification of the Common Stock of the Corporation, or any Deemed Liquidation Event; or

(c) of the voluntary or involuntary dissolution, liquidation or winding-up of the Corporation,

then, and in each such case, the Corporation will send or cause to be sent to the holders of the Preferred Stock a notice specifying, as the case may be, (i) the record date for such dividend, distribution or right, and the amount and character of such dividend, distribution or right, or (ii) the effective date on which such reorganization, reclassification, consolidation, merger, transfer, dissolution, liquidation or winding-up is proposed to take place, and the time, if any is to be fixed, as of which the holders of record of Common Stock (or such other capital stock or securities at the time issuable upon the conversion of the Preferred Stock) shall be entitled to exchange their shares of Common Stock (or such other capital stock or securities) for securities or other property deliverable upon such reorganization, reclassification, consolidation, merger,

transfer, dissolution, liquidation or winding-up, and the amount per share and character of such exchange applicable to the Preferred Stock and the Common Stock. Such notice shall be sent at least ten (10) days prior to the record date or effective date for the event specified in such notice.

5. Mandatory Conversion.

5.1 Trigger Events. Upon either (a) the closing of the sale of shares of Common Stock to the public at a price of at least $5.00 per share (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Common Stock), in a firm-commitment underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended, resulting in at least $50,000,000 of gross proceeds to the Corporation or (b) the date and time, or the occurrence of an event, specified by vote or written consent of the holders of a majority of the then outstanding shares of Preferred Stock (the time of such closing or the date and time specified or the time of the event specified in such vote or written consent is referred to herein as the "**Mandatory Conversion Time**"), then (i) all outstanding shares of Preferred Stock shall automatically be converted into shares of Common Stock, at the then effective conversion rate as calculated pursuant to Subsection 4.1.1 and (ii) such shares may not be reissued by the Corporation.

5.2 Procedural Requirements. All holders of record of shares of Preferred Stock shall be sent written notice of the Mandatory Conversion Time and the place designated for mandatory conversion of all such shares of Preferred Stock pursuant to this Section 5. Such notice need not be sent in advance of the occurrence of the Mandatory Conversion Time. Upon receipt of such notice, each holder of shares of Preferred Stock in certificated form shall surrender his, her or its certificate or certificates for all such shares (or, if such holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate) to the Corporation at the place designated in such notice. If so required by the Corporation, any certificates surrendered for conversion shall be endorsed or accompanied by written instrument or instruments of transfer, in form satisfactory to the Corporation, duly executed by the registered holder or by his, her or its attorney duly authorized in writing. All rights with respect to the Preferred Stock converted pursuant to Subsection 5.1, including the rights, if any, to receive notices and vote (other than as a holder of Common Stock), will terminate at the Mandatory Conversion Time (notwithstanding the failure of the holder or holders thereof to surrender any certificates at or prior to such time), except only the rights of the holders thereof, upon surrender of any certificate or certificates of such holders (or lost certificate affidavit and agreement) therefor, to receive the items provided for in the next sentence of this Subsection 5.2. As soon as practicable after the Mandatory Conversion Time and, if applicable, the surrender of any certificate or certificates (or lost certificate affidavit and agreement) for Preferred Stock, the Corporation shall (a) issue and deliver to such holder, or to his, her or its nominees, a certificate or certificates for the number of full shares of Common Stock issuable on such conversion in accordance with the provisions hereof and (b) pay cash as provided in Subsection 4.2 in lieu of any fraction of a share of Common Stock otherwise issuable

upon such conversion and the payment of any declared but unpaid dividends on the shares of Preferred Stock converted. Such converted Preferred Stock shall be retired and cancelled and may not be reissued as shares of such series, and the Corporation may thereafter take such appropriate action (without the need for stockholder action) as may be necessary to reduce the authorized number of shares of Preferred Stock accordingly.

5A. Special Mandatory Conversion and Special Mandatory Redemption.

5A.1. Trigger Event. In the event that any Investor (as defined in the Purchase Agreement) does not purchase the shares of Preferred Stock that such Investor has agreed to purchase in any Tranche Closing (as defined in and contemplated by the Purchase Agreement), other than as a result of the nonfulfillment of such Investor's conditions to purchase such shares (as set forth in Section 5 of the Purchase Agreement), then (i) each share of Preferred Stock originally purchased by such Investor under the Purchase Agreement shall automatically, and without any further action on the part of the holder thereof, be converted into one percent (1%) of the number of shares of Common Stock that would otherwise be issuable upon conversion of such share pursuant to Section 4.1, effective upon, subject to, and concurrently with, the consummation of such Tranche Closing and (ii) with respect to any shares of Common Stock outstanding at the time of such Tranche Closing that were issued to such Investor upon conversion of any shares of Preferred Stock originally purchased by such Investor under the Purchase Agreement pursuant to Section 4.1 prior to such Tranche Closing, ninety nine percent (99%) of the shares of Common Stock issued upon such conversion (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Common Stock occurring after the conversion and before such Tranche Closing) shall be redeemed by the Corporation at a price per share equal to $0.01. For purposes of determining the number of shares of Preferred Stock an Investor has purchased in a Tranche Closing, all Shares purchased by Affiliates of such Investor shall be aggregated with the Shares purchased by such Investor (provided that no Shares shall be attributed to more than one entity or person within any such group of affiliated entities or persons). "**Affiliate**" shall mean, with respect to any specified individual, corporation, partnership, trust, limited liability company, association or other entity (collectively, a "**Person**"), any other Person who, directly or indirectly, controls, is controlled by or is under common control with such Person, including without limitation any general partner, managing member, limited partner, member, manager, employee, officer or director of such Person or any venture capital fund now or hereafter existing that is controlled by one or more general partners or managing members of, or shares the same management company with, such Person. For purposes of this definition, (i) the term "control" when used with respect to any Person means the power to direct the management or policies of such Person, directly or indirectly, whether through ownership of voting securities, by contract or otherwise, and the terms "controlling" and "controlled" shall have meanings correlative to the foregoing, and (ii) Asia Ventures III L.P., Japan Ventures I L.P. and FIL Capital Investments (Mauritius) II Limited and their Affiliates are deemed to be Affiliates of F-Prime Capital Partners Healthcare Fund IV LP. Such conversion is referred to as a "**Special Mandatory Conversion**." Such redemption is referred to as the "**Special Mandatory Redemption**."

5A.2. Procedural Requirements for Special Mandatory Conversion. Upon a Special Mandatory Conversion, each holder of shares of Preferred Stock converted pursuant to Subsection 5A.1 shall be sent written notice of such Special Mandatory Conversion and the place designated for mandatory conversion of all such shares of Preferred Stock pursuant to this Section 5A. Upon receipt of such notice, each holder of such shares of Preferred Stock shall surrender his, her or its certificate or certificates for all such shares (or, if such holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate) to the Corporation at the place designated in such notice. If so required by the Corporation, certificates surrendered for conversion shall be endorsed or accompanied by written instrument or instruments of transfer, in form satisfactory to the Corporation, duly executed by the registered holder or by his, her or its attorney duly authorized in writing. All rights with respect to the Preferred Stock converted pursuant to Subsection 5A.1, including the rights, if any, to receive notices and vote (other than as a holder of Common Stock), will terminate at the time of the Special Mandatory Conversion (notwithstanding the failure of the holder or holders thereof to surrender the certificates for such shares at or prior to such time), except only the rights of the holders thereof, upon surrender of their certificate or certificates therefor (or lost certificate affidavit and agreement), to receive the items provided for in the next sentence of this Subsection 5A.1. As soon as practicable after the Special Mandatory Conversion and the surrender of the certificate or certificates (or lost certificate affidavit and agreement) for Preferred Stock so converted, the Corporation shall issue and deliver to such holder, or to his, her or its nominees, a certificate or certificates for the number of full shares of Common Stock issuable on such conversion in accordance with the provisions hereof, together with cash as provided in Subsection 4.2 in lieu of any fraction of a share of Common Stock otherwise issuable upon such conversion and the payment of any declared but unpaid dividends on the shares of Preferred Stock converted. Such converted Preferred Stock shall be retired and cancelled and may not be reissued as shares of such series, and the Corporation may thereafter take such appropriate action (without the need for stockholder action) as may be necessary to reduce the authorized number of shares of Preferred Stock accordingly.

5A.3. Procedural Requirements for Special Mandatory Redemption. Upon a Special Mandatory Redemption, each holder of shares of Common Stock redeemed pursuant to Subsection 5A.1 (a "**Redeemed Holder**") shall be sent written notice of such Special Mandatory Redemption and the place designated for mandatory redemption of all such shares of Common Stock pursuant to this Section 5A. Upon receipt of such notice, each Redeemed Holder shall surrender his, her or its certificate or certificates for all such shares (or, if such Redeemed Holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate) to the Corporation at the place designated in such notice. If so required by the Corporation, certificates surrendered for redemption shall be endorsed or accompanied by written instrument or instruments of transfer, in form satisfactory to the Corporation, duly executed by the registered Redeemed Holder or by his, her or its attorney duly authorized in writing. All rights with respect to the Common Stock redeemed pursuant to

Subsection 5A.1, including the rights, if any, to receive notices and vote, will terminate at the time of the Special Mandatory Redemption (notwithstanding the failure of the Redeemed Holder to surrender the certificates for such shares at or prior to such time). Such redeemed Common Stock shall be retired and cancelled and may not be reissued as shares of such series, and the Corporation may thereafter take such appropriate action (without the need for stockholder action) as may be necessary to reduce the authorized number of shares of Common Stock accordingly.

6. Redemption.

6.1 General. Unless prohibited by Delaware law governing distributions to stockholders, shares of Preferred Stock shall be redeemed by the Corporation at a price equal to the Series A-1 Original Issue Price, Series A-2 Original Issue Price, Series B-1 Original Issue Price or Series B-2 Original Issue Price, as applicable, per share, plus any Accruing Dividends accrued but unpaid thereon, whether or not declared, together with any other dividends declared but unpaid thereon (the "**Redemption Price**"), in three (3) annual installments commencing not more than sixty (60) days after receipt by the Corporation at any time on or after the fifth anniversary of the Series B-1 Original Issue Date, from the holders of a majority of the then outstanding shares of Preferred Stock, of written notice requesting redemption of all shares of Preferred Stock (the "**Redemption Request**"). Upon receipt of a Redemption Request, the Corporation shall apply all of its assets to any such redemption, and to no other corporate purpose, except to the extent prohibited by Delaware law governing distributions to stockholders. The date of each such installment shall be referred to as a "**Redemption Date**." On each Redemption Date, the Corporation shall redeem, on a pro rata basis in accordance with the number of shares of Preferred Stock owned by each holder, that number of outstanding shares of Preferred Stock determined by dividing (i) the total number of shares of Preferred Stock outstanding immediately prior to such Redemption Date by (ii) the number of remaining Redemption Dates (including the Redemption Date to which such calculation applies); provided, however, that Excluded Shares (as such term is defined in Subsection 6.2) shall not be redeemed and shall be excluded from the calculations set forth in this sentence. If on any Redemption Date Delaware law governing distributions to stockholders prevents the Corporation from redeeming all shares of Preferred Stock to be redeemed, the Corporation shall ratably redeem the maximum number of shares that it may redeem consistent with such law, and shall redeem the remaining shares as soon as it may lawfully do so under such law.

6.2 Redemption Notice. The Corporation shall send written notice of the mandatory redemption (the "**Redemption Notice**") to each holder of record of Preferred Stock not less than forty (40) days prior to each Redemption Date. Each Redemption Notice shall state:

(a) the number of shares of Preferred Stock held by the holder that the Corporation shall redeem on the Redemption Date specified in the Redemption Notice;

(b) the Redemption Date and the Redemption Price;

(c) the date upon which the holder's right to convert such shares terminates (as determined in accordance with Subsection 4.1); and

(d) for holders of shares in certificated form, that the holder is to surrender to the Corporation, in the manner and at the place designated, his, her or its certificate or certificates representing the shares of Preferred Stock to be redeemed.

If the Corporation receives, on or prior to the twentieth (20th) day after the date of delivery of the Redemption Notice to a holder of Preferred Stock, written notice from such holder that such holder elects to be excluded from the redemption provided in this Section 6, then the shares of Preferred Stock registered on the books of the Corporation in the name of such holder at the time of the Corporation's receipt of such notice shall thereafter be "**Excluded Shares**." Excluded Shares shall not be redeemed or redeemable pursuant to this Section 6, whether on such Redemption Date or thereafter.

6.3 Surrender of Certificates; Payment. On or before the applicable Redemption Date, each holder of shares of Preferred Stock to be redeemed on such Redemption Date, unless such holder has exercised his, her or its right to convert such shares as provided in Section 4, shall, if a holder of shares in certificated form, surrender the certificate or certificates representing such shares (or, if such registered holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate) to the Corporation, in the manner and at the place designated in the Redemption Notice, and thereupon the Redemption Price for such shares shall be payable to the order of the person whose name appears on such certificate or certificates as the owner thereof. In the event less than all of the shares of Preferred Stock represented by a certificate are redeemed, a new certificate, instrument, or book entry representing the unredeemed shares of Preferred Stock shall promptly be issued to such holder.

6.4 Rights Subsequent to Redemption. If the Redemption Notice shall have been duly given, and if on the applicable Redemption Date the Redemption Price payable upon redemption of the shares of Preferred Stock to be redeemed on such Redemption Date is paid or tendered for payment or deposited with an independent payment agent so as to be available therefor in a timely manner, then notwithstanding that any certificates evidencing any of the shares of Preferred Stock so called for redemption shall not have been surrendered, dividends with respect to such shares of Preferred Stock shall cease to accrue after such Redemption Date and all rights with respect to such shares shall forthwith after the Redemption Date terminate, except only the right of the holders to receive the Redemption Price without interest upon surrender of any such certificate or certificates therefor.

7. Redeemed or Otherwise Acquired Shares. Any shares of Preferred Stock that are redeemed or otherwise acquired by the Corporation or any of its subsidiaries shall be automatically and immediately cancelled and retired and shall not be reissued, sold or transferred. Neither the Corporation nor any of its subsidiaries may exercise any voting or other rights granted to the holders of Preferred Stock following redemption.

8. Waiver. Any of the rights, powers, preferences and other terms of the Preferred Stock set forth herein may be waived on behalf of all holders of Preferred Stock by the affirmative written consent or vote of the holders of a majority of the shares of Preferred Stock then outstanding, consenting or voting as a single class.

9. Notices. Any notice required or permitted by the provisions of this Article Fourth to be given to a holder of shares of Preferred Stock shall be mailed, postage prepaid, to the post office address last shown on the records of the Corporation, or given by electronic communication in compliance with the provisions of the General Corporation Law, and shall be deemed sent upon such mailing or electronic transmission.

FIFTH: Subject to any additional vote required by the Certificate of Incorporation or By-laws, in furtherance and not in limitation of the powers conferred by statute, the Board of Directors is expressly authorized to make, repeal, alter, amend and rescind any or all of the By-laws of the Corporation.

SIXTH: Subject to any additional vote required by the Certificate of Incorporation, the number of directors of the Corporation shall be determined in the manner set forth in the By-laws of the Corporation.

SEVENTH: Elections of directors need not be by written ballot unless the Bylaws of the Corporation shall so provide.

EIGHTH: Meetings of stockholders may be held within or without the State of Delaware, as the By-laws of the Corporation may provide. The books of the Corporation may be kept outside the State of Delaware at such place or places as may be designated from time to time by the Board of Directors or in the By-laws of the Corporation.

NINTH: To the fullest extent permitted by law, a director of the Corporation shall not be personally liable to the Corporation or its stockholders for monetary damages for breach of fiduciary duty as a director. If the General Corporation Law or any other law of the State of Delaware is amended after approval by the stockholders of this Article Ninth to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of a director of the Corporation shall be eliminated or limited to the fullest extent permitted by the General Corporation Law as so amended.

Any repeal or modification of the foregoing provisions of this Article Ninth by the stockholders of the Corporation shall not adversely affect any right or protection of a director of the Corporation existing at the time of, or increase the liability of any director of the Corporation with respect to any acts or omissions of such director occurring prior to, such repeal or modification.

TENTH: To the fullest extent permitted by applicable law, the Corporation is authorized to provide indemnification of (and advancement of expenses to) directors, officers and agents of the Corporation (and any other persons to which General Corporation Law permits the Corporation to provide indemnification) through By-law provisions, agreements with such agents or other persons, vote of stockholders or disinterested directors or otherwise, in excess of the indemnification and advancement otherwise permitted by Section 145 of the General Corporation Law.

Any amendment, repeal or modification of the foregoing provisions of this Article Tenth shall not adversely affect any right or protection of any director, officer or other agent of the Corporation existing at the time of such amendment, repeal or modification.

ELEVENTH: The Corporation renounces, to the fullest extent permitted by law, any interest or expectancy of the Corporation in, or in being offered an opportunity to participate in, any Excluded Opportunity. An "**Excluded Opportunity**" is any matter, transaction or interest that is presented to, or acquired, created or developed by, or which otherwise comes into the possession of (i) any director of the Corporation who is not an employee of the Corporation or any of its subsidiaries, or (ii) any holder of Preferred Stock or any partner, member, director, stockholder, employee or agent of any such holder, other than someone who is an employee of the Corporation or any of its subsidiaries (collectively, "**Covered Persons**"), unless such matter, transaction or interest is presented to, or acquired, created or developed by, or otherwise comes into the possession of, a Covered Person expressly and solely in such Covered Person's capacity as a director of the Corporation.

TWELFTH: Unless the Corporation consents in writing to the selection of an alternative forum, the Court of Chancery in the State of Delaware shall be the sole and exclusive forum for any stockholder (including a beneficial owner) to bring (i) any derivative action or proceeding brought on behalf of the Corporation, (ii) any action asserting a claim of breach of fiduciary duty owed by any director, officer or other employee of the Corporation to the Corporation or the Corporation's stockholders, (iii) any action asserting a claim against the Corporation, its directors, officers or employees arising pursuant to any provision of the Delaware General Corporation Law or the Corporation's certificate of incorporation or by-laws or (iv) any action asserting a claim against the Corporation, its directors, officers or employees governed by the internal affairs doctrine, except for, as to each of (i) through (iv) above, any claim as to which the Court of Chancery determines that there is an indispensable party not subject to the jurisdiction of the Court of Chancery (and the indispensable party does not consent to the personal jurisdiction of the Court of Chancery within ten days following such determination), which is vested in the exclusive jurisdiction of a court or forum other than the Court of Chancery, or for which the Court of Chancery does not have subject matter jurisdiction. If any provision or provisions of this Article Twelfth shall be held to be invalid, illegal or unenforceable as applied to any person or entity or circumstance for any reason whatsoever, then, to the fullest extent permitted by law, the validity, legality and enforceability of such provisions in any other circumstance and of the remaining provisions of this Article Twelfth (including, without limitation, each portion of any sentence of this Article Twelfth containing any such provision held to be invalid, illegal or unenforceable that is not itself held to be invalid, illegal or unenforceable) and the application of such provision to other persons or entities and circumstances shall not in any way be affected or impaired thereby.

* * *

3. That the foregoing amendment and restatement was approved by the holders of the requisite number of shares of this corporation in accordance with Section 228 of the General Corporation Law.

4. That this Amended and Restated Certificate of Incorporation, which restates and integrates and further amends the provisions of this Corporation's Certificate of Incorporation, has been duly adopted in accordance with Sections 242 and 245 of the General Corporation Law.

IN WITNESS WHEREOF, this Amended and Restated Certificate of Incorporation has been executed by a duly authorized officer of this corporation on this 20th day of November, 2017.

By: /s/ Ryan Watts
Name: Ryan Watts, Ph.D.
Title: President and CEO

CERTIFICATE OF AMENDMENT TO

THE AMENDED AND RESTATED

CERTIFICATE OF INCORPORATION

OF

DENALI THERAPEUTICS INC.

Denali Therapeutics Inc., a corporation organized and existing under the laws of the State of Delaware (the "**Corporation**"), hereby certifies as follows:

1. The name of the Corporation is Denali Therapeutics Inc., and the original Certificate of Incorporation of this Corporation was filed with the Secretary of State of the State of Delaware on October 14, 2013 under the name SPR Pharma Inc.

2. This Certificate of Amendment to the Amended and Restated Certificate of Incorporation (the "**Certificate of Amendment**") has been duly adopted in accordance with Section 242 of the Delaware General Corporation Law (the "**DGCL**") and amends the provisions of the Corporation's Amended and Restated Certificate of Incorporation (the "**Restated Certificate**").

3. The terms and provisions of this Certificate of Amendment have been duly approved by written consent of the required number of shares of outstanding stock of the Corporation pursuant to Subsection 228(a) of the DGCL and written notice pursuant to Subsection 228(e) of the General Corporation Law of the State of Delaware has been or will be given to those stockholders whose written consent has not been obtained.

4. The introductory paragraph of ARTICLE FOURTH of the Restated Certificate is hereby amended and restated in its entirety to read as follows:

"**FOURTH**: Immediately upon the filing of this Certificate of Amendment, each four (4) outstanding shares of Common Stock, each four (4) outstanding shares of Series A-1 Preferred Stock, each four (4) outstanding shares of Series A-2 Preferred Stock, each four (4) outstanding shares of Series B-1 Preferred Stock and each four (4) outstanding shares of Series B-2 Preferred Stock, will be exchanged and combined, automatically and without further action, into one (1) share of Common Stock, one (1) share of Series A-1 Preferred Stock, one (1) share of Series A-2 Preferred Stock, one (1) share of Series B-1 Preferred Stock, and one (1) share of Series B-2 Preferred Stock, respectively (the "**Reverse Stock Split**"). The Reverse Stock Split shall also apply to any outstanding securities or rights convertible into, or exchangeable or exercisable for, Common Stock or Preferred Stock of the Corporation. The Reverse Stock Split shall be effected on a certificate-by-certificate basis and each certificate share number will then be rounded down. No fractional shares shall be issued upon the exchange and combination. In lieu of any fractional shares to which the holder would otherwise be entitled, the Corporation shall pay an amount of cash equal to the product of (i) the fractional share to which the holder would otherwise be entitled and (ii) the then fair value of a share as determined in good faith by the Board of Directors of the Corporation.

The total number of shares of all classes of stock which the Corporation shall have authority to issue is (i) 83,587,362 shares of Common Stock, $0.01 par value per share ("**Common Stock**"), and (ii) 63,288,466 shares of Preferred Stock, $0.01 par value per share ("**Preferred Stock**")."

5. The introductory paragraph of Article FOURTH, Section B of the Restated Certificate is hereby amended and restated in its entirety to read as follows:

"B. PREFERRED STOCK

46,114,433 shares of the authorized Preferred Stock of the Corporation are hereby designated "**Series A-1 Preferred Stock**," 4,361,533 shares of the authorized Preferred Stock of the Corporation are hereby designated "**Series A-2 Preferred Stock**" (together with the Series A-1 Preferred Stock, the "**Series A Preferred Stock**"), 8,125,000 shares of the authorized Preferred Stock of the Corporation are hereby designated "**Series B-1 Preferred Stock**," and 4,687,500 shares of the authorized Preferred Stock of the Corporation are hereby designated "**Series B-2 Preferred Stock**" (together with the Series B-1 Preferred Stock, the "**Series B Preferred Stock**"), each with the following rights, preferences, powers, privileges and restrictions, qualifications and limitations. Unless otherwise indicated, references to "sections" or "subsections" in this Part B of this Article Fourth refer to sections and subsections of Part B of this Article Fourth."

* * *

IN WITNESS WHEREOF, DENALI THERAPEUTICS INC. has caused this Certificate of Amendment to be signed by its President and Chief Executive Officer this ____ day of _____, 2017.

DENALI THERAPEUTICS INC.

By: _____

Ryan J. Watts, Ph.D.
President and Chief Executive Officer

Exhibit 3.2

AMENDED AND RESTATED

CERTIFICATE OF INCORPORATION OF

DENALI THERAPEUTICS INC.

Denali Therapeutics Inc., a corporation organized and existing under the laws of the State of Delaware (the "Corporation"), does hereby certify as follows:

A. The name of the Corporation is Denali Therapeutics Inc. The original Certificate of Incorporation of the Corporation was filed with the Secretary of State of the State of Delaware on October 14, 2013 under the name SPR Pharma Inc.

B. This Amended and Restated Certificate of Incorporation (this "Amended and Restated Certificate of Incorporation") was duly adopted by the Board of Directors of the Corporation (the "Board of Directors") in accordance with Sections 242 and 245 of the General Corporation Law of the State of Delaware "DGCL"), and has been duly approved by the written consent of the stockholders of the Corporation in accordance with Section 228 of the DGCL.

C. The text of the Amended and Restated Certificate of Incorporation is hereby amended and restated in its entirety to read as follows:

ARTICLE I

The name of the Corporation is Denali Therapeutics Inc.

ARTICLE II

The address of the Corporation's registered office in the State of Delaware is 1209 Orange Street, City of Wilmington, County of New Castle, Delaware 19801. The name of its registered agent at such address is The Corporation Trust Company.

ARTICLE III

The nature of the business or purposes to be conducted or promoted by the Corporation is to engage in any lawful act or activity for which corporations may be organized under the General Corporation Law of the State of Delaware ("DGCL").

ARTICLE IV

Section 1. This Corporation is authorized to issue two classes of stock, to be designated, respectively, Common Stock and Preferred Stock. The total number of shares of stock that the Corporation shall have authority to issue is four hundred forty million (440,000,000) shares, of which four hundred million (400,000,000) shares are Common Stock, $0.01 par value, and forty million (40,000,000) shares are Preferred Stock, $0.01 par value.

Section 2. Each share of Common Stock shall entitle the holder thereof to one (1) vote on any matter submitted to a vote at a meeting of stockholders.

Section 3. The Preferred Stock may be issued from time to time in one or more series pursuant to a resolution or resolutions providing for such issue duly adopted by the Board of Directors (authority to do so being hereby expressly vested in the Board of Directors). The Board of Directors is further authorized, subject to limitations prescribed by law, to fix by resolution or resolutions the designations, powers, preferences and rights, and the qualifications, limitations or restrictions thereof, of any wholly unissued series of Preferred Stock, including, without limitation, authority to fix by resolution or resolutions the dividend rights, dividend rate, conversion rights, voting rights, rights and terms of redemption (including sinking fund provisions), redemption price or prices, and liquidation preferences of any such series, and the number of shares constituting any such series and the designation thereof, or any of the foregoing. The Board of Directors is further authorized to increase (but not above the total number of authorized shares of the class) or decrease (but not below the number of shares of any such series then outstanding) the number of shares of any series, the number of which was fixed by it, subsequent to the issuance of shares of such series then outstanding, subject to the powers, preferences and rights, and the qualifications, limitations and restrictions thereof stated in this Amended and Restated Certificate of Incorporation or the resolution of the Board of Directors originally fixing the number of shares of such series. If the number of shares of any series is so decreased, then the Corporation shall take all such steps as are necessary to cause the shares constituting such decrease to resume the status which they had prior to the adoption of the resolution originally fixing the number of shares of such series.

Section 4. Except as otherwise required by law, holders of Common Stock shall not be entitled to vote on any amendment to this Amended and Restated Certificate of Incorporation (including any certificate of designation filed with respect to any series of Preferred Stock) that relates solely to the terms of one or more outstanding series of Preferred Stock if the holders of such affected series are entitled, either separately or together as a class with the holders of one or more other such series, to vote thereon by law or pursuant to this Amended and Restated Certificate of Incorporation (including any certificate of designation filed with respect to any series of Preferred Stock).

ARTICLE V

Section 1. The number of directors that constitutes the entire Board of Directors of the Corporation shall be determined in the manner set forth in the Bylaws of the Corporation. At each annual meeting of stockholders, directors of the Corporation shall be elected to hold office until the expiration of the term for which they are elected and until their successors have been duly elected and qualified or until their earlier resignation or removal; except that if any such meeting shall not be so held, such election shall take place at a stockholders' meeting called and held in accordance with the DGCL.

Section 2. From and after the effectiveness of this Amended and Restated Certificate of Incorporation, the directors of the Corporation (other than any who may be elected by holders of Preferred Stock under specified circumstances) shall be divided into three classes as nearly equal in size as is practicable, hereby designated Class I, Class II and Class III. Directors already in office shall be assigned to each class at the time such classification becomes effective in accordance with a resolution or resolutions adopted by the Board of Directors. At the first annual meeting of stockholders following the date hereof, the term of office of the Class I directors shall expire and Class I directors shall be elected for a full term of three years. At the second annual meeting of stockholders following the date hereof, the term of office of the Class II directors shall expire and Class II directors shall be elected for a full term of three years. At the third annual meeting of stockholders following the date hereof, the term of office of the Class III directors shall expire and Class III directors shall be elected for a full term of three years. At each succeeding annual meeting of stockholders, directors shall be elected for a full term of three years to succeed the directors of the class whose terms expire at such annual meeting. If the number of directors is changed, any newly created directorships or decrease in directorships shall be so apportioned hereafter among the classes as to make all classes as nearly equal in number as is practicable, *provided that* no decrease in the number of directors constituting the Board of Directors shall shorten the term of any incumbent director.

ARTICLE VI

Section 1. Any director or the entire Board of Directors may be removed from office at any time, but only for cause, and only by the affirmative vote of the holders of at least a majority of the voting power of the issued and outstanding capital stock of the Corporation entitled to vote in the election of directors.

Section 2. Except as otherwise provided for or fixed by or pursuant to the provisions of Article IV hereof in relation to the rights of the holders of Preferred Stock to elect directors under specified circumstances, newly created directorships resulting from any increase in the number of directors, created in accordance with the Bylaws of the Corporation, and any vacancies on the Board of Directors resulting from death, resignation, disqualification, removal or other cause shall be filled only by the affirmative vote of a majority of the remaining directors then in office, even though less than a quorum of the Board of Directors, or by a sole remaining director, and not by the stockholders. A person so elected by the Board of Directors to fill a vacancy or newly created directorship shall hold office until the next election of the class for which such director shall have been chosen until his or her successor shall have been duly elected and qualified, or until such director’s earlier death, resignation or removal. No decrease in the number of directors constituting the Board of Directors shall shorten the term of any incumbent director.

ARTICLE VII

Section 1. The Corporation is to have perpetual existence.

Section 2. The business and affairs of the Corporation shall be managed by or under the direction of the Board of Directors. In addition to the powers and authority expressly conferred upon them by statute or by this Amended and Restated Certificate of Incorporation or the Bylaws of the Corporation, the directors are hereby empowered to exercise all such powers and do all such acts and things as may be exercised or done by the Corporation.

Section 3. In furtherance and not in limitation of the powers conferred by statute, the Board of Directors is expressly authorized to adopt, alter, amend or repeal the Bylaws of the Corporation. The affirmative vote of at least a majority of the Board of Directors then in office shall be required in order for the Board of Directors to adopt, amend, alter or repeal the Corporation's Bylaws. The Corporation's Bylaws may also be adopted, amended, altered or repealed by the stockholders of the Corporation. Notwithstanding the above or any other provision of this Amended and Restated Certificate of Incorporation, the Bylaws of the Corporation may not be amended, altered or repealed except in accordance with Article X of the Bylaws. No Bylaw hereafter legally adopted, amended, altered or repealed shall invalidate any prior act of the directors or officers of the Corporation that would have been valid if such Bylaw had not been adopted, amended, altered or repealed.

Section 4. The election of directors need not be by written ballot unless the Bylaws of the Corporation shall so provide.

Section 5. No stockholder will be permitted to cumulate votes at any election of directors.

ARTICLE VIII

Section 1. Any action required or permitted to be taken by the stockholders of the Corporation must be effected at a duly called annual or special meeting of stockholders of the Corporation and may not be effected by any consent in writing by such stockholders.

Section 2. Special meetings of stockholders of the Corporation may be called only by the Chairperson of the Board of Directors, the Chief Executive Officer, the President or the Board of Directors acting pursuant to a resolution adopted by a majority of the Board of Directors, and any power of stockholders to call a special meeting of stockholders is specifically denied. Only such business shall be considered at a special meeting of stockholders as shall have been stated in the notice for such meeting.

Section 3. Advance notice of stockholder nominations for the election of directors and of business to be brought by stockholders before any meeting of the stockholders of the Corporation shall be given in the manner and to the extent provided in the Bylaws of the Corporation.

ARTICLE IX

Section 1. To the fullest extent permitted by the DGCL as the same exists or as may hereafter be amended from time to time, a director of the Corporation shall not be personally liable to the Corporation or its stockholders for monetary damages for breach of fiduciary duty as a director. If the DGCL is amended to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of a director of the Corporation shall be eliminated or limited to the fullest extent permitted by the DGCL, as so amended.

Section 2. The Corporation shall indemnify, to the fullest extent permitted by applicable law, any director or officer of the Corporation who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (a "Proceeding") by reason of the fact that he or she is or was a director, officer, employee or agent of the Corporation or is or was serving at the request of the Corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, including service with respect to employee benefit plans, against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by such person in connection with any such Proceeding. The Corporation shall be required to indemnify a person in connection with a Proceeding initiated by such person only if the Proceeding was authorized by the Board of Directors.

Section 3. The Corporation shall have the power to indemnify, to the extent permitted by applicable law, any employee or agent of the Corporation who was or is a party or is threatened to be made a party to any Proceeding by reason of the fact that he or she is or was a director, officer, employee or agent of the Corporation or is or was serving at the request of the Corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, including service with respect to employee benefit plans, against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by such person in connection with any such Proceeding.

Section 4. Neither any amendment nor repeal of any Section of this Article IX, nor the adoption of any provision of this Amended and Restated Certificate of Incorporation or the Bylaws of the Corporation inconsistent with this Article IX, shall eliminate or reduce the effect of this Article IX in respect of any matter occurring, or any cause of action, suit, claim or proceeding accruing or arising or that, but for this Article IX, would accrue or arise, prior to such amendment, repeal or adoption of an inconsistent provision.

ARTICLE X

Meetings of stockholders may be held within or outside of the State of Delaware, as the Bylaws may provide. The books of the Corporation may be kept (subject to any provision contained in the statutes) outside of the State of Delaware at such place or places as may be designated from time to time by the Board of Directors or in the Bylaws of the Corporation.

ARTICLE XI

Unless the Corporation consents in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for (A) any derivative action or proceeding brought on behalf of the Corporation, (B) any action or proceeding asserting a claim of breach of a fiduciary duty owed by any director, officer or other employee of the Corporation to the Corporation or the Corporation's stockholders, (C) any action or proceeding asserting a claim arising pursuant to any provision of the DGCL or the Corporation's Certificate of Incorporation or Bylaws, or (D) any action or proceeding asserting a claim governed by the internal affairs doctrine.

Unless the Corporation consents in writing to the selection of an alternative forum, the federal district courts of the United States of America shall be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act of 1933, as amended.

ARTICLE XII

The Corporation reserves the right to amend or repeal any provision contained in this Amended and Restated Certificate of Incorporation in the manner prescribed by the laws of the State of Delaware and all rights conferred upon stockholders are granted subject to this reservation; *provided*, *however*, that notwithstanding any other provision of this Amended and Restated Certificate of Incorporation or any provision of law that might otherwise permit a lesser vote or no vote, the Board of Directors acting pursuant to a resolution adopted by a majority of the Board of Directors and the affirmative vote of sixty-six and two-thirds percent (66 2/3%) of the then outstanding voting securities of the Corporation, voting together as a single class, shall be required for the amendment, repeal or modification of the provisions of Section 3 of Article IV, Section 2 of Article V, Article VI, Section 5 of Article VII, Article VIII, Article XI or Article XII of this Amended and Restated Certificate of Incorporation.

***

IN WITNESS WHEREOF, Denali Therapeutics Inc. has caused this Amended and Restated Certificate of Incorporation to be signed by Ryan Watts, a duly authorized officer of the Corporation, on this ____ day of _____, 2017.

Ryan Watts, Ph.D.
President and Chief Executive Officer

Exhibit 3.4

AMENDED AND RESTATED BYLAWS OF

DENALI THERAPEUTICS INC.

(as amended and restated on November 25, 2017, and effective immediately as of the closing of the corporation's initial public offering)

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AMENDED AND RESTATED BYLAWS OF DENALI THERAPEUTICS INC.

ARTICLE I — CORPORATE OFFICES

1.1 REGISTERED OFFICE

The registered office of Denali Therapeutics Inc. shall be fixed in the corporation's certificate of incorporation. References in these bylaws to the certificate of incorporation shall mean the certificate of incorporation of the corporation, as amended from time to time, including the terms of any certificate of designations of any series of Preferred Stock.

1.2 OTHER OFFICES

The corporation's board of directors may at any time establish other offices at any place or places where the corporation is qualified to do business.

ARTICLE II — MEETINGS OF STOCKHOLDERS

2.1 PLACE OF MEETINGS

Meetings of stockholders shall be held at any place, within or outside the State of Delaware, designated by the board of directors. The board of directors may, in its sole discretion, determine that a meeting of stockholders shall not be held at any place, but may instead be held solely by means of remote communication as authorized by Section 211(a)(2) of the General Corporation Law of the State of Delaware (the "DGCL"). In the absence of any such designation or determination, stockholders' meetings shall be held at the corporation's principal executive office.

2.2 ANNUAL MEETING

The annual meeting of stockholders shall be held on such date, at such time, and at such place (if any) within or without the State of Delaware as shall be designated from time to time by the board of directors and stated in the corporation's notice of the meeting. At the annual meeting, directors shall be elected and any other proper business may be transacted.

2.3 SPECIAL MEETING

(i) A special meeting of the stockholders, other than those required by statute, may be called at any time only by (A) the board of directors, (B) the chairperson of the board of directors, (C) the chief executive officer or (D) the president (in the absence of a chief executive officer). A special meeting of the stockholders may not be called by any other person or persons. The board of directors may cancel, postpone or reschedule any previously scheduled special meeting at any time, before or after the notice for such meeting has been sent to the stockholders.

(ii) The notice of a special meeting shall include the purpose for which the meeting is called. Only such business shall be conducted at a special meeting of stockholders as shall have been brought before the meeting by or at the direction of the board of directors, the chairperson of the board of directors, the chief executive officer or the president (in the absence of a chief executive officer). Nothing contained in this Section 2.3(ii) shall be construed as limiting, fixing or affecting the time when a meeting of stockholders called by action of the board of directors may be held.

2.4 ADVANCE NOTICE PROCEDURES

(i) *Advance Notice of Stockholder Business.* At an annual meeting of the stockholders, only such business shall be conducted as shall have been properly brought before the meeting. To be properly brought before an annual meeting, business must be brought: (A) pursuant to the corporation's proxy materials with respect to such meeting, (B) by or at the direction of the board of directors, or (C) by a stockholder of the corporation who (1) is a stockholder of record at the time of the giving of the notice required by this Section 2.4(i) and on the record date for the determination of stockholders entitled to vote at the annual meeting and (2) has timely complied in proper written form with the notice procedures set forth in this Section 2.4(i). In addition, for business to be properly brought before an annual meeting by a stockholder, such business must be a proper matter for stockholder action pursuant to these bylaws and applicable law. Except for proposals properly made in accordance with Rule 14a-8 under the Securities Exchange Act of 1934, as amended (the "1934 Act") and the rules and regulations thereunder (as so amended and inclusive of such rules and regulations), and included in the notice of meeting given by or at the direction of the board of directors, for the avoidance of doubt, clause (C) above shall be the exclusive means for a stockholder to bring business before an annual meeting of stockholders.

(a) To comply with clause (C) of Section 2.4(i) above, a stockholder's notice must set forth all information required under this Section 2.4(i) and must be timely received by the secretary of the corporation. To be timely, a stockholder's notice must be received by the secretary at the principal executive offices of the corporation not later than the 45th day nor earlier than the 75th day before the one-year anniversary of the date on which the corporation first mailed its proxy materials or a notice of availability of proxy materials (whichever is earlier) for the preceding year's annual meeting; *provided*, *however*, that in the event that no annual meeting was held in the previous year or if the date of the annual meeting is advanced by more than 30 days prior to or delayed by more than 60 days after the one-year anniversary of the date of the previous year's annual meeting, then, for notice by the stockholder to be timely, it must be so received by the secretary not earlier than the close of business on the 120th day prior to such annual meeting and not later than the close of business on the later of (i) the 90th day prior to such annual meeting, or (ii) the tenth day following the day on which Public Announcement (as defined below) of the date of such annual meeting is first made. In no event shall any adjournment or postponement of an annual meeting or the announcement thereof commence a new time period for the giving of a stockholder's notice as described in this Section 2.4(i)(a). "Public Announcement" shall mean disclosure in a press release reported by the Dow Jones News Service, Associated Press or a comparable national news service or in a document publicly filed by the corporation with the Securities and Exchange Commission pursuant to Section 13, 14 or 15(d) of the 1934 Act.

(b) To be in proper written form, a stockholder's notice to the secretary must set forth as to each matter of business the stockholder intends to bring before the annual meeting: (1) a brief description of the business intended to be brought before the annual meeting and the reasons for conducting such

business at the annual meeting, (2) the name and address, as they appear on the corporation's books, of the stockholder proposing such business and any Stockholder Associated Person (as defined below), (3) the class and number of shares of the corporation that are held of record or are beneficially owned by the stockholder or any Stockholder Associated Person and any derivative positions held or beneficially held by the stockholder or any Stockholder Associated Person, (4) whether and the extent to which any hedging or other transaction or series of transactions has been entered into by or on behalf of such stockholder or any Stockholder Associated Person with respect to any securities of the corporation, and a description of any other agreement, arrangement or understanding (including any short position or any borrowing or lending of shares), the effect or intent of which is to mitigate loss to, or to manage the risk or benefit from share price changes for, or to increase or decrease the voting power of, such stockholder or any Stockholder Associated Person with respect to any securities of the corporation, (5) any material interest of the stockholder or a Stockholder Associated Person in such business, and (6) a statement whether either such stockholder or any Stockholder Associated Person will deliver a proxy statement and form of proxy to holders of at least the percentage of the corporation's voting shares required under applicable law to carry the proposal (such information provided and statements made as required by clauses (1) through (6), a "Business Solicitation Statement"). In addition, to be in proper written form, a stockholder's notice to the secretary must be supplemented not later than ten days following the record date for notice of the meeting to disclose the information contained in clauses (3) and (4) above as of the record date for notice of the meeting. For purposes of this Section 2.4, a "Stockholder Associated Person" of any stockholder shall mean (i) any person controlling, directly or indirectly, or acting in concert with, such stockholder, (ii) any beneficial owner of shares of stock of the corporation owned of record or beneficially by such stockholder and on whose behalf the proposal or nomination, as the case may be, is being made, or (iii) any person controlling, controlled by or under common control with such person referred to in the preceding clauses (i) and (ii).

(c) Without exception, no business shall be conducted at any annual meeting except in accordance with the provisions set forth in this Section 2.4(i) and, if applicable, Section 2.4(ii). In addition, business proposed to be brought by a stockholder may not be brought before the annual meeting if such stockholder or a Stockholder Associated Person, as applicable, takes action contrary to the representations made in the Business Solicitation Statement applicable to such business or if the Business Solicitation Statement applicable to such business contains an untrue statement of a material fact or omits to state a material fact necessary to make the statements therein not misleading. The chairperson of the annual meeting shall, if the facts warrant, determine and declare at the annual meeting that business was not properly brought before the annual meeting and in accordance with the provisions of this Section 2.4(i), and, if the chairperson should so determine, he or she shall so declare at the annual meeting that any such business not properly brought before the annual meeting shall not be conducted.

(ii) *Advance Notice of Director Nominations at Annual Meetings.* Notwithstanding anything in these bylaws to the contrary, only persons who are nominated in accordance with the procedures set forth in this Section 2.4(ii) shall be eligible for election or re-election as directors at an annual meeting of stockholders. Nominations of persons for election or re-election to the board of directors of the corporation shall be made at an annual meeting of stockholders only (A) by or at the direction of the board of directors or (B) by a stockholder of the corporation who (1) was a stockholder of record at the time of the giving of the notice required by this Section 2.4(ii) and on the record date for the determination of stockholders entitled to vote at the annual meeting and (2) has complied with the notice procedures set forth in this Section 2.4(ii). In addition to any other applicable requirements, for a nomination to be made by a stockholder, the stockholder must have given timely notice thereof in proper written form to the secretary of the corporation.

(a) To comply with clause (B) of Section 2.4(ii) above, a nomination to be made by a stockholder must set forth all information required under this Section 2.4(ii) and must be received by the secretary of the corporation at the principal executive offices of the corporation at the time set forth in, and in accordance with, the final three sentences of Section 2.4(i)(a) above.

(b) To be in proper written form, such stockholder's notice to the secretary must set forth:

(1) as to each person (a "nominee") whom the stockholder proposes to nominate for election or re-election as a director: (A) the name, age, business address and residence address of the nominee, (B) the principal occupation or employment of the nominee, (C) the class and number of shares of the corporation that are held of record or are beneficially owned by the nominee and any derivative positions held or beneficially held by the nominee, (D) whether and the extent to which any hedging or other transaction or series of transactions has been entered into by or on behalf of the nominee with respect to any securities of the corporation, and a description of any other agreement, arrangement or understanding (including any short position or any borrowing or lending of shares), the effect or intent of which is to mitigate loss to, or to manage the risk or benefit of share price changes for, or to increase or decrease the voting power of the nominee, (E) a description of all arrangements or understandings between the stockholder and each nominee and any other person or persons (naming such person or persons) pursuant to which the nominations are to be made by the stockholder, (F) a written statement executed by the nominee acknowledging that as a director of the corporation, the nominee will owe a fiduciary duty under Delaware law with respect to the corporation and its stockholders, and (G) any other information relating to the nominee that would be required to be disclosed about such nominee if proxies were being solicited for the election or re-election of the nominee as a director, or that is otherwise required, in each case pursuant to Regulation 14A under the 1934 Act (including without limitation the nominee's written consent to being named in the proxy statement, if any, as a nominee and to serving as a director if elected or re-elected, as the case may be); and

(2) as to such stockholder giving notice, (A) the information required to be provided pursuant to clauses (2) through (5) of Section 2.4(i)(b) above, and the supplement referenced in the second sentence of Section 2.4(i)(b) above (except that the references to "business" in such clauses shall instead refer to nominations of directors for purposes of this paragraph), and (B) a statement whether either such stockholder or Stockholder Associated Person will deliver a proxy statement and form of proxy to holders of a number of the corporation's voting shares reasonably believed by such stockholder or Stockholder Associated Person to be necessary to elect or re-elect such nominee(s) (such information provided and statements made as required by clauses (A) and (B) above, a "Nominee Solicitation Statement").

(c) At the request of the board of directors, any person nominated by a stockholder for election or re-election as a director must furnish to the secretary of the corporation (1) that information required to be set forth in the stockholder's notice of nomination of such person as a director as of a date subsequent to the date on which the notice of such person's nomination was given and (2) such other information as may reasonably be required by the corporation to determine the eligibility of such proposed nominee to serve as an independent director or audit committee financial expert of the corporation under applicable law, securities

exchange rule or regulation, or any publicly-disclosed corporate governance guideline or committee charter of the corporation and (3) that could be material to a reasonable stockholder's understanding of the independence, or lack thereof, of such nominee; in the absence of the furnishing of such information if requested, such stockholder's nomination shall not be considered in proper form pursuant to this Section 2.4(ii).

(d) Without exception, no person shall be eligible for election or re-election as a director of the corporation at an annual meeting of stockholders unless nominated in accordance with the provisions set forth in this Section 2.4(ii). In addition, a nominee shall not be eligible for election or re-election if a stockholder or Stockholder Associated Person, as applicable, takes action contrary to the representations made in the Nominee Solicitation Statement applicable to such nominee or if the Nominee Solicitation Statement applicable to such nominee contains an untrue statement of a material fact or omits to state a material fact necessary to make the statements therein not misleading. The chairperson of the annual meeting shall, if the facts warrant, determine and declare at the annual meeting that a nomination was not made in accordance with the provisions prescribed by these bylaws, and if the chairperson should so determine, he or she shall so declare at the annual meeting, and the defective nomination shall be disregarded.

(iii) Advance Notice of Director Nominations for Special Meetings.

(a) For a special meeting of stockholders at which directors are to be elected or re-elected, nominations of persons for election or re-election to the board of directors shall be made only (1) by or at the direction of the board of directors or (2) by any stockholder of the corporation who (A) is a stockholder of record at the time of the giving of the notice required by this Section 2.4(iii) and on the record date for the determination of stockholders entitled to vote at the special meeting and (B) delivers a timely written notice of the nomination to the secretary of the corporation that includes the information set forth in Sections 2.4(ii)(b) and (ii)(c) above. To be timely, such notice must be received by the secretary at the principal executive offices of the corporation not later than the close of business on the later of the 90th day prior to such special meeting or the tenth day following the day on which Public Announcement is first made of the date of the special meeting and of the nominees proposed by the board of directors to be elected or re-elected at such meeting. A person shall not be eligible for election or re-election as a director at a special meeting unless the person is nominated (i) by or at the direction of the board of directors or (ii) by a stockholder in accordance with the notice procedures set forth in this Section 2.4(iii). In addition, a nominee shall not be eligible for election or re-election if a stockholder or Stockholder Associated Person, as applicable, takes action contrary to the representations made in the Nominee Solicitation Statement applicable to such nominee or if the Nominee Solicitation Statement applicable to such nominee contains an untrue statement of a material fact or omits to state a material fact necessary to make the statements therein not misleading.

(b) The chairperson of the special meeting shall, if the facts warrant, determine and declare at the meeting that a nomination or business was not made in accordance with the procedures prescribed by these bylaws, and if the chairperson should so determine, he or she shall so declare at the meeting, and the defective nomination or business shall be disregarded.

(iv) Other Requirements and Rights. In addition to the foregoing provisions of this Section 2.4, a stockholder must also comply with all applicable requirements of state law and of the 1934 Act and the rules and regulations thereunder with respect to the matters set forth in this Section 2.4. Nothing in this Section 2.4 shall be deemed to affect any rights of:

(a) a stockholder to request inclusion of proposals in the corporation's proxy statement pursuant to Rule 14a-8 (or any successor provision) under the 1934 Act; or

(b) the corporation to omit a proposal from the corporation's proxy statement pursuant to Rule 14a-8 (or any successor provision) under the 1934 Act.

2.5 NOTICE OF STOCKHOLDERS' MEETINGS

Whenever stockholders are required or permitted to take any action at a meeting, a written notice of the meeting shall be given which shall state the place, if any, date and hour of the meeting, the means of remote communications, if any, by which stockholders and proxy holders may be deemed to be present in person and vote at such meeting, the record date for determining the stockholders entitled to vote at the meeting, if such date is different from the record date for determining stockholders entitled to notice of the meeting, and, in the case of a special meeting, the purpose or purposes for which the meeting is called. Except as otherwise provided in the DGCL, the certificate of incorporation or these bylaws, the written notice of any meeting of stockholders shall be given not less than 10 nor more than 60 days before the date of the meeting to each stockholder entitled to vote at such meeting as of the record date for determining the stockholders entitled to notice of the meeting.

2.6 QUORUM

The holders of a majority of the stock issued and outstanding and entitled to vote, present in person or represented by proxy, shall constitute a quorum for the transaction of business at all meetings of the stockholders. Where a separate vote by a class or series or classes or series is required, a majority of the outstanding shares of such class or series or classes or series, present in person or represented by proxy, shall constitute a quorum entitled to take action with respect to that vote on that matter, except as otherwise provided by law, the certificate of incorporation or these bylaws.

If a quorum is not present or represented at any meeting of the stockholders, then either (i) the chairperson of the meeting, or (ii) the stockholders entitled to vote at the meeting, present in person or represented by proxy, shall have power to adjourn the meeting from time to time, without notice other than announcement at the meeting, until a quorum is present or represented. At such adjourned meeting at which a quorum is present or represented, any business may be transacted that might have been transacted at the meeting as originally noticed.

2.7 ADJOURNED MEETING; NOTICE

When a meeting is adjourned to another time or place, unless these bylaws otherwise require, notice need not be given of the adjourned meeting if the time, place, if any, thereof, and the means of remote communications, if any, by which stockholders and proxy holders may be deemed to be present in person and vote at such adjourned meeting are announced at the meeting at which the adjournment is taken. At the adjourned meeting, the corporation may transact any business which might have been transacted at the original meeting. If the adjournment is for more than 30(days, a notice of the adjourned meeting shall be given to each stockholder of record entitled to vote at the meeting. If after the adjournment a new record date for stockholders entitled to vote is fixed for the adjourned meeting, the board of directors shall fix a new record date for notice of such adjourned meeting in accordance with Section 213(a) of the DGCL and Section 2.11 of these bylaws, and shall give notice of the adjourned meeting to each stockholder of record entitled to vote at such adjourned meeting as of the record date fixed for notice of such adjourned meeting.

2.8 CONDUCT OF BUSINESS

The chairperson of any meeting of stockholders shall determine the order of business and the procedure at the meeting, including such regulation of the manner of voting and the conduct of business. The chairperson of any meeting of stockholders shall be designated by the board of directors; in the absence of such designation, the chairperson of the board, if any, the chief executive officer (in the absence of the chairperson) or the president (in the absence of the chairperson of the board and the chief executive officer), or in their absence any other executive officer of the corporation, shall serve as chairperson of the stockholder meeting.

2.9 VOTING

The stockholders entitled to vote at any meeting of stockholders shall be determined in accordance with the provisions of Section 2.11 of these bylaws, subject to Section 217 (relating to voting rights of fiduciaries, pledgors and joint owners of stock) and Section 218 (relating to voting trusts and other voting agreements) of the DGCL.

Except as may be otherwise provided in the certificate of incorporation or these bylaws, each stockholder shall be entitled to one vote for each share of capital stock held by such stockholder.

Except as otherwise required by law, the certificate of incorporation or these bylaws, in all matters other than the election of directors, the affirmative vote of a majority of the voting power of the shares present in person or represented by proxy at the meeting and entitled to vote on the subject matter shall be the act of the stockholders. Except as otherwise required by law, the certificate of incorporation or these bylaws, directors shall be elected by a plurality of the voting power of the shares present in person or represented by proxy at the meeting and entitled to vote on the election of directors. Where a separate vote by a class or series or classes or series is required, in all matters other than the election of directors, the affirmative vote of the majority of shares of such class or series or classes or series present in person or represented by proxy at the meeting shall be the act of such class or series or classes or series, except as otherwise provided by law, the certificate of incorporation or these bylaws.

2.10 STOCKHOLDER ACTION BY WRITTEN CONSENT WITHOUT A MEETING

Subject to the rights of the holders of the shares of any series of Preferred Stock or any other class of stock or series thereof that have been expressly granted the right to take action by written consent, any action required or permitted to be taken by the stockholders of the corporation must be effected at a duly called annual or special meeting of stockholders of the corporation and may not be effected by any consent in writing by such stockholders.

2.11 RECORD DATES

In order that the corporation may determine the stockholders entitled to notice of any meeting of stockholders or any adjournment thereof, the board of directors may fix a record date, which record date shall not precede the date upon which the resolution fixing the record date is adopted by the board of directors and which record date shall not be more than 60 nor less than 10 days before the date of such meeting. If the board of directors so fixes a date, such date shall also be the record date for determining the stockholders entitled to vote at such meeting unless the board of directors determines, at the time it fixes such record date, that a later date on or before the date of the meeting shall be the date for making such determination.

If no record date is fixed by the board of directors, the record date for determining stockholders entitled to notice of and to vote at a meeting of stockholders shall be at the close of business on the day next preceding the day on which notice is given, or, if notice is waived, at the close of business on the day next preceding the day on which the meeting is held.

A determination of stockholders of record entitled to notice of or to vote at a meeting of stockholders shall apply to any adjournment of the meeting; *provided, however,* that the board of directors may fix a new record date for determination of stockholders entitled to vote at the adjourned meeting, and in such case shall also fix as the record date for stockholders entitled to notice of such adjourned meeting the same or an earlier date as that fixed for determination of stockholders entitled to vote in accordance with the provisions of Section 213 of the DGCL and this Section 2.11 at the adjourned meeting.

In order that the corporation may determine the stockholders entitled to receive payment of any dividend or other distribution or allotment of any rights or the stockholders entitled to exercise any rights in respect of any change, conversion or exchange of stock, or for the purpose of any other lawful action, the board of directors may fix a record date, which record date shall not precede the date upon which the resolution fixing the record date is adopted, and which record date shall be not more than 60 days prior to such action. If no record date is fixed, the record date for determining stockholders for any such purpose shall be at the close of business on the day on which the board of directors adopts the resolution relating thereto.

2.12 PROXIES

Each stockholder entitled to vote at a meeting of stockholders may authorize another person or persons to act for such stockholder by proxy authorized by an instrument in writing or by a transmission permitted by law filed in accordance with the procedure established for the meeting, but no such proxy shall be voted or acted upon after three years from its date, unless the proxy provides for a longer period. The revocability of a proxy that states on its face that it is irrevocable shall be governed by the provisions of Section 212 of the DGCL. A written proxy may be in the form of a telegram, cablegram, or other means of electronic transmission which sets forth or is submitted with information from which it can be determined that the telegram, cablegram, or other means of electronic transmission was authorized by the person.

2.13 LIST OF STOCKHOLDERS ENTITLED TO VOTE

The officer who has charge of the stock ledger of the corporation shall prepare and make, at least 10 days before every meeting of stockholders, a complete list of the stockholders entitled to vote at the meeting; *provided, however,* if the record date for determining the stockholders entitled to vote is less than 10 days before the meeting date, the list shall reflect the stockholders entitled to vote as of the tenth day before the meeting date. The stockholder list shall be arranged in alphabetical order and show the address of each stockholder and the number of shares registered in the name of each stockholder. The corporation shall not be required to include electronic

mail addresses or other electronic contact information on such list. Such list shall be open to the examination of any stockholder for any purpose germane to the meeting for a period of at least 10 days prior to the meeting (i) on a reasonably accessible electronic network, provided that the information required to gain access to such list is provided with the notice of the meeting, or (ii) during ordinary business hours, at the corporation's principal place of business. In the event that the corporation determines to make the list available on an electronic network, the corporation may take reasonable steps to ensure that such information is available only to stockholders of the corporation. If the meeting is to be held at a place, then the list shall be produced and kept at the time and place of the meeting during the whole time thereof, and may be examined by any stockholder who is present. If the meeting is to be held solely by means of remote communication, then the list shall also be open to the examination of any stockholder during the whole time of the meeting on a reasonably accessible electronic network, and the information required to access such list shall be provided with the notice of the meeting. Such list shall presumptively determine the identity of the stockholders entitled to vote at the meeting and the number of shares held by each of them.

2.14 INSPECTORS OF ELECTION

Before any meeting of stockholders, the board of directors shall appoint an inspector or inspectors of election to act at the meeting or its adjournment. The number of inspectors shall be either one (1) or three (3). If any person appointed as inspector fails to appear or fails or refuses to act, then the chairperson of the meeting may, and upon the request of any stockholder or a stockholder's proxy shall, appoint a person to fill that vacancy.

Each inspector, before entering upon the discharge of his or her duties, shall take and sign an oath to execute faithfully the duties of inspector with strict impartiality and according to the best of his or her ability. The inspector or inspectors so appointed and designated shall (i) ascertain the number of shares of capital stock of the corporation outstanding and the voting power of each share, (ii) determine the shares of capital stock of the corporation represented at the meeting and the validity of proxies and ballots, (iii) count all votes and ballots, (iv) determine and retain for a reasonable period a record of the disposition of any challenges made to any determination by the inspectors, and (v) certify their determination of the number of shares of capital stock of the corporation represented at the meeting and such inspector or inspectors' count of all votes and ballots.

In determining the validity and counting of proxies and ballots cast at any meeting of stockholders of the corporation, the inspector or inspectors may consider such information as is permitted by applicable law. If there are three (3) inspectors of election, the decision, act or certificate of a majority is effective in all respects as the decision, act or certificate of all.

ARTICLE III — DIRECTORS

3.1 POWERS

The business and affairs of the corporation shall be managed by or under the direction of the board of directors, except as may be otherwise provided in the DGCL or the certificate of incorporation.

3.2 NUMBER OF DIRECTORS

The board of directors shall consist of one or more members, each of whom shall be a natural person. Unless the certificate of incorporation fixes the number of directors, the number of directors shall be determined from time to time solely by resolution of the board of directors. No reduction of the authorized number of directors shall have the effect of removing any director before that director's term of office expires.

3.3 ELECTION, QUALIFICATION AND TERM OF OFFICE OF DIRECTORS

Except as provided in Section 3.4 of these bylaws, each director, including a director elected to fill a vacancy, shall hold office until the expiration of the term for which elected and until such director's successor is elected and qualified or until such director's earlier death, resignation or removal. Directors need not be stockholders unless so required by the certificate of incorporation or these bylaws. The certificate of incorporation or these bylaws may prescribe other qualifications for directors.

3.4 RESIGNATION AND VACANCIES

Any director may resign at any time upon notice given in writing or by electronic transmission to the corporation; *provided, however*, that if such notice is given by electronic transmission, such electronic transmission must either set forth or be submitted with information from which it can be determined that the electronic transmission was authorized by the director. A resignation is effective when the resignation is delivered unless the resignation specifies a later effective date or an effective date determined upon the happening of an event or events. Acceptance of such resignation shall not be necessary to make it effective. A resignation which is conditioned upon the director failing to receive a specified vote for reelection as a director may provide that it is irrevocable. Unless otherwise provided in the certificate of incorporation or these bylaws, when one or more directors resign from the board of directors, effective at a future date, a majority of the directors then in office, including those who have so resigned, shall have power to fill such vacancy or vacancies, the vote thereon to take effect when such resignation or resignations shall become effective.

Unless otherwise provided in the certificate of incorporation or these bylaws, vacancies and newly created directorships resulting from any increase in the authorized number of directors elected by all of the stockholders having the right to vote as a single class shall be filled only by a majority of the directors then in office, although less than a quorum, or by a sole remaining director. If the directors are divided into classes, a person so elected by the directors then in office to fill a vacancy or newly created directorship shall hold office until the next election of the class for which such director shall have been chosen and until his or her successor shall have been duly elected and qualified.

If, at the time of filling any vacancy or any newly created directorship, the directors then in office constitute less than a majority of the whole board of directors (as constituted immediately prior to any such increase), the Court of Chancery may, upon application of any stockholder or stockholders holding at least 10% of the voting stock at the time outstanding having the right to vote for such directors, summarily order an election to be held to fill any such vacancies or newly created directorships, or to replace the directors chosen by the directors then in office as aforesaid, which election shall be governed by the provisions of Section 211 of the DGCL as far as applicable.

3.5 PLACE OF MEETINGS; MEETINGS BY TELEPHONE

The board of directors may hold meetings, both regular and special, either within or outside the State of Delaware.

Unless otherwise restricted by the certificate of incorporation or these bylaws, members of the board of directors, or any committee designated by the board of directors, may participate in a meeting of the board of directors, or any committee, by means of conference telephone or other communications equipment by means of which all persons participating in the meeting can hear each other, and such participation in a meeting shall constitute presence in person at the meeting.

3.6 REGULAR MEETINGS

Regular meetings of the board of directors may be held without notice at such time and at such place as shall from time to time be determined by the board of directors.

3.7 SPECIAL MEETINGS; NOTICE

Special meetings of the board of directors for any purpose or purposes may be called at any time by the chairperson of the board of directors, the chief executive officer, the president, the secretary or a majority of the authorized number of directors, at such times and places as he or she or they shall designate.

Notice of the time and place of special meetings shall be:

(i) delivered personally by hand, by courier or by telephone;

(ii) sent by United States first-class mail, postage prepaid;

(iii) sent by facsimile; or

(iv) sent by electronic mail,

directed to each director at that director’s address, telephone number, facsimile number or electronic mail address, as the case may be, as shown on the corporation’s records.

If the notice is (i) delivered personally by hand, by courier or by telephone, (ii) sent by facsimile or (iii) sent by electronic mail, it shall be delivered or sent at least 24 hours before the time of the holding of the meeting. If the notice is sent by United States mail, it shall be deposited in the United States mail at least four days before the time of the holding of the meeting. Any oral notice may be communicated to the director. The notice need not specify the place of the meeting (if the meeting is to be held at the corporation’s principal executive office) nor the purpose of the meeting.

3.8 QUORUM; VOTING

At all meetings of the board of directors, a majority of the total authorized number of directors shall constitute a quorum for the transaction of business. If a quorum is not present at any meeting of the board of directors, then the directors present thereat may adjourn the meeting from time to time, without notice other than announcement at the meeting, until a quorum is present. A meeting at which a quorum is initially present may continue to transact business notwithstanding the withdrawal of directors, if any action taken is approved by at least a majority of the required quorum for that meeting.

The vote of a majority of the directors present at any meeting at which a quorum is present shall be the act of the board of directors, except as may be otherwise specifically provided by statute, the certificate of incorporation or these bylaws.

If the certificate of incorporation provides that one or more directors shall have more or less than one vote per director on any matter, every reference in these bylaws to a majority or other proportion of the directors shall refer to a majority or other proportion of the votes of the directors.

3.9 BOARD ACTION BY WRITTEN CONSENT WITHOUT A MEETING

Unless otherwise restricted by the certificate of incorporation or these bylaws, any action required or permitted to be taken at any meeting of the board of directors, or of any committee thereof, may be taken without a meeting if all members of the board of directors or committee, as the case may be, consent thereto in writing or by electronic transmission and the writing or writings or electronic transmission or transmissions are filed with the minutes of proceedings of the board of directors or committee. Such filing shall be in paper form if the minutes are maintained in paper form and shall be in electronic form if the minutes are maintained in electronic form.

3.10 FEES AND COMPENSATION OF DIRECTORS

Unless otherwise restricted by the certificate of incorporation or these bylaws, the board of directors shall have the authority to fix the compensation of directors.

3.11 REMOVAL OF DIRECTORS

A director may be removed from office by the stockholders of the corporation only for cause.

No reduction of the authorized number of directors shall have the effect of removing any director prior to the expiration of such director’s term of office.

ARTICLE IV — COMMITTEES

4.1 COMMITTEES OF DIRECTORS

The board of directors may designate one or more committees, each committee to consist of one or more of the directors of the corporation. The board of directors may designate one or more directors as alternate members of any committee, who may replace any absent or disqualified member at any meeting of the committee. In the absence or disqualification of a member of a committee, the member or members thereof present at any meeting and not disqualified from voting, whether or not such member or members constitute a quorum, may unanimously appoint another member of the board of directors to act at the meeting in the place of any such absent or disqualified member. Any such committee, to the extent provided in the resolution of the board of directors or in these bylaws, shall have and may exercise all the powers and authority of the board of directors in the management of the business and affairs of the corporation, and may authorize the seal of the corporation to be affixed to all papers that may require it; but no such committee shall have the power or authority to (i) approve or adopt, or recommend to the stockholders, any action or matter (other than the election or removal of directors) expressly required by the DGCL to be submitted to stockholders for approval, or (ii) adopt, amend or repeal any bylaw of the corporation.

4.2 COMMITTEE MINUTES

Each committee shall keep regular minutes of its meetings and report the same to the board of directors when required.

4.3 MEETINGS AND ACTION OF COMMITTEES

Meetings and actions of committees shall be governed by, and held and taken in accordance with, the provisions of:

(i) Section 3.5 (place of meetings; meetings by telephone);

(ii) Section 3.6 (regular meetings);

(iii) Section 3.7 (special meetings; notice);

(iv) Section 3.8 (quorum; voting);

(v) Section 3.9 (action by written consent without a meeting); and

(vi) Section 7.5 (waiver of notice)

with such changes in the context of those bylaws as are necessary to substitute the committee and its members for the board of directors and its members. *However*:

(i) the time of regular meetings of committees may be determined by resolution of the committee;

(ii) special meetings of committees may also be called by resolution of the committee; and

(iii) notice of special meetings of committees shall also be given to all alternate members, who shall have the right to attend all meetings of the committee. The board of directors may adopt rules for the government of any committee not inconsistent with the provisions of these bylaws.

Any provision in the certificate of incorporation providing that one or more directors shall have more or less than one vote per director on any matter shall apply to voting in any committee or subcommittee, unless otherwise provided in the certificate of incorporation or these bylaws.

4.4 SUBCOMMITTEES

Unless otherwise provided in the certificate of incorporation, these bylaws or the resolutions of the board of directors designating the committee, a committee may create one or more subcommittees, each subcommittee to consist of one or more members of the committee, and delegate to a subcommittee any or all of the powers and authority of the committee.

ARTICLE V — OFFICERS

5.1 OFFICERS

The officers of the corporation shall be a president and a secretary. The corporation may also have, at the discretion of the board of directors, a chairperson of the board of directors, a vice chairperson of the board of directors, a chief executive officer, a chief financial officer or treasurer, one or more vice presidents, one or more assistant vice presidents, one or more assistant treasurers, one or more assistant secretaries, and any such other officers as may be appointed in accordance with the provisions of these bylaws. Any number of offices may be held by the same person.

5.2 APPOINTMENT OF OFFICERS

The board of directors shall appoint the officers of the corporation, except such officers as may be appointed in accordance with the provisions of Section 5.3 of these bylaws, subject to the rights, if any, of an officer under any contract of employment. A vacancy in any office because of death, resignation, removal, disqualification or any other cause shall be filled in the manner prescribed in this Section 5 for the regular election to such office.

5.3 SUBORDINATE OFFICERS

The board of directors may appoint, or empower the chief executive officer or, in the absence of a chief executive officer, the president, to appoint, such other officers and agents as the business of the corporation may require. Each of such officers and agents shall hold office for such period, have such authority, and perform such duties as are provided in these bylaws or as the board of directors may from time to time determine.

5.4 REMOVAL AND RESIGNATION OF OFFICERS

Subject to the rights, if any, of an officer under any contract of employment, any officer may be removed, either with or without cause, by an affirmative vote of the majority of the board of directors at any regular or special meeting of the board of directors or, except in the case of an officer chosen by the board of directors, by any officer upon whom such power of removal may be conferred by the board of directors.

Any officer may resign at any time by giving written or electronic notice to the corporation; *provided*, *however*, that if such notice is given by electronic transmission, such electronic transmission must either set forth or be submitted with information from which it can be determined that the electronic transmission was authorized by the officer. Any resignation shall take effect at the date of the receipt of that notice or at any later time specified in that notice. Unless otherwise specified in the notice of resignation, the acceptance of the resignation shall not be necessary to make it effective. Any resignation is without prejudice to the rights, if any, of the corporation under any contract to which the officer is a party.

5.5 VACANCIES IN OFFICES

Any vacancy occurring in any office of the corporation shall be filled by the board of directors or as provided in Section 5.3.

5.6 REPRESENTATION OF SHARES OF OTHER CORPORATIONS

The chairperson of the board of directors, the president, any vice president, the treasurer, the secretary or assistant secretary of this corporation, or any other person authorized by the board of directors or the president or a vice president, is authorized to vote, represent, and exercise on behalf of this corporation all rights incident to any and all shares of any other corporation or corporations standing in the name of this corporation. The authority granted herein may be exercised either by such person directly or by any other person authorized to do so by proxy or power of attorney duly executed by such person having the authority.

5.7 AUTHORITY AND DUTIES OF OFFICERS

All officers of the corporation shall respectively have such authority and perform such duties in the management of the business of the corporation as may be designated from time to time by the board of directors and, to the extent not so provided, as generally pertain to their respective offices, subject to the control of the board of directors.

ARTICLE VI — STOCK

6.1 STOCK CERTIFICATES; PARTLY PAID SHARES

The shares of the corporation shall be represented by certificates, provided that the board of directors may provide by resolution or resolutions that some or all of any or all classes or series of its stock shall be uncertificated shares. Any such resolution shall not apply to shares represented by a certificate until such certificate is surrendered to the corporation. Every holder of stock represented by certificates shall be entitled to have a certificate signed by, or in the name of the corporation by the chairperson of the board of directors or vice-chairperson of the board of directors, or the president or a vice-president, and by the treasurer or an assistant treasurer, or the secretary or an assistant secretary of the corporation representing the number of shares registered in certificate form. Any or all of the signatures on the certificate may be a facsimile. In case any officer, transfer agent or registrar who has signed or whose facsimile signature has been placed upon a certificate has ceased to be such officer, transfer agent or registrar before such certificate is issued, it may be issued by the corporation with the same effect as if such person were such officer, transfer agent or registrar at the date of issue. The corporation shall not have power to issue a certificate in bearer form.

The corporation may issue the whole or any part of its shares as partly paid and subject to call for the remainder of the consideration to be paid therefor. Upon the face or back of each stock certificate issued to represent any such partly-paid shares, or upon the books and records of the corporation in the case of uncertificated partly-paid shares, the total amount of the consideration to be paid therefor and the amount paid thereon shall be stated. Upon the declaration of any dividend on fully-paid shares, the corporation shall declare a dividend upon partly-paid shares of the same class, but only upon the basis of the percentage of the consideration actually paid thereon.

6.2 SPECIAL DESIGNATION ON CERTIFICATES

If the corporation is authorized to issue more than one class of stock or more than one series of any class, then the powers, the designations, the preferences, and the relative, participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights shall be set forth in full or summarized on the face or back of the certificate that the corporation shall issue to represent such class or series of stock; *provided*, *however*, that, except as otherwise provided in Section 202 of the DGCL, in lieu of the foregoing requirements there may be set forth on the face or back of the certificate that the corporation shall issue to represent such class or series of stock, a statement that the corporation will furnish without charge to each stockholder who so requests the powers, designations, preferences and relative, participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights. Within a reasonable time after the issuance or transfer of uncertificated stock, the corporation shall send to the registered owner thereof a written notice containing the information required to be set forth or stated on certificates pursuant to this section 6.2 or Sections 156, 202(a) or 218(a) of the DGCL or with respect to this section 6.2 a statement that the corporation will furnish without charge to each stockholder who so requests the powers, designations, preferences and relative, participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights. Except as otherwise expressly provided by law, the rights and obligations of the holders of uncertificated stock and the rights and obligations of the holders of certificates representing stock of the same class and series shall be identical.

6.3 LOST, STOLEN OR DESTROYED CERTIFICATES

Except as provided in this Section 6.3, no new certificates for shares shall be issued to replace a previously issued certificate unless the latter is surrendered to the corporation and cancelled at the same time. The corporation may issue a new certificate of stock or uncertificated shares in the place of any certificate theretofore issued by it, alleged to have been lost, stolen or destroyed, and the corporation may require the owner of the lost, stolen or destroyed certificate, or such owner’s legal representative, to give the corporation a bond sufficient to indemnify it against any claim that may be made against it on account of the alleged loss, theft or destruction of any such certificate or the issuance of such new certificate or uncertificated shares.

6.4 DIVIDENDS

The board of directors, subject to any restrictions contained in the certificate of incorporation or applicable law, may declare and pay dividends upon the shares of the corporation's capital stock. Dividends may be paid in cash, in property, or in shares of the corporation's capital stock, subject to the provisions of the certificate of incorporation.

The board of directors may set apart out of any of the funds of the corporation available for dividends a reserve or reserves for any proper purpose and may abolish any such reserve. Such purposes shall include but not be limited to equalizing dividends, repairing or maintaining any property of the corporation, and meeting contingencies.

6.5 TRANSFER OF STOCK

Transfers of record of shares of stock of the corporation shall be made only upon its books by the holders thereof, in person or by an attorney duly authorized, and, if such stock is certificated, upon the surrender of a certificate or certificates for a like number of shares, properly endorsed or accompanied by proper evidence of succession, assignation or authority to transfer; *provided, however,* that such succession, assignment or authority to transfer is not prohibited by the certificate of incorporation, these bylaws, applicable law or contract.

6.6 STOCK TRANSFER AGREEMENTS

The corporation shall have power to enter into and perform any agreement with any number of stockholders of any one or more classes of stock of the corporation to restrict the transfer of shares of stock of the corporation of any one or more classes owned by such stockholders in any manner not prohibited by the DGCL.

6.7 REGISTERED STOCKHOLDERS

The corporation:

(i) shall be entitled to recognize the exclusive right of a person registered on its books as the owner of shares to receive dividends and to vote as such owner;

(ii) shall be entitled to hold liable for calls and assessments the person registered on its books as the owner of shares; and

(iii) shall not be bound to recognize any equitable or other claim to or interest in such share or shares on the part of another person, whether or not it shall have express or other notice thereof, except as otherwise provided by the laws of Delaware.

ARTICLE VII — MANNER OF GIVING NOTICE AND WAIVER

7.1 NOTICE OF STOCKHOLDERS' MEETINGS

Notice of any meeting of stockholders, if mailed, is given when deposited in the United States mail, postage prepaid, directed to the stockholder at such stockholder's address as it appears on the corporation's records. An affidavit of the secretary or an assistant secretary of the corporation or of the transfer agent or other agent of the corporation that the notice has been given shall, in the absence of fraud, be *prima facie* evidence of the facts stated therein.

7.2 NOTICE BY ELECTRONIC TRANSMISSION

Without limiting the manner by which notice otherwise may be given effectively to stockholders pursuant to the DGCL, the certificate of incorporation or these bylaws, any notice to stockholders given by the corporation under any provision of the DGCL, the certificate of incorporation or these bylaws shall be effective if given by a form of electronic transmission consented to by the stockholder to whom the notice is given. Any such consent shall be revocable by the stockholder by written notice to the corporation. Any such consent shall be deemed revoked if:

(i) the corporation is unable to deliver by electronic transmission two consecutive notices given by the corporation in accordance with such consent; and

(ii) such inability becomes known to the secretary or an assistant secretary of the corporation or to the transfer agent, or other person responsible for the giving of notice.

However, the inadvertent failure to treat such inability as a revocation shall not invalidate any meeting or other action.

Any notice given pursuant to the preceding paragraph shall be deemed given:

(i) if by facsimile telecommunication, when directed to a number at which the stockholder has consented to receive notice;

(ii) if by electronic mail, when directed to an electronic mail address at which the stockholder has consented to receive notice;

(iii) if by a posting on an electronic network together with separate notice to the stockholder of such specific posting, upon the later of (A) such posting and (B) the giving of such separate notice; and

(iv) if by any other form of electronic transmission, when directed to the stockholder.

An affidavit of the secretary or an assistant secretary or of the transfer agent or other agent of the corporation that the notice has been given by a form of electronic transmission shall, in the absence of fraud, be *prima facie* evidence of the facts stated therein.

An "electronic transmission" means any form of communication, not directly involving the physical transmission of paper, that creates a record that may be retained, retrieved, and reviewed by a recipient thereof, and that may be directly reproduced in paper form by such a recipient through an automated process.

7.3 NOTICE TO STOCKHOLDERS SHARING AN ADDRESS

Except as otherwise prohibited under the DGCL, without limiting the manner by which notice otherwise may be given effectively to stockholders, any notice to stockholders given by the corporation under the provisions of the DGCL, the certificate of incorporation or these bylaws shall be effective if given by a single written notice to stockholders who share an address if consented to by the stockholders at that address to whom such notice is given. Any such consent shall be revocable by the stockholder by written notice to the corporation. Any stockholder who fails to object in writing to the corporation, within 60 days of having been given written notice by the corporation of its intention to send the single notice, shall be deemed to have consented to receiving such single written notice.

7.4 NOTICE TO PERSON WITH WHOM COMMUNICATION IS UNLAWFUL

Whenever notice is required to be given, under the DGCL, the certificate of incorporation or these bylaws, to any person with whom communication is unlawful, the giving of such notice to such person shall not be required and there shall be no duty to apply to any governmental authority or agency for a license or permit to give such notice to such person. Any action or meeting which shall be taken or held without notice to any such person with whom communication is unlawful shall have the same force and effect as if such notice had been duly given. In the event that the action taken by the corporation is such as to require the filing of a certificate under the DGCL, the certificate shall state, if such is the fact and if notice is required, that notice was given to all persons entitled to receive notice except such persons with whom communication is unlawful.

7.5 WAIVER OF NOTICE

Whenever notice is required to be given to stockholders, directors or other persons under any provision of the DGCL, the certificate of incorporation or these bylaws, a written waiver, signed by the person entitled to notice, or a waiver by electronic transmission by the person entitled to notice, whether before or after the time of the event for which notice is to be given, shall be deemed equivalent to notice. Attendance of a person at a meeting shall constitute a waiver of notice of such meeting, except when the person attends a meeting for the express purpose of objecting at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened. Neither the business to be transacted at, nor the purpose of, any regular or special meeting of the stockholders or the board of directors, as the case may be, need be specified in any written waiver of notice or any waiver by electronic transmission unless so required by the certificate of incorporation or these bylaws.

ARTICLE VIII — INDEMNIFICATION

8.1 INDEMNIFICATION OF DIRECTORS AND OFFICERS IN THIRD PARTY PROCEEDINGS

Subject to the other provisions of this Article VIII, the corporation shall indemnify, to the fullest extent permitted by the DGCL, as now or hereinafter in effect, any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (a "Proceeding") (other than an action by or in the right of the corporation) by reason of the fact that such person is or was a director of the corporation or an officer of the corporation, or while a director of the corporation or officer of the corporation is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by such person in connection with such Proceeding if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe such person's conduct was unlawful. The termination of any Proceeding by judgment, order, settlement, conviction, or upon a plea of *nolo contendere* or its equivalent, shall not, of itself, create a presumption that the person did not act in good faith and in a manner which such person reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had reasonable cause to believe that such person's conduct was unlawful.

8.2 INDEMNIFICATION OF DIRECTORS AND OFFICERS IN ACTIONS BY OR IN THE RIGHT OF THE CORPORATION

Subject to the other provisions of this Article VIII, the corporation shall indemnify, to the fullest extent permitted by the DGCL, as now or hereinafter in effect, any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to procure a judgment in its favor by reason of the fact that such person is or was a director or officer of the corporation, or while a director or officer of the corporation is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise against expenses (including attorneys' fees) actually and reasonably incurred by such person in connection with the defense or settlement of such action or suit if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the corporation; except that no indemnification shall be made in respect of any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or the court in which such action or suit was brought shall determine upon application that, despite the adjudication of liability but in view of all the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or such other court shall deem proper.

8.3 SUCCESSFUL DEFENSE

To the extent that a present or former director or officer of the corporation has been successful on the merits or otherwise in defense of any action, suit or proceeding described in Section 8.1 or Section 8.2, or in defense of any claim, issue or matter therein, such person shall be indemnified against expenses (including attorneys' fees) actually and reasonably incurred by such person in connection therewith.

8.4 INDEMNIFICATION OF OTHERS

Subject to the other provisions of this Article VIII, the corporation shall have power to indemnify its employees and its agents to the extent not prohibited by the DGCL or other applicable law. The board of directors shall have the power to delegate the determination of whether employees or agents shall be indemnified to such person or persons as the board of determines.

8.5 ADVANCED PAYMENT OF EXPENSES

Expenses (including attorneys' fees) incurred by an officer or director of the corporation in defending any Proceeding shall be paid by the corporation in advance of the final disposition of such Proceeding upon receipt of a written request therefor (together with documentation reasonably evidencing such expenses) and an undertaking by or on behalf of the person to repay such amounts if it shall ultimately be determined that the person is not entitled to be indemnified under this Article VIII or the DGCL. Such expenses (including attorneys' fees) incurred by former directors and officers or other employees and agents may be so paid upon such terms and conditions, if any, as the corporation deems reasonably appropriate and shall be subject to the corporation's expense guidelines. The right to advancement of expenses shall not apply to any claim for which indemnity is excluded pursuant to these bylaws, but shall apply to any Proceeding referenced in Section 8.6(ii) or 8.6(iii) prior to a determination that the person is not entitled to be indemnified by the corporation.

8.6 LIMITATION ON INDEMNIFICATION

Subject to the requirements in Section 8.3 and the DGCL, the corporation shall not be obligated to indemnify any person pursuant to this Article VIII in connection with any Proceeding (or any part of any Proceeding):

(i) for which payment has actually been made to or on behalf of such person under any statute, insurance policy, indemnity provision, vote or otherwise, except with respect to any excess beyond the amount paid;

(ii) for an accounting or disgorgement of profits pursuant to Section 16(b) of the 1934 Act, or similar provisions of federal, state or local statutory law or common law, if such person is held liable therefor (including pursuant to any settlement arrangements);

(iii) for any reimbursement of the corporation by such person of any bonus or other incentive-based or equity-based compensation or of any profits realized by such person from the sale of securities of the corporation, as required in each case under the 1934 Act (including any such reimbursements that arise from an accounting restatement of the corporation pursuant to Section 304 of the Sarbanes-Oxley Act of 2002 (the "Sarbanes-Oxley Act"), or the payment to the corporation of profits arising from the purchase and sale by such person of securities in violation of Section 306 of the Sarbanes-Oxley Act), if such person is held liable therefor (including pursuant to any settlement arrangements);

(iv) initiated by such person against the corporation or its directors, officers, employees, agents or other indemnitees, unless (a) the board of directors authorized the Proceeding (or the relevant part of the Proceeding) prior to its initiation, (b) the corporation provides the indemnification, in its sole discretion, pursuant to the powers vested in the corporation under applicable law, (c) otherwise required to be made under Section 8.7 or (d) otherwise required by applicable law; or

(v) if prohibited by applicable law; *provided, however*, that if any provision or provisions of this Article VIII shall be held to be invalid, illegal or unenforceable for any reason whatsoever: (1) the validity, legality and enforceability of the remaining provisions of this Article VIII (including, without limitation, each portion of any paragraph or clause containing any such provision held to be invalid, illegal or unenforceable, that is not itself held to be invalid, illegal or unenforceable) shall not in any way be affected or impaired thereby; and (2) to the fullest extent possible, the provisions of this Article VIII (including, without limitation, each such portion of any paragraph or clause containing any such provision held to be invalid, illegal or unenforceable) shall be construed so as to give effect to the intent manifested by the provision held invalid, illegal or unenforcebable.

8.7 DETERMINATION; CLAIM

If a claim for indemnification or advancement of expenses under this Article VIII is not paid in full within 90 days after receipt by the corporation of the written request therefor, the claimant shall be entitled to an adjudication by a court of competent jurisdiction of his or her entitlement to such indemnification or advancement of expenses. The corporation shall indemnify such person against any and all expenses that are incurred by such person in connection with any action for indemnification or advancement of expenses from the corporation under this Article VIII, to the extent such person is successful in such action, and to the extent not prohibited by law. In any such suit, the corporation shall, to the fullest extent not prohibited by law, have the burden of proving that the claimant is not entitled to the requested indemnification or advancement of expenses.

8.8 NON-EXCLUSIVITY OF RIGHTS

The indemnification and advancement of expenses provided by, or granted pursuant to, this Article VIII shall not be deemed exclusive of any other rights to which those seeking indemnification or advancement of expenses may be entitled under the certificate of incorporation or any statute, bylaw, agreement, vote of stockholders or disinterested directors or otherwise, both as to action in such person’s official capacity and as to action in another capacity while holding such office. The corporation is specifically authorized to enter into individual contracts with any or all of its directors, officers, employees or agents respecting indemnification and advancement of expenses, to the fullest extent not prohibited by the DGCL or other applicable law.

8.9 INSURANCE

The corporation may purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise against any liability asserted against such person and incurred by such person in any such capacity, or arising out of such person’s status as such, whether or not the corporation would have the power to indemnify such person against such liability under the provisions of the DGCL.

8.10 SURVIVAL

The rights to indemnification and advancement of expenses conferred by this Article VIII shall continue as to a person who has ceased to be a director, officer, employee or agent and shall inure to the benefit of the heirs, executors and administrators of such a person.

8.11 EFFECT OF REPEAL OR MODIFICATION

Any amendment, alteration or repeal of this Article VIII shall not adversely affect any right or protection hereunder of any person in respect of any act or omission occurring prior to such amendment, alteration or repeal.

8.12 CERTAIN DEFINITIONS

For purposes of this Article VIII, references to the "corporation" shall include, in addition to the resulting corporation, any constituent corporation (including any constituent of a constituent) absorbed in a consolidation or merger which, if its separate existence had continued, would have had power and authority to indemnify its directors, officers, employees or agents, so that any person who is or was a director, officer, employee or agent of such constituent corporation, or is or was serving at the request of such constituent corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, shall stand in the same position under the provisions of this Article VIII with respect to the resulting or surviving corporation as such person would have with respect to such constituent corporation if its separate existence had continued. For purposes of this Article VIII, references to "other enterprises" shall include employee benefit plans; references to "fines" shall include any excise taxes assessed on a person with respect to an employee benefit plan (excluding any "parachute payments" within the meanings of Sections 280G and 4999 of the Internal Revenue Code of 1986, as amended); and references to "serving at the request of the corporation" shall include any service as a director, officer, employee or agent of the corporation which imposes duties on, or involves services by, such director, officer, employee or agent with respect to an employee benefit plan, its participants or beneficiaries; and a person who acted in good faith and in a manner such person reasonably believed to be in the interest of the participants and beneficiaries of an employee benefit plan shall be deemed to have acted in a manner "not opposed to the best interests of the corporation" as referred to in this Article VIII.

ARTICLE IX — GENERAL MATTERS

9.1 EXECUTION OF CORPORATE CONTRACTS AND INSTRUMENTS

Except as otherwise provided by law, the certificate of incorporation or these bylaws, the board of directors may authorize any officer or officers, or agent or agents, to enter into any contract or execute any document or instrument in the name of and on behalf of the corporation; such authority may be general or confined to specific instances. Unless so authorized or ratified by the board of directors or within the agency power of an officer, no officer, agent or employee shall have any power or authority to bind the corporation by any contract or engagement or to pledge its credit or to render it liable for any purpose or for any amount.

9.2 FISCAL YEAR

The fiscal year of the corporation shall be fixed by resolution of the board of directors and may be changed by the board of directors.

9.3 SEAL

The corporation may adopt a corporate seal, which shall be adopted and which may be altered by the board of directors. The corporation may use the corporate seal by causing it or a facsimile thereof to be impressed or affixed or in any other manner reproduced.

9.4 CONSTRUCTION; DEFINITIONS

Unless the context requires otherwise, the general provisions, rules of construction, and definitions in the DGCL shall govern the construction of these bylaws. Without limiting the generality of this provision, the singular number includes the plural, the plural number includes the singular, and the term "person" includes both an entity and a natural person.

ARTICLE X — AMENDMENTS

These bylaws may be adopted, amended or repealed by the stockholders entitled to vote; *provided*, *however*, that the affirmative vote of the holders of at least 66 2/3% of the total voting power of outstanding voting securities, voting together as a single class, shall be required for the stockholders of the corporation to alter, amend or repeal, or adopt any bylaw inconsistent with, the following provisions of these bylaws: Article II, Sections 3.1, 3.2, 3.4 and 3.11 of Article III, Article VIII and this Article X (including, without limitation, any such Article or Section as renumbered as a result of any amendment, alteration, change, repeal, or adoption of any other Bylaw). The board of directors shall also have the power to adopt, amend or repeal bylaws; *provided*, *however*, that a bylaw amendment adopted by stockholders which specifies the votes that shall be necessary for the election of directors shall not be further amended or repealed by the board of directors.

Exhibit 4.2

NUMBER
DN

DENALI™
THERAPEUTICS

SHARES

INCORPORATED UNDER THE
LAWS OF THE STATE
OF DELAWARE

CUSIP 24823R 10 5

SEE REVERSE FOR CERTAIN DEFINITIONS

This certifies that

is the record holder of

FULLY PAID AND NONASSESSABLE SHARES OF COMMON STOCK, $.01 PAR VALUE, OF

DENALI THERAPEUTICS INC.

transferable on the books of the corporation in person or by duly authorized attorney upon surrender of this Certificate properly endorsed. This Certificate is not valid until countersigned by the Transfer Agent and registered by the Registrar.

WITNESS the facsimile seal of the Corporation and the facsimile signatures of its duly authorized officers.

Dated:

President

DENALI THERAPEUTICS INC. CORPORATE SEAL OCTOBER 14, 2013 DELAWARE

Secretary

COUNTERSIGNED AND REGISTERED
AMERICAN STOCK TRANSFER & TRUST COMPANY, LLC
(NEW YORK, NY)
TRANSFER AGENT
AND REGISTRAR

BY

AUTHORIZED SIGNATURE

The Corporation shall furnish without charge to each stockholder who so requests a statement of the powers, designations, preferences and relative, participating, optional or other special rights of each class of stock of the Corporation or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights. Such requests shall be made to the Corporation's Secretary at the principal office of the Corporation.

KEEP THIS CERTIFICATE IN A SAFE PLACE. IF IT IS LOST, STOLEN,OR DESTROYED THE CORPORATION WILL REQUIRE A BOND INDEMNITY AS A CONDITION TO THE ISSUANCE OF A REPLACEMENT CERTIFICATE.

The following abbreviations, when used in the inscription on the face of this certificate, shall be construed as though they were written out in full according to applicable laws or regulations:

TEN COM	–	as tenants in common
TEN ENT	–	as tenants by the entireties
JT TEN	–	as joint tenants with right of survivorship and not as tenants in common
COM PROP	–	as community property

UNIF GIFT MIN ACT – ..... Custodian .....
(Cust) (Minor)
under Uniform Gifts to Minors
Act .....
(State)

UNIF TRF MIN ACT – ..... Custodian (until age .....)
(Cust)
..... under Uniform Transfers
(Minor)
to Minors Act .....
(State)

Additional abbreviations may also be used though not in the above list.

FOR VALUE RECEIVED, _____ hereby sell(s), assign(s) and transfer(s) unto

PLEASE INSERT SOCIAL SECURITY OR OTHER IDENTIFYING NUMBER OF ASSIGNEE

_____
(PLEASE PRINT OR TYPEWRITE NAME AND ADDRESS, INCLUDING ZIP CODE, OF ASSIGNEE)

_____

_____

_____ shares of the capital stock represented by within Certificate, and do hereby irrevocably constitute and appoint

_____ attorney-in-fact to transfer the said stock on the books of the within named Corporation with full power of the substitution in the premises.

Dated _____

X _____

X _____

Signature(s) Guaranteed:

NOTICE: THE SIGNATURE TO THIS ASSIGNMENT MUST CORRESPOND WITH THE NAME AS WRITTEN UPON THE FACE OF THE CERTIFICATE IN EVERY PARTICULAR, WITHOUT ALTERATION OR ENLARGEMENT OR ANY CHANGE WHATSOEVER.

By _____

THE SIGNATURE(S) SHOULD BE GUARANTEED BY AN ELIGIBLE GUARANTOR INSTITUTION (BANKS, STOCKBROKERS, SAVINGS AND LOAN ASSOCIATIONS AND CREDIT UNIONS WITH MEMBERSHIP IN AN APPROVED SIGNATURE GUARANTEE MEDALLION PROGRAM), PURSUANT TO S.E.C. RULE 17Ad-15. GUARANTEES BY A NOTARY PUBLIC ARE NOT ACCEPTABLE. SIGNATURE GUARANTEES MUST NOT BE DATED.

Exhibit 5.1

Wilson Sonsini Goodrich & Rosati
PROFESSIONAL CORPORATION

650 Page Mill Road
Palo Alto, CA 94304-1050

PHONE 650.493.9300
FAX 650.493.6811
www.wsgr.com

November 27, 2017

Denali Therapeutics Inc.
151 Oyster Point Blvd., 2nd Floor
South San Francisco, California 94080

Re: Registration Statement on Form S-1

Ladies and Gentlemen:

This opinion is furnished to you in connection with the Registration Statement on Form S-1 (Registration No. 333-221522), as amended (the "**Registration Statement**"), filed by Denali Therapeutics Inc. (the "**Company**") with the Securities and Exchange Commission in connection with the registration under the Securities Act of 1933, as amended, of up to 9,583,333 shares (including up to 1,250,000 shares issuable upon exercise of an option granted to the underwriters by the Company) of the Company's common stock, $0.01 par value per share (the "**Shares**"), to be issued and sold by the Company. We understand that the Shares are to be sold to the underwriters for resale to the public as described in the Registration Statement and pursuant to an underwriting agreement, substantially in the form filed as an exhibit to the Registration Statement, to be entered into by and among the Company and the underwriters (the "**Underwriting Agreement**").

We are acting as counsel for the Company in connection with the sale of the Shares by the Company. In such capacity, we have examined originals or copies, certified or otherwise identified to our satisfaction, of such documents, corporate records, certificates of public officials and other instruments as we have deemed necessary for the purposes of rendering this opinion. In our examination, we have assumed the genuineness of all signatures, the authenticity of all documents submitted to us as originals, the conformity with the originals of all documents submitted to us as copies, the authenticity of the originals of such documents and the legal competence of all signatories to such documents.

We express no opinion herein as to the laws of any state or jurisdiction other than the General Corporation Law of the State of Delaware (including the statutory provisions and all applicable judicial decisions interpreting those laws) and the federal laws of the United States of America.

On the basis of the foregoing, we are of the opinion that upon the effectiveness of the Company's Amended and Restated Certificate of Incorporation, a form of which has been filed as Exhibit 3.2 to the Registration Statement, the Shares to be issued and sold by the Company have been duly authorized and, when such Shares are issued and paid for in accordance with the terms of the Underwriting Agreement, will be validly issued, fully paid and nonassessable.

We consent to the use of this opinion as an exhibit to the Registration Statement, and we consent to the reference of our name under the caption “Legal Matters” in the prospectus forming part of the Registration Statement.

Very truly yours,

/s/ Wilson Sonsini Goodrich & Rosati

WILSON SONSINI GOODRICH & ROSATI
Professional Corporation

Exhibit 10.1

DENALI THERAPEUTICS INC.

INDEMNIFICATION AGREEMENT

This Indemnification Agreement (this "***Agreement***") is dated as of _____, 2017 and is between Denali Therapeutics Inc., a Delaware corporation (the "***Company***"), and _____ ("***Indemnitee***").

RECITALS

A. Indemnitee's service to the Company substantially benefits the Company.

B. Individuals are reluctant to serve as directors or officers of corporations or in certain other capacities unless they are provided with adequate protection through insurance or indemnification against the risks of claims and actions against them arising out of such service to and activities on behalf of the Company.

C. Indemnitee does not regard the protection currently provided by applicable law, the Company's governing documents and any insurance as adequate under the present circumstances, and Indemnitee may not be willing to serve as a director or officer without additional protection.

D. In order to induce Indemnitee to continue to provide services to the Company, it is reasonable, prudent and necessary for the Company to contractually obligate itself to indemnify, and to advance expenses on behalf of, Indemnitee as permitted by applicable law.

E. This Agreement shall supersede any prior indemnification agreement between the Company and the Indemnitee, which is hereby terminated.

F. This Agreement is a supplement to and in furtherance of the indemnification provided in the Company's certificate of incorporation and bylaws, and any resolutions adopted pursuant thereto, and this Agreement shall not be deemed a substitute therefor, nor shall this Agreement be deemed to limit, diminish or abrogate any rights of Indemnitee thereunder.

G. In light of the considerations referred to in the preceding recitals, it is the Company's intention and desire that the provisions of this Agreement be construed liberally, subject to their express terms, to maximize the protections to be provided to Indemnitee hereunder.

In consideration of Indemnitee's agreement to serve as a director or officer of the Company after the date hereof, the parties hereto agree as follows:

1. **Definitions**.

(a) A "***Change in Control***" shall be deemed to occur upon the earliest to occur after the date of this Agreement of any of the following events:

(i) *Acquisition of Stock by Third Party*. Any Person (as defined below) is or becomes the Beneficial Owner (as defined below), directly or indirectly, of securities of the Company representing fifteen percent (15%) or more of the combined voting power of the Company's then outstanding securities;

(ii) *Change in Board Composition*. During any period of two consecutive years (not including any period prior to the execution of this Agreement), individuals who at the beginning of such period constitute the Company's board of directors, and any new directors (other than a director designated by a person who has entered into an agreement with the Company to effect a transaction described in Sections 1(a)(i), 1(a)(iii) or 1(a)(iv)) whose election by the board of directors or nomination for election by the Company's stockholders was approved by a vote of at least two-thirds of the directors then still in office who either were directors at the beginning of the period or whose election or nomination for election was previously so approved, cease for any reason to constitute at least a majority of the members of the Company's board of directors;

(iii) *Corporate Transactions*. The effective date of a merger or consolidation of the Company with any other entity, other than a merger or consolidation which would result in the voting securities of the Company outstanding immediately prior to such merger or consolidation continuing to represent (either by remaining outstanding or by being converted into voting securities of the surviving entity or its ultimate parent, as applicable) more than 50% of the combined voting power of the voting securities of the surviving entity or its ultimate parent, as applicable, outstanding immediately after such merger or consolidation and with the power to elect at least a majority of the board of directors or other governing body of such surviving entity or its ultimate parent, as applicable;

(iv) *Liquidation*. The approval by the stockholders of the Company of a complete liquidation of the Company or an agreement for the sale or disposition by the Company of all or substantially all of the Company's assets; and

(v) *Other Events*. Any other event of a nature that would be required to be reported in response to Item 6(e) of Schedule 14A of Regulation 14A (or in response to any similar item on any similar schedule or form) promulgated under the Securities Exchange Act of 1934, as amended, whether or not the Company is then subject to such reporting requirement.

For purposes of this Section 1(a), the following terms shall have the following meanings:

(1) "***Person***" shall have the meaning as set forth in Sections 13(d) and 14(d) of the Securities Exchange Act of 1934, as amended; *provided*, *however*, that "***Person***" shall exclude (i) the Company, (ii) any trustee or other fiduciary holding securities under an employee benefit plan of the Company, and (iii) any corporation owned, directly or indirectly, by the stockholders of the Company in substantially the same proportions as their ownership of stock of the Company.

(2) "***Beneficial Owner***" shall have the meaning given to such term in Rule 13d-3 under the Securities Exchange Act of 1934, as amended; *provided*, *however*, that "***Beneficial Owner***" shall exclude any Person otherwise becoming a Beneficial Owner by reason of (i) the stockholders of the Company approving a merger of the Company with another entity or (ii) the Company's board of directors approving a sale of securities by the Company to such Person.

(b) "***Corporate Status***" describes the status of a person who is or was a director, trustee, general partner, managing member, officer, employee, agent or fiduciary of the Company or any other Enterprise.

(c) "***DGCL***" means the General Corporation Law of the State of Delaware.

(d) "***Disinterested Director***" means a director of the Company who is not and was not a party to the Proceeding in respect of which indemnification is sought by Indemnitee.

(e) "***Enterprise***" means the Company and any other corporation, partnership, limited liability company, joint venture, trust, employee benefit plan or other enterprise of which Indemnitee is or was serving at the request of the Company as a director, trustee, general partner, managing member, officer, employee, agent or fiduciary.

(f) "***Expenses***" include all reasonable attorneys' fees, retainers, court costs, transcript costs, fees and costs of experts, witness fees, travel expenses, duplicating costs, printing and binding costs, telephone charges, postage, delivery service fees, and all other disbursements or expenses of the types customarily incurred in connection with prosecuting, defending, preparing to prosecute or defend, investigating, being or preparing to be a witness in, or otherwise participating in, a Proceeding. Expenses also include (i) Expenses incurred in connection with any appeal resulting from any Proceeding, including without limitation the premium, security for, and other costs relating to any cost bond, supersedeas bond or other appeal bond or their equivalent, and (ii) for purposes of Section 13(d), Expenses incurred by Indemnitee in connection with the interpretation, enforcement or defense of Indemnitee's rights under this Agreement or under any directors' and officers' liability insurance policies maintained by the Company. Expenses, however, shall not include amounts paid in settlement by Indemnitee or the amount of judgments or fines against Indemnitee.

(g) "***Independent Counsel***" means a law firm, or a partner or member of a law firm, that is experienced in matters of corporation law and neither presently is, nor in the past five years has been, retained to represent (i) the Company or Indemnitee in any matter material to either such party (other than as Independent Counsel with respect to matters concerning Indemnitee under this Agreement, or other indemnitees under similar indemnification agreements), or (ii) any other party to the Proceeding giving rise to a claim for indemnification hereunder. Notwithstanding the foregoing, the term "***Independent Counsel***" shall not include any person who, under the applicable standards of professional conduct then prevailing, would have a conflict of interest in representing either the Company or Indemnitee in an action to determine Indemnitee's rights under this Agreement.

(h) "***Proceeding***" means any threatened, pending or completed action, suit, arbitration, mediation, alternate dispute resolution mechanism, investigation, inquiry, administrative hearing or proceeding, whether brought in the right of the Company or otherwise and whether of a civil, criminal, administrative or investigative nature, including any appeal therefrom and including without limitation any such Proceeding pending as of the date of this Agreement, in which Indemnitee was, is or will be involved as a party, a potential party, a non-party witness or otherwise by reason of (i) the fact that Indemnitee is or was a director or officer of the Company, (ii) any action taken by Indemnitee or any action or inaction on Indemnitee's part while acting as a director or officer of the Company, or (iii) the fact that he or she is or was serving at the request of the Company as a director, trustee, general partner, managing member, officer, employee, agent or fiduciary of the Company or any other Enterprise, in each case whether or not serving in such capacity at the time any liability or Expense is incurred for which indemnification or advancement of expenses can be provided under this Agreement.

(i) Reference to "***other enterprises***" shall include employee benefit plans; references to "***fines***" shall include any excise taxes assessed on a person with respect to any employee benefit plan; references to "***serving at the request of the Company***" shall include any service as a director, officer, employee or agent of the Company which imposes duties on, or involves services by, such director, officer, employee or agent with respect to an employee benefit plan, its participants or beneficiaries; and a person who acted in good faith and in a manner he or she reasonably believed to be in the best interests of the participants and beneficiaries of an employee benefit plan shall be deemed to have acted in a manner "***not opposed to the best interests of the Company***" as referred to in this Agreement.

2. **Indemnity in Third-Party Proceedings**. The Company shall indemnify Indemnitee in accordance with the provisions of this Section 2 if Indemnitee is, or is threatened to be made, a party to or a participant in any Proceeding, other than a Proceeding by or in the right of the Company to procure a judgment in its favor. Pursuant to this Section 2, Indemnitee shall be indemnified to the fullest extent permitted by applicable law against all Expenses, judgments, fines and amounts paid in settlement actually and reasonably incurred by Indemnitee or on his or her behalf in connection with such Proceeding or any claim, issue or matter therein, if Indemnitee acted in good faith and in a manner he or she reasonably believed to be in or not *opposed to the best* interests of the Company and, with respect to any criminal action or proceeding, had no reasonable cause to believe that his or her conduct was unlawful.

3. **Indemnity in Proceedings by or in the Right of the Company**. The Company shall indemnify Indemnitee in accordance with the provisions of this Section 3 if Indemnitee is, or is threatened to be made, a party to or a participant in any Proceeding by or in the right of the Company to procure a judgment in its favor. Pursuant to this Section 3, Indemnitee shall be indemnified to the fullest extent permitted by applicable law against all Expenses actually and reasonably incurred by Indemnitee or on Indemnitee's behalf in connection with such Proceeding or any claim, issue or matter therein, if Indemnitee acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the Company. No indemnification for Expenses shall be made under this Section 3 in respect of any claim, issue or matter as to which Indemnitee shall have been adjudged by a court of competent jurisdiction to be liable to the Company, unless and only to the extent that the Delaware Court of Chancery or any court in which the Proceeding was brought shall determine upon application that, despite the adjudication of liability but in view of all the circumstances of the case, Indemnitee is fairly and reasonably entitled to indemnification for such expenses as the Delaware Court of Chancery or such other court shall deem proper.

4. **Indemnification for Expenses of a Party Who is Wholly or Partly Successful**. To the extent that Indemnitee is a party to or a participant in and is successful (on the merits or otherwise) in defense of any Proceeding or any claim, issue or matter therein, the Company shall indemnify Indemnitee against all Expenses actually and reasonably incurred by Indemnitee or on Indemnitee's behalf in connection therewith. To the extent permitted by applicable law, if Indemnitee is not wholly successful in such Proceeding but is successful, on the merits or otherwise, in defense of one or more but less than all claims, issues or matters in such Proceeding, the Company shall indemnify Indemnitee against all Expenses actually and reasonably incurred by Indemnitee or on Indemnitee's behalf in connection with (a) each successfully resolved claim, issue or matter, and (b) any claim, issue or matter related to any such successfully resolved claim, issue or matter. For purposes of this section, the termination of any claim, issue or matter in such a Proceeding by dismissal, with or without prejudice, shall be deemed to be a successful result as to such claim, issue or matter.

5. **Partial Indemnification**. If Indemnitee is entitled under any provision of this Agreement to indemnification by the Company for some or a portion of Expenses, but not, however, for the total amount thereof, the Company shall nevertheless indemnify Indemnitee for the portion thereof to which Indemnitee is entitled.

6. **Indemnification for Expenses of a Witness**. To the extent that Indemnitee is, by reason of his or her Corporate Status, a witness in any Proceeding to which Indemnitee is not a party, Indemnitee shall be indemnified to the extent permitted by applicable law against all Expenses actually and reasonably incurred by Indemnitee or on Indemnitee's behalf in connection therewith.

7. **Additional Indemnification**.

(a) Notwithstanding any limitation in Sections 2, 3 or 4, the Company shall indemnify Indemnitee to the fullest extent permitted by applicable law if Indemnitee is, or is threatened to be made, a party to or a participant in any Proceeding (including a Proceeding by or in the right of the Company to procure a judgment in its favor) against all Expenses, judgments, fines and amounts paid in settlement actually and reasonably incurred by Indemnitee or on his or her behalf in connection with the Proceeding or any claim, issue or matter therein.

(b) For purposes of Section 7(a), the meaning of the phrase "***to the fullest extent permitted by applicable law***" shall include, but not be limited to:

(i) the fullest extent permitted by the provision of the DGCL that authorizes or contemplates additional indemnification by agreement, or the corresponding provision of any amendment to or replacement of the DGCL; and

(ii) the fullest extent authorized or permitted by any amendments to or replacements of the DGCL adopted after the date of this Agreement that increase the extent to which a corporation may indemnify its officers and directors.

8. **Exclusions**. Notwithstanding any provision in this Agreement, the Company shall not be obligated under this Agreement to make any indemnity in connection with any Proceeding (or any part of any Proceeding):

(a) for which payment has actually been made to or on behalf of Indemnitee under any statute, insurance policy, indemnity provision, vote or otherwise, except with respect to any excess beyond the amount paid;

(b) for an accounting or disgorgement of profits pursuant to Section 16(b) of the Securities Exchange Act of 1934, as amended, or similar provisions of federal, state or local statutory law or common law, if Indemnitee is held liable therefor;

(c) for any reimbursement of the Company by Indemnitee of any bonus or other incentive-based or equity-based compensation or of any profits realized by Indemnitee from the sale of securities of the Company, as required in each case under the Securities Exchange Act of 1934, as amended (including any such reimbursements that arise from an accounting restatement of the Company pursuant to Section 304 of the Sarbanes-Oxley Act of 2002 (the "***Sarbanes-Oxley Act***"), or the payment to the Company of profits arising from the purchase and sale by Indemnitee of securities in violation of Section 306 of the Sarbanes-Oxley Act), if Indemnitee is held liable therefor;

(d) initiated by Indemnitee and not by way of defense, including any Proceeding (or any part of any Proceeding) initiated by Indemnitee against the Company or its directors, officers, employees, agents or other indemnitees, unless (i) the Company's board of directors authorized the Proceeding (or the relevant part of the Proceeding) prior to its initiation, (ii) the Company provides the indemnification, in its sole discretion, pursuant to the powers vested in the Company under applicable law, (iii) otherwise authorized in Section 13(d) or (iv) otherwise required by applicable law; or

(e) if prohibited by applicable law.

9. **Advances of Expenses**.

(a) The Company shall advance the Expenses incurred by Indemnitee in connection with any Proceeding prior to its final resolution, and such advancement shall be made as soon as reasonably practicable, but in any event no later than 60 days, after the receipt by the Company of a written statement or statements requesting such advances from time to time (which shall include invoices received by Indemnitee in connection with such Expenses but, in the case of invoices in connection with legal services, any references to legal work performed or to expenditure made that would cause Indemnitee to waive any privilege accorded by applicable law shall not be included with the invoice). Advances shall be unsecured and interest free and made without regard to Indemnitee's ability to repay such advances. Indemnitee hereby undertakes to repay any advance to the extent that it is ultimately determined that Indemnitee is not entitled to be indemnified by the Company. This Section 9 shall not apply to the extent advancement is prohibited by law and shall not apply to any Proceeding for which indemnity is not permitted under this Agreement, but shall apply to any Proceeding referenced in Section 8(b) or 8(c) prior to a determination that Indemnitee is not entitled to be indemnified by the Company.

10. **Procedures for Notification and Defense of Claim**.

(a) Indemnitee shall notify the Company in writing of any matter with respect to which Indemnitee intends to seek indemnification or advancement of Expenses as soon as reasonably practicable following the receipt by Indemnitee of notice thereof. The written notification to the Company shall include, in reasonable detail, a description of the nature of the Proceeding and the facts underlying the Proceeding. The failure or delay by Indemnitee to notify the Company will not relieve the Company from any liability which it may have to Indemnitee hereunder or otherwise than under this Agreement, except to the extent that such failure or delay materially prejudices the Company.

(b) If, at the time of the receipt of a notice of a Proceeding pursuant to the terms hereof, the Company has directors' and officers' liability insurance in effect, the Company shall give prompt notice of the commencement of the Proceeding to the insurers in accordance with the procedures set forth in the applicable policies. The Company shall thereafter take all commercially-reasonable action to cause such insurers to pay, on behalf of Indemnitee, all amounts payable as a result of such Proceeding in accordance with the terms of such policies.

(c) In the event the Company may be obligated to make any indemnity in connection with a Proceeding, the Company shall be entitled to assume the defense of such Proceeding with counsel approved by Indemnitee, which approval shall not be unreasonably withheld. After the retention of such counsel by the Company, the Company will not be liable to Indemnitee for any fees or expenses of counsel subsequently incurred by Indemnitee with respect to the same Proceeding. Notwithstanding the Company's assumption of the defense of any such Proceeding, the Company shall be obligated to pay the fees and expenses of Indemnitee's separate counsel to the extent (i) the employment of separate counsel by Indemnitee is authorized by the Company, (ii) counsel for the Company or Indemnitee shall have reasonably concluded that there is a conflict of interest between the Company and Indemnitee in the conduct of any such defense such that Indemnitee needs to be separately represented, (iii) the fees and expenses are non-duplicative and reasonably incurred in connection with Indemnitee's role in the Proceeding despite the Company's assumption of the defense; (iv) the Company is not financially or legally able to perform its indemnification obligations, or (v) the Company shall not have retained, or shall not continue to retain, such counsel to defend such Proceeding. The Company shall have the right to conduct such defense as it sees fit in its sole discretion. Regardless of any provision in this Agreement, Indemnitee shall have the right to employ counsel in any Proceeding at Indemnitee's personal expense. The Company shall not be entitled, without the consent of Indemnitee, to assume the defense of any claim brought by or in the right of the Company.

(d) Indemnitee shall give the Company such information and cooperation in connection with the Proceeding as may be reasonably appropriate.

(e) The Company shall not be liable to indemnify Indemnitee for any settlement of any Proceeding (or any part thereof) without the Company's prior written consent, which shall not be unreasonably withheld.

(f) The Company shall not settle any Proceeding (or any part thereof) in a manner that imposes any penalty or liability on Indemnitee without Indemnitee's prior written consent, which shall not be unreasonably withheld.

11. **Procedures upon Application for Indemnification**.

(a) To obtain indemnification, Indemnitee shall submit to the Company a written request, including therein or therewith such documentation and information as is reasonably available to Indemnitee *and as is reasonably* necessary to determine whether and to what extent Indemnitee is entitled to indemnification following the final disposition of the Proceeding. Any delay in providing the request will not relieve the Company from its obligations under this Agreement, except to the extent such delay is prejudicial.

(b) Upon written request by Indemnitee for indemnification pursuant to Section 11(a), a determination with respect to Indemnitee's entitlement thereto shall be made in the specific case (i) if a Change in Control shall have occurred, by Independent Counsel in a written opinion to the Company's board of directors, a copy of which shall be delivered to Indemnitee or (ii) if a Change in Control shall not have occurred, if required by applicable law (A) by a majority vote of the Disinterested Directors, even though less than a quorum of the Company's board of directors, (B) by a committee of Disinterested Directors designated by a majority vote of the Disinterested Directors, even though less than a quorum of the Company's board of directors, (C) if there are no such Disinterested Directors or, if such Disinterested Directors so direct, by Independent Counsel in a written opinion to the Company's board of directors, a copy of which shall be delivered to Indemnitee or (D) if so directed by the Company's board of directors, by the stockholders of the Company. If it is determined that Indemnitee is entitled to indemnification, payment to Indemnitee shall be made within ten days after such determination. Indemnitee shall cooperate with the person, persons or entity making the determination with respect to Indemnitee's entitlement to indemnification, including providing to such person, persons or entity upon reasonable advance request any documentation or information that is not privileged or otherwise protected from disclosure and that is reasonably available to Indemnitee and reasonably necessary to such determination. Any costs or expenses (including attorneys' fees and disbursements) reasonably incurred by Indemnitee in so cooperating with the person, persons or entity making such determination shall be borne by the Company, to the extent permitted by applicable law.

(c) In the event the determination of entitlement to indemnification is to be made by Independent Counsel pursuant to Section 11(b), the Independent Counsel shall be selected as provided in this Section 11(c). If a Change in Control shall not have occurred, the Independent Counsel shall be selected by the Company's board of directors, and the Company shall give written notice to Indemnitee advising him or her of the identity of the Independent Counsel so selected. If a Change in Control shall have occurred, the Independent Counsel shall be selected by Indemnitee (unless Indemnitee shall request that such selection be made by the Company's board of directors, in which event the preceding sentence shall apply), and Indemnitee shall give written notice to the Company advising it of the identity of the Independent Counsel so selected. In either event, Indemnitee or the Company, as the case may be, may, within ten days after such written notice of selection shall have been given, deliver to the Company or to Indemnitee, as the case may be, a written objection to such selection; *provided*, *however*, that such objection may be asserted only on the ground that the Independent Counsel so selected does not meet the requirements of "Independent Counsel" as

defined in Section 1 of this Agreement, and the objection shall set forth with particularity the factual basis of such assertion. Absent a proper and timely objection, the person so selected shall act as Independent Counsel. If such written objection is so made and substantiated, the Independent Counsel so selected may not serve as Independent Counsel unless and until such objection is withdrawn or a court has determined that such objection is without merit. If, within 20 days after the later of (i) submission by Indemnitee of a written request for indemnification pursuant to Section 11(a) hereof and (ii) the final disposition of the Proceeding, the parties have not agreed upon an Independent Counsel, either the Company or Indemnitee may petition a court of competent jurisdiction for resolution of any objection which shall have been made by the Company or Indemnitee to the other's selection of Independent Counsel and for the appointment as Independent Counsel of a person selected by the court or by such other person as the court shall designate, and the person with respect to whom all objections are so resolved or the person so appointed shall act as Independent Counsel under Section 11(b) hereof. Upon the due commencement of any judicial proceeding or arbitration pursuant to Section 13(a) of this Agreement, the Independent Counsel shall be discharged and relieved of any further responsibility in such capacity (subject to the applicable standards of professional conduct then prevailing). The Company shall pay the reasonable fees and expenses of any Independent Counsel.

12. **Presumptions and Effect of Certain Proceedings**.

(a) In making a determination with respect to entitlement to indemnification hereunder, the person, persons or entity making such determination shall, to the fullest extent not prohibited by law, presume that Indemnitee is entitled to indemnification under this Agreement, and the Company shall, to the fullest extent not prohibited by law, have the burden of proof to overcome that presumption.

(b) The termination of any Proceeding or of any claim, issue or matter therein, by judgment, order, settlement or conviction, or upon a plea of *nolo contendere* or its equivalent, shall not (except as otherwise expressly provided in this Agreement) of itself create a presumption that Indemnitee did not act in good faith and in a manner which he or she reasonably believed to be in or not opposed to the best interests of the Company or, with respect to any criminal Proceeding, that Indemnitee had reasonable cause to believe that his or her conduct was unlawful.

(c) Neither the knowledge, actions nor failure to act of any other director, officer, agent or employee of the Enterprise shall be imputed to Indemnitee for purposes of determining the right to indemnification under this Agreement.

13. **Remedies of Indemnitee**.

(a) Subject to Section 13(e), in the event that (i) a determination is made pursuant to Section 11 of this Agreement that Indemnitee is not entitled to indemnification under this Agreement, (ii) advancement of Expenses is not timely made pursuant to Section 9 or 13(d) of this Agreement, (iii) no determination of entitlement to indemnification shall have been made pursuant to Section 11 of this Agreement within 90 days after the later of the receipt by the Company of the request for indemnification or the final disposition of the Proceeding, (iv) payment of indemnification pursuant to this Agreement is not made (A) within ten days after a determination has been made that Indemnitee is entitled to indemnification or (B) with respect to indemnification pursuant to Sections 4, 5 and 13(d) of this Agreement, within 30 days after receipt by the Company of a written request therefor, or (v) the Company or any other person or entity takes or threatens to take any action to declare this Agreement void or unenforceable, or institutes any litigation or other action or proceeding designed to deny, or to recover from, Indemnitee the benefits provided or intended to be provided to Indemnitee hereunder, Indemnitee shall be entitled to an adjudication by a court of competent jurisdiction of his or her entitlement to such indemnification or advancement of Expenses. Alternatively, Indemnitee, at his or her option, may seek an award in arbitration with respect to his or her

entitlement to such indemnification or advancement of Expenses, to be conducted by a single arbitrator pursuant to the Commercial Arbitration Rules of the American Arbitration Association. Indemnitee shall commence such proceeding seeking an adjudication or an award in arbitration within 180 days following the date on which Indemnitee first has the right to commence such proceeding pursuant to this Section 13(a); *provided, however*, that the foregoing clause shall not apply in respect of a proceeding brought by Indemnitee to enforce his or her rights under Section 4 of this Agreement. The Company shall not oppose Indemnitee's right to seek any such adjudication or award in arbitration in accordance with this Agreement.

(b) Neither (i) the failure of the Company, its board of directors, any committee or subgroup of the board of directors, Independent Counsel or stockholders to have made a determination that indemnification of Indemnitee is proper in the circumstances because Indemnitee has met the applicable standard of conduct, nor (ii) an actual determination by the Company, its board of directors, any committee or subgroup of the board of directors, Independent Counsel or stockholders that Indemnitee has not met the applicable standard of conduct, shall create a presumption that Indemnitee has or has not met the applicable standard of conduct. In the event that a determination shall have been made pursuant to Section 11 of this Agreement that Indemnitee is not entitled to indemnification, any judicial proceeding or arbitration *commenced pursuant* to this Section 13 shall be conducted in all respects as a *de novo* trial, or arbitration, on the merits, and Indemnitee shall not be prejudiced by reason of that adverse determination. In any judicial proceeding or arbitration commenced pursuant to this Section 12, the Company shall, to the fullest extent not prohibited by law, have the burden of proving Indemnitee is not entitled to indemnification or advancement of Expenses, as the case may be.

(c) To the fullest extent not prohibited by law, the Company shall be precluded from asserting in any judicial proceeding or arbitration commenced pursuant to this Section 13 that the procedures and presumptions of this Agreement are not valid, binding and enforceable and shall stipulate in any such court or before any such arbitrator that the Company is bound by all the provisions of this Agreement. If a determination shall have been made pursuant to Section 11 of this Agreement that Indemnitee is entitled to indemnification, the Company shall be bound by such determination in any judicial proceeding or arbitration commenced pursuant to this Section 13, absent (i) a misstatement by Indemnitee of a material fact, or an omission of a material fact necessary to make Indemnitee's statements not materially misleading, in connection with the request for indemnification, or (ii) a prohibition of such indemnification under applicable law.

(d) To the extent not prohibited by law, the Company shall indemnify Indemnitee against all Expenses that are incurred by Indemnitee in connection with any action for indemnification or advancement of Expenses from the Company under this Agreement or under any directors' and officers' liability insurance policies maintained by the Company, unless the court (or arbitrator) finds that each material argument or defense advanced by Indemnitee in such action or arbitration was either frivolous or not made in good faith. Further, if requested by Indemnitee, the Company shall (as soon as reasonably practicable, but in any event no later than 60 days, after receipt by the Company of a written request therefor) advance such Expenses to Indemnitee, subject to the provisions of Section 8, subject to Indemnitee's agreement to repay the sums advanced if the court (or arbitrator) finds that each material argument or defense advanced by Indemnitee in such action or arbitration was either frivolous or not made in good faith.

(e) Notwithstanding anything in this Agreement to the contrary, no determination as to entitlement to indemnification shall be required to be made prior to the final disposition of the Proceeding.

14. **Contribution**. To the fullest extent permissible under applicable law, if the indemnification provided for in this Agreement is unavailable to Indemnitee, the Company, in lieu of indemnifying Indemnitee, shall contribute to the amounts incurred by Indemnitee, whether for Expenses, judgments, fines

or amounts paid or to be paid in settlement, in connection with any claim relating to an indemnifiable event under this Agreement, in such proportion as is deemed fair and reasonable in light of all of the circumstances of such Proceeding in order to reflect (i) the relative benefits received by the Company and Indemnitee as a result of the events and transactions giving rise to such Proceeding; and (ii) the relative fault of Indemnitee and the Company (and its other directors, officers, employees and agents) in connection with such events and transactions.

15. **Non-exclusivity**. The rights of indemnification and to receive advancement of Expenses as provided by this Agreement shall not be deemed exclusive of any other rights to which Indemnitee may at any time be entitled under applicable law, the Company's certificate of incorporation or bylaws, any agreement, a vote of stockholders or a resolution of directors, or otherwise. To the extent that a change in Delaware law, whether by statute or judicial decision, permits greater indemnification or advancement of Expenses than would be afforded currently under the Company's certificate of incorporation and bylaws and this Agreement, it is the intent of the parties hereto that Indemnitee shall enjoy by this Agreement the greater benefits so afforded by such change, subject to the restrictions expressly set forth herein or therein. Except as expressly set forth herein, no right or remedy herein conferred is intended to be exclusive of any other right or remedy, and every other right and remedy shall be cumulative and in addition to every other right and remedy given hereunder or now or hereafter existing at law or in equity or otherwise. Except as expressly set forth herein, the *assertion* or employment of any right or remedy hereunder, or otherwise, shall not prevent the concurrent assertion or employment of any other right or remedy.

16. **Primary Responsibility**. The Company acknowledges that to the extent Indemnitee is serving as a director on the Company's board of directors at the request or direction of a venture capital fund or other entity and/or certain of its affiliates (collectively, the "***Secondary Indemnitors***"), Indemnitee may have certain rights to indemnification and advancement of expenses provided by such Secondary Indemnitors. The Company agrees that, as between the Company and the Secondary Indemnitors, the Company is primarily responsible for amounts required to be indemnified or advanced under the Company's certificate of incorporation or bylaws or this Agreement and any obligation of the Secondary Indemnitors to provide indemnification or advancement for the same amounts is secondary to those Company obligations. To the extent not in contravention of any insurance policy or policies providing liability or other insurance for the Company or any director, trustee, general partner, managing member, officer, employee, agent or fiduciary of the Company or any other Enterprise, the Company waives any right of contribution or subrogation against the Secondary Indemnitors with respect to the liabilities for which the Company is primarily responsible under this Section 16. In the event of any payment by the Secondary Indemnitors of amounts otherwise required to be indemnified or advanced by the Company under the Company's certificate of incorporation or bylaws or this Agreement, the Secondary Indemnitors shall be subrogated to the extent of such payment to all of the rights of recovery of Indemnitee for indemnification or advancement of expenses under the Company's certificate of incorporation or bylaws or this Agreement or, to the extent such subrogation is unavailable and contribution is found to be the applicable remedy, shall have a right of contribution with respect to the amounts paid. The Secondary Indemnitors are express third-party beneficiaries of the terms of this Section 16.

17. **No Duplication of Payments**. The Company shall not be liable under this Agreement to make any payment of amounts otherwise indemnifiable hereunder (or for which advancement is provided hereunder) if and to the extent that Indemnitee has otherwise actually received payment for such amounts under any insurance policy, contract, agreement or otherwise.

18. **Insurance**. To the extent that the Company maintains an insurance policy or policies providing liability insurance for directors, trustees, general partners, managing members, officers, employees, agents or fiduciaries of the Company or any other Enterprise, Indemnitee shall be covered by such policy or policies to the same extent as the most favorably-insured persons under such policy or policies in a comparable position.

19. **Subrogation**. In the event of any payment under this Agreement, the Company shall be subrogated to the extent of such payment to all of the rights of recovery of Indemnitee, who shall execute all papers required and take all action necessary to secure such rights, including execution of such documents as are necessary to enable the Company to bring suit to enforce such rights.

20. **Services to the Company**. Indemnitee agrees to serve as a director or officer of the Company or, at the request of the Company, as a director, trustee, general partner, managing member, officer, employee, agent or fiduciary of another Enterprise, for so long as Indemnitee is duly elected or appointed or until Indemnitee tenders his or her resignation or is removed from such position. Indemnitee may at any time and for any reason resign from such position (subject to any other contractual obligation or any obligation imposed by operation of law), in which event the Company shall have no obligation under this Agreement to continue Indemnitee in such position. This Agreement shall not be deemed an employment contract between the Company (or any of its subsidiaries or any Enterprise) and Indemnitee. Indemnitee specifically acknowledges that any employment with the Company (or any of its subsidiaries or any Enterprise) is at will, and Indemnitee may be discharged at any time for any reason, with or without cause, with or without notice, except as may be otherwise expressly provided in any executed, written employment contract between Indemnitee and the Company (or any of its subsidiaries or any Enterprise), any existing formal severance policies adopted by the Company's board of directors or, with respect to service as a director or officer of the Company, the Company's certificate of incorporation or bylaws or the DGCL. No such document shall be subject to any oral modification thereof.

21. **Duration**. This Agreement shall continue until and terminate upon the later of (a) ten years after the date that Indemnitee shall have ceased to serve as a director or officer of the Company or as a director, trustee, general partner, managing member, officer, employee, agent or fiduciary of any other Enterprise, as applicable; or (b) one year after the final termination of any Proceeding, including any appeal, then pending in respect of which Indemnitee is granted rights of indemnification or advancement of Expenses hereunder and of any proceeding commenced by Indemnitee pursuant to Section 13 of this Agreement relating thereto.

22. **Successors and Assigns**. This Agreement shall be binding upon the Company and its successors and assigns, including any direct or indirect successor by purchase, merger, consolidation or otherwise to all or substantially all of the business or assets of the Company, and shall inure to the benefit of Indemnitee and Indemnitee's personal or legal representatives, heirs, executors, administrators, distributees, legatees and other successors. The Company shall require and cause any successor (whether direct or indirect by purchase, merger, consolidation or otherwise) to all or substantially all of the business or assets of the Company, by written agreement, expressly to assume and agree to perform this Agreement in the same manner and to the same extent that the Company would be required to perform if no such succession had taken place.

23. **Severability**. Nothing in this Agreement is intended to require or shall be construed as requiring the Company to do or fail to do any act in violation of applicable law. The Company's inability, pursuant to court order or other applicable law, to perform its obligations under this Agreement shall not constitute a breach of this Agreement. If any provision or provisions of this Agreement shall be held to be invalid, illegal or unenforceable for any reason whatsoever: (i) the validity, legality and enforceability of the remaining provisions of this Agreement (including without limitation, each portion of any section of this Agreement containing any such provision held to be invalid, illegal or unenforceable, that is not itself invalid, illegal or unenforceable) shall not in any way be affected or impaired thereby and shall remain enforceable to

the fullest extent permitted by law; (ii) such provision or provisions shall be deemed reformed to the extent necessary to conform to applicable law and to give the maximum effect to the intent of the parties hereto; and (iii) to the fullest extent possible, the provisions of this Agreement (including, without limitation, each portion of any section of this Agreement containing any such provision held to be invalid, illegal or unenforceable, that is not itself invalid, illegal or unenforceable) shall be construed so as to give effect to the intent manifested thereby.

24. **Enforcement**. The Company expressly confirms and agrees that it has entered into this Agreement and assumed the obligations imposed on it hereby in order to induce Indemnitee to serve as a director or officer of the Company, and the Company acknowledges that Indemnitee is relying upon this Agreement in serving as a director or officer of the Company.

25. **Entire Agreement**. This Agreement constitutes the entire agreement between the parties hereto with respect to the subject matter hereof and supersedes all prior agreements and understandings, oral, written and implied, between the parties hereto with respect to the subject matter hereof; *provided, however*, that this Agreement is a supplement to and in furtherance of the Company's certificate of incorporation and bylaws and applicable law.

26. **Modification and Waiver**. No supplement, modification or amendment to this Agreement shall be binding unless executed in writing by the parties hereto. No amendment, alteration or repeal of this Agreement shall adversely affect any right of Indemnitee under this Agreement in respect of any action taken or omitted by such Indemnitee in his or her Corporate Status prior to such amendment, alteration or repeal. No waiver of any of the provisions of this Agreement shall constitute or be deemed a waiver of any other provision of this Agreement nor shall any waiver constitute a continuing waiver.

27. **Notices**. All notices and other communications required or permitted hereunder shall be in writing and shall be mailed by registered or certified mail, postage prepaid, or otherwise delivered by hand, messenger or courier service addressed:

(a) if to Indemnitee, to Indemnitee's address, as shown on the signature page of this Agreement or in the Company's records, as may be updated in accordance with the provisions hereof; or

(b) if to the Company, to the attention of the Chief Executive Officer or Chief Financial Officer of the Company at 151 Oyster Point Blvd., 2nd Floor, South San Francisco, CA 94010, or at such other current address as the Company shall have furnished to Indemnitee, with a copy (which shall not constitute notice) to Kenneth Clark and Tony Jeffries at Wilson Sonsini Goodrich & Rosati, P.C., 650 Page Mill Road, Palo Alto, California 94304.

Each such notice or other communication shall for all purposes of this Agreement be treated as effective or having been given (i) if delivered by hand, messenger or courier service, when delivered (or if sent *via* a nationally-recognized overnight courier service, freight prepaid, specifying next-business-day delivery, one business day after deposit with the courier), or (ii) if sent *via* mail, at the earlier of its receipt or five days after the same has been deposited in a regularly-maintained receptacle for the deposit of the United States mail, addressed and mailed as aforesaid.

28. **Applicable Law and Consent to Jurisdiction**. This Agreement and the legal relations among the parties shall be governed by, and construed and enforced in accordance with, the laws of the State of Delaware, without regard to its conflict of laws rules. Except with respect to any arbitration commenced by Indemnitee pursuant to Section 13(a) of this Agreement, or except as mutually agreed by the parties in writing, the Company and Indemnitee hereby irrevocably and unconditionally (i) agree that any action or

proceeding arising out of or in connection with this Agreement shall be brought only in the Delaware Court of Chancery, and not in any other state or federal court in the United States of America or any court in any other country, (ii) consent to submit to the exclusive jurisdiction of the Delaware Court of Chancery for purposes of any action or proceeding arising out of or in connection with this Agreement, (iii) appoint, to the extent such party is not otherwise subject to service of process in the State of Delaware, The Corporation Trust Company, Wilmington, Delaware as its agent in the State of Delaware as such party's agent for acceptance of legal process in connection with any such action or proceeding against such party with the same legal force and validity as if served upon such party personally within the State of Delaware, (iv) waive any objection to the laying of venue of any such action or proceeding in the Delaware Court of Chancery, and (v) waive, and agree not to plead or to make, any claim that any such action or proceeding brought in the Delaware Court of Chancery has been brought in an improper or inconvenient forum.

29. **Counterparts**. This Agreement may be executed in one or more counterparts, each of which shall for all purposes be deemed to be an original but all of which together shall constitute one and the same Agreement. This Agreement may also be executed and delivered by facsimile signature and in counterparts, each of which shall for all purposes be deemed to be an original but all of which together shall constitute one and the same Agreement. Only one such counterpart signed by the party against whom enforceability is sought needs to be produced to evidence the existence of this Agreement.

30. **Captions**. The headings of the paragraphs of this Agreement are inserted for convenience only and shall not be deemed to constitute part of this Agreement or to affect the construction thereof.

(*signature page follows*)

The parties are signing this Indemnification Agreement as of the date stated in the introductory sentence.

DENALI THERAPEUTICS INC.

_____

(Signature)

_____

(Print Name)

_____

(Title)

INDEMNITEE

_____

(Signature)

_____

(Print Name)

_____

(Street address)

_____

(City, State and ZIP)

DENALI THERAPEUTICS INC.

2017 EQUITY INCENTIVE PLAN

1. Purposes of the Plan. The purposes of this Plan are:

- to attract and retain the best available personnel for positions of substantial responsibility,
- to provide additional incentive to Employees, Directors and Consultants, and
- to promote the success of the Company's business.

The Plan permits the grant of Incentive Stock Options, Nonstatutory Stock Options, Restricted Stock, Restricted Stock Units, Stock Appreciation Rights, Performance Units and Performance Shares.

2. Definitions. As used herein, the following definitions will apply:

(a) "Administrator" means the Board or any of its Committees as will be administering the Plan, in accordance with Section 4 of the Plan.

(b) "Applicable Laws" means the legal and regulatory requirements relating to the administration of equity-based awards, including but not limited to the related issuance of shares of Common Stock, including but not limited to, under U.S. state corporate laws, U.S. federal and state securities laws, the Code, any stock exchange or quotation system on which the Common Stock is listed or quoted and the applicable laws of any foreign country or jurisdiction where Awards are, or will be, granted under the Plan.

(c) "Award" means, individually or collectively, a grant under the Plan of Options, Stock Appreciation Rights, Restricted Stock, Restricted Stock Units, Performance Units or Performance Shares.

(d) "Award Agreement" means the written or electronic agreement setting forth the terms and provisions applicable to each Award granted under the Plan. The Award Agreement is subject to the terms and conditions of the Plan.

(e) "Board" means the Board of Directors of the Company.

(f) "Change in Control" means the occurrence of any of the following events:

(i) A change in the ownership of the Company which occurs on the date that any one person, or more than one person acting as a group ("Person"), acquires ownership of the stock of the Company that, together with the stock held by such Person, constitutes more than fifty percent (50%) of the total voting power of the stock of the Company; provided, however, that for purposes of this subsection, the acquisition of additional stock by any one Person, who is considered

to own more than fifty percent (50%) of the total voting power of the stock of the Company will not be considered a Change in Control. Further, if the stockholders of the Company immediately before such change in ownership continue to retain immediately after the change in ownership, in substantially the same proportions as their ownership of shares of the Company's voting stock immediately prior to the change in ownership, direct or indirect beneficial ownership of fifty percent (50%) or more of the total voting power of the stock of the Company or of the ultimate parent entity of the Company, such event shall not be considered a Change in Control under this subsection (i). For this purpose, indirect beneficial ownership shall include, without limitation, an interest resulting from ownership of the voting securities of one or more corporations or other business entities which own the Company, as the case may be, either directly or through one or more subsidiary corporations or other business entities; or

(ii) A change in the effective control of the Company which occurs on the date that a majority of members of the Board is replaced during any twelve (12) month period by Directors whose appointment or election is not endorsed by a majority of the members of the Board prior to the date of the appointment or election. For purposes of this subsection (ii), if any Person is considered to be in effective control of the Company, the acquisition of additional control of the Company by the same Person will not be considered a Change in Control; or

(iii) A change in the ownership of a substantial portion of the Company's assets which occurs on the date that any Person acquires (or has acquired during the twelve (12) month period ending on the date of the most recent acquisition by such person or persons) assets from the Company that have a total gross fair market value equal to or more than fifty percent (50%) of the total gross fair market value of all of the assets of the Company immediately prior to such acquisition or acquisitions; provided, however, that for purposes of this subsection (iii), the following will not constitute a change in the ownership of a substantial portion of the Company's assets: (A) a transfer to an entity that is controlled by the Company's stockholders immediately after the transfer, or (B) a transfer of assets by the Company to: (1) a stockholder of the Company (immediately before the asset transfer) in exchange for or with respect to the Company's stock, (2) an entity, fifty percent (50%) or more of the total value or voting power of which is owned, directly or indirectly, by the Company, (3) a Person, that owns, directly or indirectly, fifty percent (50%) or more of the total value or voting power of all the outstanding stock of the Company, or (4) an entity, at least fifty percent (50%) of the total value or voting power of which is owned, directly or indirectly, by a Person described in this subsection (iii)(B)(3). For purposes of this subsection (iii), gross fair market value means the value of the assets of the Company, or the value of the assets being disposed of, determined without regard to any liabilities associated with such assets.

For purposes of this definition, persons will be considered to be acting as a group if they are owners of a corporation that enters into a merger, consolidation, purchase or acquisition of stock, or similar business transaction with the Company.

Notwithstanding the foregoing, a transaction will not be deemed a Change in Control unless the transaction qualifies as a change in control event within the meaning of Code Section 409A, as it has been and may be amended from time to time, and any proposed or final Treasury Regulations and Internal Revenue Service guidance that has been promulgated or may be promulgated thereunder from time to time.

Further and for the avoidance of doubt, a transaction will not constitute a Change in Control if: (i) its sole purpose is to change the jurisdiction of the Company's incorporation, or (ii) its sole purpose is to create a holding company that will be owned in substantially the same proportions by the persons who held the Company's securities immediately before such transaction.

(g) "Code" means the Internal Revenue Code of 1986, as amended. Reference to a specific section of the Code or regulation thereunder shall include such section or regulation, any valid regulation promulgated under such section, and any comparable provision of any future legislation or regulation amending, supplementing or superseding such section or regulation.

(h) "Committee" means a committee of Directors or of other individuals satisfying Applicable Laws appointed by the Board, or a duly authorized committee of the Board, in accordance with Section 4 hereof.

(i) "Common Stock" means the common stock of the Company.

(j) "Company" means Denali Therapeutics Inc., a Delaware corporation, or any successor thereto.

(k) "Consultant" means any natural person, including an advisor, engaged by the Company or a Parent or Subsidiary to render bona fide services to such entity, provided the services (i) are not in connection with the offer or sale of securities in a capital-raising transaction, and (ii) do not directly promote or maintain a market for the Company's securities, in each case, within the meaning of Form S-8 promulgated under the Securities Act, and provided, further, that a Consultant will include only those persons to whom the issuance of Shares may be registered under Form S-8 promulgated under the Securities Act.

(l) "Director" means a member of the Board.

(m) "Disability" means total and permanent disability as defined in Section 22(e)(3) of the Code, provided that in the case of Awards other than Incentive Stock Options, the Administrator in its discretion may determine whether a permanent and total disability exists in accordance with uniform and non-discriminatory standards adopted by the Administrator from time to time.

(n) "Employee" means any person, including Officers and Directors, employed by the Company or any Parent or Subsidiary of the Company. Neither service as a Director nor payment of a director's fee by the Company will be sufficient to constitute "employment" by the Company.

(o) "Exchange Act" means the Securities Exchange Act of 1934, as amended.

(p) "Exchange Program" means a program under which (i) outstanding Awards are surrendered or cancelled in exchange for awards of the same type (which may have higher or lower exercise prices and different terms), awards of a different type, and/or cash, (ii) Participants would have the opportunity to transfer any outstanding Awards to a financial institution or other person or entity selected by the Administrator, and/or (iii) the exercise price of an outstanding Award is increased or reduced. The Administrator will determine the terms and conditions of any Exchange Program in its sole discretion.

(q) "Fair Market Value" means, as of any date, the value of Common Stock determined as follows:

(i) If the Common Stock is listed on any established stock exchange or a national market system, including without limitation the New York Stock Exchange, the NASDAQ Global Select Market, the NASDAQ Global Market or the NASDAQ Capital Market of The NASDAQ Stock Market, its Fair Market Value will be the closing sales price for such stock (or, if no closing sales price was reported on that date, as applicable, on the last trading date such closing sales price was reported) as quoted on such exchange or system on the day of determination, as reported in *The Wall Street Journal* or such other source as the Administrator deems reliable;

(ii) If the Common Stock is regularly quoted by a recognized securities dealer but selling prices are not reported, the Fair Market Value of a Share will be the mean between the high bid and low asked prices for the Common Stock on the day of determination (or, if no bids and asks were reported on that date, as applicable, on the last trading date such bids and asks were reported), as reported in *The Wall Street Journal* or such other source as the Administrator deems reliable;

(iii) For purposes of any Awards granted on the Registration Date, the Fair Market Value will be the initial price to the public as set forth in the final prospectus included within the registration statement on Form S-1 filed with the Securities and Exchange Commission for the initial public offering of the Common Stock; or

(iv) In the absence of an established market for the Common Stock, the Fair Market Value will be determined in good faith by the Administrator.

(r) "Fiscal Year" means the fiscal year of the Company.

(s) "Incentive Stock Option" means an Option intended to qualify as an incentive stock option within the meaning of Section 422 of the Code and the regulations promulgated thereunder.

(t) "Inside Director" means a Director who is an Employee.

(u) "Nonstatutory Stock Option" means an Option that by its terms does not qualify or is not intended to qualify as an Incentive Stock Option.

(v) "Officer" means a person who is an officer of the Company within the meaning of Section 16 of the Exchange Act and the rules and regulations promulgated thereunder.

(w) "Option" means a stock option granted pursuant to the Plan.

(x) "Outside Director" means a Director who is not an Employee.

(y) "Parent" means a "parent corporation," whether now or hereafter existing, as defined in Section 424(e) of the Code.

(z) "Participant" means the holder of an outstanding Award.

(aa) "Performance Share" means an Award denominated in Shares which may be earned in whole or in part upon attainment of performance goals or other vesting criteria as the Administrator may determine pursuant to Section 10.

(bb) "Performance Unit" means an Award which may be earned in whole or in part upon attainment of performance goals or other vesting criteria as the Administrator may determine and which may be settled for cash, Shares or other securities or a combination of the foregoing pursuant to Section 10.

(cc) "Period of Restriction" means the period during which the transfer of Shares of Restricted Stock are subject to restrictions and therefore, the Shares are subject to a substantial risk of forfeiture. Such restrictions may be based on the passage of time, the achievement of target levels of performance, or the occurrence of other events as determined by the Administrator.

(dd) "Plan" means this Denali Therapeutics Inc. 2017 Equity Incentive Plan.

(ee) "Registration Date" means the effective date of the first registration statement that is filed by the Company and declared effective pursuant to Section 12(g) of the Exchange Act, with respect to any class of the Company's securities.

(ff) "Restricted Stock" means Shares issued pursuant to a Restricted Stock award under Section 7 of the Plan, or issued pursuant to the early exercise of an Option.

(gg) "Restricted Stock Unit" means a bookkeeping entry representing an amount equal to the Fair Market Value of one Share, granted pursuant to Section 8. Each Restricted Stock Unit represents an unfunded and unsecured obligation of the Company.

(hh) "Rule 16b-3" means Rule 16b-3 of the Exchange Act or any successor to Rule 16b-3, as in effect when discretion is being exercised with respect to the Plan.

(ii) "Section 16(b)" means Section 16(b) of the Exchange Act.

(jj) "Service Provider" means an Employee, Director or Consultant.

(kk) "Share" means a share of the Common Stock, as adjusted in accordance with Section 14 of the Plan.

(ll) "Stock Appreciation Right" means an Award, granted alone or in connection with an Option, that pursuant to Section 9 is designated as a Stock Appreciation Right.

(mm) "Subsidiary" means a "subsidiary corporation," whether now or hereafter existing, as defined in Section 424(f) of the Code.

3. Stock Subject to the Plan.

(a) Stock Subject to the Plan. Subject to the provisions of Section 14 of the Plan and the automatic increase set forth in Section 3(b), the maximum aggregate number of Shares that may be issued under the Plan is 6,210,000 Shares, plus (i) any Shares that, as of immediately prior to the termination of the 2015 Stock Incentive Plan (the "2015 Plan"), have been reserved but not issued pursuant to any awards granted under the 2015 Plan and are not subject to any awards thereunder, plus (ii) any Shares subject to stock options, restricted stock units or similar awards granted under the 2015 Plan that, on or after the termination of the 2015 Plan, expire or otherwise terminate without having been exercised or issued in full and Shares issued pursuant to awards granted under the 2015 Plan that, on or after the termination of the 2015 Plan, are forfeited to or repurchased by the Company, with the maximum number of Shares to be added to the Plan pursuant to clauses (i) and (ii) equal to 8,325,000 Shares. In addition, Shares may become available for issuance under the Plan pursuant to Sections 3(b) and 3(c). The Shares may be authorized, but unissued, or reacquired Common Stock.

(b) Automatic Share Reserve Increase. Subject to the provisions of Section 14 of the Plan, the number of Shares available for issuance under the Plan will be increased on the first day of each Fiscal Year beginning with the 2019 Fiscal Year, in an amount equal to the least of (i) 10,000,000 Shares, (ii) five percent (5%) of the outstanding Shares on the last day of the immediately preceding Fiscal Year, or (iii) such number of Shares determined by the Administrator.

(c) Lapsed Awards. If an Award expires or becomes unexercisable without having been exercised in full, is surrendered pursuant to an Exchange Program, or, with respect to Restricted Stock, Restricted Stock Units, Performance Units or Performance Shares, is forfeited to or repurchased by the Company due to failure to vest, the unpurchased Shares (or for Awards other than Options or Stock Appreciation Rights the forfeited or repurchased Shares), which were subject thereto will become available for future grant or sale under the Plan (unless the Plan has terminated). With respect to Stock Appreciation Rights, only Shares actually issued (i.e., the net Shares issued) pursuant to a Stock Appreciation Right will cease to be available under the Plan; all remaining Shares under Stock Appreciation Rights will remain available for future grant or sale under the Plan (unless the Plan has terminated). Shares that have actually been issued under the Plan under any Award will not be returned to the Plan and will not become available for future distribution under the Plan; provided, however, that if Shares issued pursuant to Awards of Restricted Stock, Restricted Stock Units, Performance Shares or Performance Units are repurchased by the Company or are forfeited to the Company, such Shares will become available for future grant under the Plan. Shares used to pay the exercise price of an Award or to satisfy the tax withholding obligations related to an Award will become available for future grant or sale under the Plan. To the extent an Award under the Plan is paid out in cash rather than Shares, such cash payment will not result in reducing the number of Shares available for issuance under the Plan. Notwithstanding the foregoing and, subject to adjustment as provided in Section 14, the maximum number of Shares that may be issued upon the exercise of Incentive Stock Options will equal the aggregate Share number stated in Section 3(a), plus, to the extent allowable under Section 422 of the Code and the Treasury Regulations promulgated thereunder, any Shares that become available for issuance under the Plan pursuant to Sections 3(b) and 3(c).

(d) Share Reserve. The Company, during the term of this Plan, will at all times reserve and keep available such number of Shares as will be sufficient to satisfy the requirements of the Plan.

4. Administration of the Plan.

(a) Procedure.

(i) Multiple Administrative Bodies. Different Committees with respect to different groups of Service Providers may administer the Plan.

(ii) Section 162(m). To the extent that the Administrator determines it to be desirable to qualify Awards granted hereunder as "performance-based compensation" within the meaning of Section 162(m) of the Code, the Plan will be administered by a Committee of two (2) or more "outside directors" within the meaning of Section 162(m) of the Code.

(iii) Rule 16b-3. To the extent desirable to qualify transactions hereunder as exempt under Rule 16b-3, the transactions contemplated hereunder will be structured to satisfy the requirements for exemption under Rule 16b-3.

(iv) Other Administration. Other than as provided above, the Plan will be administered by (A) the Board or (B) a Committee, which committee will be constituted to satisfy Applicable Laws.

(b) Powers of the Administrator. Subject to the provisions of the Plan, and in the case of a Committee, subject to the specific duties delegated by the Board to such Committee, the Administrator will have the authority, in its discretion:

(i) to determine the Fair Market Value;

(ii) to select the Service Providers to whom Awards may be granted hereunder;

(iii) to determine the number of Shares to be covered by each Award granted hereunder;

(iv) to approve forms of Award Agreements for use under the Plan;

(v) to determine the terms and conditions, not inconsistent with the terms of the Plan, of any Award granted hereunder. Such terms and conditions include, but are not limited to, the exercise price, the time or times when Awards may be exercised (which may be based on performance criteria), any vesting acceleration or waiver of forfeiture restrictions, and any restriction or limitation regarding any Award or the Shares relating thereto, based in each case on such factors as the Administrator will determine;

(vi) to institute and determine the terms and conditions of an Exchange Program;

(vii) to construe and interpret the terms of the Plan and Awards granted pursuant to the Plan;

(viii) to prescribe, amend and rescind rules and regulations relating to the Plan, including rules and regulations relating to sub-plans established for the purpose of satisfying applicable foreign laws or for qualifying for favorable tax treatment under applicable foreign laws;

(ix) to modify or amend each Award (subject to Section 19 of the Plan), including but not limited to the discretionary authority to extend the post-termination exercisability period of Awards; provided, however, that in no case will an Option or Stock Appreciation right be extended beyond its original maximum term;

(x) to allow Participants to satisfy tax withholding obligations in such manner as prescribed in Section 15 of the Plan;

(xi) to authorize any person to execute on behalf of the Company any instrument required to effect the grant of an Award previously granted by the Administrator;

(xii) to allow a Participant to defer the receipt of the payment of cash or the delivery of Shares that would otherwise be due to such Participant under an Award; and

(xiii) to make all other determinations deemed necessary or advisable for administering the Plan.

(c) Effect of Administrator's Decision. The Administrator's decisions, determinations and interpretations will be final and binding on all Participants and any other holders of Awards and will be given the maximum deference permitted by Applicable Laws.

5. Eligibility. Nonstatutory Stock Options, Stock Appreciation Rights, Restricted Stock, Restricted Stock Units, Performance Shares and Performance Units may be granted to Service Providers. Incentive Stock Options may be granted only to Employees.

6. Stock Options.

(a) Limitations. Each Option will be designated in the Award Agreement as either an Incentive Stock Option or a Nonstatutory Stock Option. However, notwithstanding such designation, to the extent that the aggregate Fair Market Value of the Shares with respect to which Incentive Stock Options are exercisable for the first time by the Participant during any calendar year (under all plans of the Company and any Parent or Subsidiary) exceeds one hundred thousand dollars ($100,000), such Options will be treated as Nonstatutory Stock Options. For purposes of this Section 6(a), Incentive Stock Options will be taken into account in the order in which they were granted. The Fair Market Value of the Shares will be determined as of the time the Option with respect to such Shares is granted.

(b) Term of Option. The term of each Option will be stated in the Award Agreement. In the case of an Incentive Stock Option, the term will be ten (10) years from the date of grant or such shorter term as may be provided in the Award Agreement. Moreover, in the case of an Incentive Stock Option granted to a Participant who, at the time the Incentive Stock Option is

granted, owns stock representing more than ten percent (10%) of the total combined voting power of all classes of stock of the Company or any Parent or Subsidiary, the term of the Incentive Stock Option will be five (5) years from the date of grant or such shorter term as may be provided in the Award Agreement.

(c) Option Exercise Price and Consideration.

(i) Exercise Price. The per share exercise price for the Shares to be issued pursuant to exercise of an Option will be determined by the Administrator, subject to the following:

(1) In the case of an Incentive Stock Option

(A) granted to an Employee who, at the time the Incentive Stock Option is granted, owns stock representing more than ten percent (10%) of the voting power of all classes of stock of the Company or any Parent or Subsidiary, the per Share exercise price will be no less than one hundred ten percent (110%) of the Fair Market Value per Share on the date of grant.

(B) granted to any Employee other than an Employee described in paragraph (A) immediately above, the per Share exercise price will be no less than one hundred percent (100%) of the Fair Market Value per Share on the date of grant.

(2) In the case of a Nonstatutory Stock Option, the per Share exercise price will be no less than one hundred percent (100%) of the Fair Market Value per Share on the date of grant.

(3) Notwithstanding the foregoing, Options may be granted with a per Share exercise price of less than one hundred percent (100%) of the Fair Market Value per Share on the date of grant pursuant to a transaction described in, and in a manner consistent with, Section 424(a) of the Code.

(ii) Waiting Period and Exercise Dates. At the time an Option is granted, the Administrator will fix the period within which the Option may be exercised and will determine any conditions that must be satisfied before the Option may be exercised.

(iii) Form of Consideration. The Administrator will determine the acceptable form of consideration for exercising an Option, including the method of payment. In the case of an Incentive Stock Option, the Administrator will determine the acceptable form of consideration at the time of grant. Such consideration may consist entirely of: (1) cash; (2) check; (3) promissory note, to the extent permitted by Applicable Laws, (4) other Shares, provided that such Shares have a Fair Market Value on the date of surrender equal to the aggregate exercise price of the Shares as to which such Option will be exercised and provided that accepting such Shares will not result in any adverse accounting consequences to the Company, as the Administrator determines in its sole discretion; (5) consideration received by the Company under a broker-assisted (or other) cashless exercise program (whether through a broker or otherwise) implemented by the Company in connection with the Plan; (6) by net exercise; (7) such other consideration and method of payment for the issuance of Shares to the extent permitted by Applicable Laws; or (8) any combination of the foregoing methods of payment.

(d) Exercise of Option.

(i) Procedure for Exercise; Rights as a Stockholder. Any Option granted hereunder will be exercisable according to the terms of the Plan and at such times and under such conditions as determined by the Administrator and set forth in the Award Agreement. An Option may not be exercised for a fraction of a Share.

An Option will be deemed exercised when the Company receives: (i) a notice of exercise (in such form as the Administrator may specify from time to time) from the person entitled to exercise the Option, and (ii) full payment for the Shares with respect to which the Option is exercised (together with applicable tax withholdings). Full payment may consist of any consideration and method of payment authorized by the Administrator and permitted by the Award Agreement and the Plan. Shares issued upon exercise of an Option will be issued in the name of the Participant or, if requested by the Participant, in the name of the Participant and his or her spouse. Until the Shares are issued (as evidenced by the appropriate entry on the books of the Company or of a duly authorized transfer agent of the Company), no right to vote or receive dividends or any other rights as a stockholder will exist with respect to the Shares subject to an Option, notwithstanding the exercise of the Option. The Company will issue (or cause to be issued) such Shares promptly after the Option is exercised. No adjustment will be made for a dividend or other right for which the record date is prior to the date the Shares are issued, except as provided in Section 14 of the Plan.

Exercising an Option in any manner will decrease the number of Shares thereafter available, both for purposes of the Plan and for sale under the Option, by the number of Shares as to which the Option is exercised.

(ii) Termination of Relationship as a Service Provider. If a Participant ceases to be a Service Provider, other than upon the Participant's termination as the result of the Participant's death or Disability, the Participant may exercise his or her Option within such period of time as is specified in the Award Agreement to the extent that the Option is vested on the date of termination (but in no event later than the expiration of the term of such Option as set forth in the Award Agreement). In the absence of a specified time in the Award Agreement, the Option will remain exercisable for three (3) months following the Participant's termination. Unless otherwise provided by the Administrator, if on the date of termination the Participant is not vested as to his or her entire Option, the Shares covered by the unvested portion of the Option will revert to the Plan. If after termination the Participant does not exercise his or her Option within the time specified by the Administrator, the Option will terminate, and the Shares covered by such Option will revert to the Plan.

(iii) Disability of Participant. If a Participant ceases to be a Service Provider as a result of the Participant's Disability, the Participant may exercise his or her Option within such period of time as is specified in the Award Agreement to the extent the Option is vested on the date of termination (but in no event later than the expiration of the term of such Option as set forth in the Award Agreement). In the absence of a specified time in the Award Agreement, the Option will remain exercisable for twelve (12) months following the Participant's termination. Unless otherwise provided by the Administrator, if on the date of termination the Participant is not vested as to his or her entire Option, the Shares covered by the unvested portion of the Option will revert to the Plan. If after termination the Participant does not exercise his or her Option within the time specified herein, the Option will terminate, and the Shares covered by such Option will revert to the Plan.

(iv) Death of Participant. If a Participant dies while a Service Provider, the Option may be exercised following the Participant's death within such period of time as is specified in the Award Agreement to the extent that the Option is vested on the date of death (but in no event may the option be exercised later than the expiration of the term of such Option as set forth in the Award Agreement), by the Participant's designated beneficiary, provided such beneficiary has been designated prior to Participant's death in a form acceptable to the Administrator. If no such beneficiary has been designated by the Participant, then such Option may be exercised by the personal representative of the Participant's estate or by the person(s) to whom the Option is transferred pursuant to the Participant's will or in accordance with the laws of descent and distribution. In the absence of a specified time in the Award Agreement, the Option will remain exercisable for twelve (12) months following Participant's death. Unless otherwise provided by the Administrator, if at the time of death Participant is not vested as to his or her entire Option, the Shares covered by the unvested portion of the Option will immediately revert to the Plan. If the Option is not so exercised within the time specified herein, the Option will terminate, and the Shares covered by such Option will revert to the Plan.

7. Restricted Stock.

(a) Grant of Restricted Stock. Subject to the terms and provisions of the Plan, the Administrator, at any time and from time to time, may grant Shares of Restricted Stock to Service Providers in such amounts as the Administrator, in its sole discretion, will determine.

(b) Restricted Stock Agreement. Each Award of Restricted Stock will be evidenced by an Award Agreement that will specify the Period of Restriction, the number of Shares granted, and such other terms and conditions as the Administrator, in its sole discretion, will determine. Unless the Administrator determines otherwise, the Company as escrow agent will hold Shares of Restricted Stock until the restrictions on such Shares have lapsed.

(c) Transferability. Except as provided in this Section 7 or the Award Agreement, Shares of Restricted Stock may not be sold, transferred, pledged, assigned, or otherwise alienated or hypothecated until the end of the applicable Period of Restriction.

(d) Other Restrictions. The Administrator, in its sole discretion, may impose such other restrictions on Shares of Restricted Stock as it may deem advisable or appropriate.

(e) Removal of Restrictions. Except as otherwise provided in this Section 7, Shares of Restricted Stock covered by each Restricted Stock grant made under the Plan will be released from escrow as soon as practicable after the last day of the Period of Restriction or at such other time as the Administrator may determine. The Administrator, in its discretion, may accelerate the time at which any restrictions will lapse or be removed.

(f) Voting Rights. During the Period of Restriction, Service Providers holding Shares of Restricted Stock granted hereunder may exercise full voting rights with respect to those Shares, unless the Administrator determines otherwise.

(g) Dividends and Other Distributions. During the Period of Restriction, Service Providers holding Shares of Restricted Stock will be entitled to receive all dividends and other distributions paid with respect to such Shares, unless the Administrator provides otherwise. If any such dividends or distributions are paid in Shares, the Shares will be subject to the same restrictions on transferability and forfeitability as the Shares of Restricted Stock with respect to which they were paid.

(h) Return of Restricted Stock to Company. On the date set forth in the Award Agreement, the Restricted Stock for which restrictions have not lapsed will revert to the Company and again will become available for grant under the Plan.

8. Restricted Stock Units.

(a) Grant. Restricted Stock Units may be granted at any time and from time to time as determined by the Administrator. After the Administrator determines that it will grant Restricted Stock Units under the Plan, it will advise the Participant in an Award Agreement of the terms, conditions, and restrictions related to the grant, including the number of Restricted Stock Units.

(b) Vesting Criteria and Other Terms. The Administrator will set vesting criteria in its discretion, which, depending on the extent to which the criteria are met, will determine the number of Restricted Stock Units that will be paid out to the Participant. The Administrator may set vesting criteria based upon the achievement of Company-wide, divisional, business unit, or individual goals (including, but not limited to, continued employment or service), applicable federal or state securities laws or any other basis determined by the Administrator in its discretion.

(c) Earning Restricted Stock Units. Upon meeting the applicable vesting criteria, the Participant will be entitled to receive a payout as determined by the Administrator. Notwithstanding the foregoing, at any time after the grant of Restricted Stock Units, the Administrator, in its sole discretion, may reduce or waive any vesting criteria that must be met to receive a payout.

(d) Form and Timing of Payment. Payment of earned Restricted Stock Units will be made as soon as practicable after the date(s) determined by the Administrator and set forth in the Award Agreement. The Administrator, in its sole discretion, may only settle earned Restricted Stock Units in cash, Shares, or a combination of both.

(e) Cancellation. On the date set forth in the Award Agreement, all unearned Restricted Stock Units will be forfeited to the Company.

9. Stock Appreciation Rights.

(a) Grant of Stock Appreciation Rights. Subject to the terms and conditions of the Plan, a Stock Appreciation Right may be granted to Service Providers at any time and from time to time as will be determined by the Administrator, in its sole discretion.

(b) Number of Shares. The Administrator will have complete discretion to determine the number of Stock Appreciation Rights granted to any Service Provider.

(c) Exercise Price and Other Terms. The per share exercise price for the Shares to be issued pursuant to exercise of a Stock Appreciation Right will be determined by the Administrator and will be no less than one hundred percent (100%) of the Fair Market Value per Share on the date of grant. Otherwise, the Administrator, subject to the provisions of the Plan, will have complete discretion to determine the terms and conditions of Stock Appreciation Rights granted under the Plan.

(d) Stock Appreciation Right Agreement. Each Stock Appreciation Right grant will be evidenced by an Award Agreement that will specify the exercise price, the term of the Stock Appreciation Right, the conditions of exercise, and such other terms and conditions as the Administrator, in its sole discretion, will determine.

(e) Expiration of Stock Appreciation Rights. A Stock Appreciation Right granted under the Plan will expire upon the date determined by the Administrator, in its sole discretion, and set forth in the Award Agreement. Notwithstanding the foregoing, the rules of Section 6(b) relating to the maximum term and Section 6(d) relating to exercise also will apply to Stock Appreciation Rights.

(f) Payment of Stock Appreciation Right Amount. Upon exercise of a Stock Appreciation Right, a Participant will be entitled to receive payment from the Company in an amount determined by multiplying:

(i) The difference between the Fair Market Value of a Share on the date of exercise over the exercise price; times

(ii) The number of Shares with respect to which the Stock Appreciation Right is exercised.

At the discretion of the Administrator, the payment upon Stock Appreciation Right exercise may be in cash, in Shares of equivalent value, or in some combination thereof.

10. Performance Units and Performance Shares.

(a) Grant of Performance Units/Shares. Performance Units and Performance Shares may be granted to Service Providers at any time and from time to time, as will be determined by the Administrator, in its sole discretion. The Administrator will have complete discretion in determining the number of Performance Units and Performance Shares granted to each Participant.

(b) Value of Performance Units/Shares. Each Performance Unit will have an initial value that is established by the Administrator on or before the date of grant. Each Performance Share will have an initial value equal to the Fair Market Value of a Share on the date of grant.

(c) Performance Objectives and Other Terms. The Administrator will set performance objectives or other vesting provisions (including, without limitation, continued status as a Service Provider) in its discretion which, depending on the extent to which they are met, will determine the number or value of Performance Units/Shares that will be paid out to the Service Providers. The time period during which the performance objectives or other vesting provisions

must be met will be called the "Performance Period." Each Award of Performance Units/Shares will be evidenced by an Award Agreement that will specify the Performance Period, and such other terms and conditions as the Administrator, in its sole discretion, will determine. The Administrator may set performance objectives based upon the achievement of Company-wide, divisional, business unit or individual goals (including, but not limited to, continued employment or service), applicable federal or state securities laws, or any other basis determined by the Administrator in its discretion.

(d) Earning of Performance Units/Shares. After the applicable Performance Period has ended, the holder of Performance Units/Shares will be entitled to receive a payout of the number of Performance Units/Shares earned by the Participant over the Performance Period, to be determined as a function of the extent to which the corresponding performance objectives or other vesting provisions have been achieved. After the grant of a Performance Unit/Share, the Administrator, in its sole discretion, may reduce or waive any performance objectives or other vesting provisions for such Performance Unit/Share.

(e) Form and Timing of Payment of Performance Units/Shares. Payment of earned Performance Units/Shares will be made as soon as practicable after the expiration of the applicable Performance Period. The Administrator, in its sole discretion, may pay earned Performance Units/Shares in the form of cash, in Shares (which have an aggregate Fair Market Value equal to the value of the earned Performance Units/Shares at the close of the applicable Performance Period) or in a combination thereof.

(f) Cancellation of Performance Units/Shares. On the date set forth in the Award Agreement, all unearned or unvested Performance Units/Shares will be forfeited to the Company, and again will be available for grant under the Plan.

11. Outside Director Limitations. No Outside Director may be granted, in any Fiscal Year, Awards with a grant date fair value (determined in accordance with U.S. generally accepted accounting principles) of more than $1,000,000, increased to $1,600,000 in connection with his or her initial service. Any Awards granted to an individual while he or she was an Employee, or while he or she was a Consultant but not an Outside Director, will not count for purposes of the limitations under this Section 11.

12. Leaves of Absence/Transfer Between Locations. Unless the Administrator provides otherwise, vesting of Awards granted hereunder will be suspended during any unpaid leave of absence. A Participant will not cease to be an Employee in the case of (i) any leave of absence approved by the Company or (ii) transfers between locations of the Company or between the Company, its Parent, or any Subsidiary. For purposes of Incentive Stock Options, no such leave may exceed three (3) months, unless reemployment upon expiration of such leave is guaranteed by statute or contract. If reemployment upon expiration of a leave of absence approved by the Company is not so guaranteed, then six (6) months following the first (1st) day of such leave any Incentive Stock Option held by the Participant will cease to be treated as an Incentive Stock Option and will be treated for tax purposes as a Nonstatutory Stock Option.

13. Transferability of Awards. Unless determined otherwise by the Administrator, an Award may not be sold, pledged, assigned, hypothecated, transferred, or disposed of in any manner other than by will or by the laws of descent or distribution and may be exercised, during the lifetime of the Participant, only by the Participant. If the Administrator makes an Award transferable, such Award will contain such additional terms and conditions as the Administrator deems appropriate.

14. Adjustments; Dissolution or Liquidation; Merger or Change in Control.

(a) Adjustments. In the event that any dividend or other distribution (whether in the form of cash, Shares, other securities, or other property), recapitalization, stock split, reverse stock split, reorganization, merger, consolidation, split-up, spin-off, combination, repurchase, or exchange of Shares or other securities of the Company, or other change in the corporate structure of the Company affecting the Shares occurs, the Administrator, in order to prevent diminution or enlargement of the benefits or potential benefits intended to be made available under the Plan, will adjust the number and class of shares of stock that may be delivered under the Plan and/or the number, class, and price of shares of stock covered by each outstanding Award, and the numerical Share limits in Sections 3 and 11 of the Plan.

(b) Dissolution or Liquidation. In the event of the proposed dissolution or liquidation of the Company, the Administrator will notify each Participant as soon as practicable prior to the effective date of such proposed transaction. To the extent it has not been previously exercised, an Award will terminate immediately prior to the consummation of such proposed action.

(c) Change in Control. In the event of a merger of the Company with or into another corporation or other entity or a Change in Control, each outstanding Award will be treated as the Administrator determines (subject to the provisions of the following paragraph) without a Participant's consent, including, without limitation, that (i) Awards will be assumed, or substantially equivalent awards will be substituted, by the acquiring or succeeding corporation (or an affiliate thereof) with appropriate adjustments as to the number and kind of shares and prices; (ii) upon written notice to a Participant, that the Participant's Awards will terminate upon or immediately prior to the consummation of such merger or Change in Control; (iii) outstanding Awards will vest and become exercisable, realizable, or payable, or restrictions applicable to an Award will lapse, in whole or in part prior to or upon consummation of such merger or Change in Control, and, to the extent the Administrator determines, terminate upon or immediately prior to the effectiveness of such merger or Change in Control; (iv) (A) the termination of an Award in exchange for an amount of cash and/or property, if any, equal to the amount that would have been attained upon the exercise of such Award or realization of the Participant's rights as of the date of the occurrence of the transaction (and, for the avoidance of doubt, if as of the date of the occurrence of the transaction the Administrator determines in good faith that no amount would have been attained upon the exercise of such Award or realization of the Participant's rights, then such Award may be terminated by the Company without payment), or (B) the replacement of such Award with other rights or property selected by the Administrator in its sole discretion; or (v) any combination of the foregoing. In taking any of the actions permitted under this subsection 14(c), the Administrator will not be obligated to treat all Awards, all Awards held by a Participant, or all Awards of the same type, similarly.

In the event that the successor corporation does not assume or substitute for the Award (or portion thereof), the Participant will fully vest in and have the right to exercise such outstanding Option and Stock Appreciation Right, including Shares as to which such Award would not otherwise be vested or exercisable, all restrictions on such Restricted Stock and Restricted Stock

Units will lapse, and, with respect to such Awards with performance-based vesting, all performance goals or other vesting criteria will be deemed achieved at one hundred percent (100%) of target levels and all other terms and conditions met, in all cases, unless specifically provided otherwise under the applicable Award Agreement or other written agreement between the Participant and the Company or any of its Subsidiaries or Parents, as applicable. In addition, if an Option or Stock Appreciation Right is not assumed or substituted in the event of a merger or Change in Control, the Administrator will notify the Participant in writing or electronically that such Option or Stock Appreciation Right will be exercisable for a period of time determined by the Administrator in its sole discretion, and the Option or Stock Appreciation Right will terminate upon the expiration of such period.

For the purposes of this subsection (c) (and subsection (d) below), an Award will be considered assumed if, following the merger or Change in Control, the Award confers the right to purchase or receive, for each Share subject to the Award immediately prior to the merger or Change in Control, the consideration (whether stock, cash, or other securities or property) received in the merger or Change in Control by holders of Common Stock for each Share held on the effective date of the transaction (and if holders were offered a choice of consideration, the type of consideration chosen by the holders of a majority of the outstanding Shares); provided, however, that if such consideration received in the merger or Change in Control is not solely common stock of the successor corporation or its Parent, the Administrator may, with the consent of the successor corporation, provide for the consideration to be received upon the exercise of an Option or Stock Appreciation Right or upon the payout of a Restricted Stock Unit, Performance Unit or Performance Share, for each Share subject to such Award, to be solely common stock of the successor corporation or its Parent equal in fair market value to the per share consideration received by holders of Common Stock in the merger or Change in Control.

Notwithstanding anything in this Section 14(c) to the contrary, and unless otherwise provided in an Award Agreement, an Award that vests, is earned or paid-out upon the satisfaction of one or more performance goals will not be considered assumed if the Company or its successor modifies any of such performance goals without the Participant's consent; provided, however, a modification to such performance goals only to reflect the successor corporation's post-Change in Control corporate structure will not be deemed to invalidate an otherwise valid Award assumption.

Notwithstanding anything in this Section 14(c) to the contrary, if a payment under an Award Agreement is subject to Code Section 409A and if the change in control definition contained in the Award Agreement does not comply with the definition of "change of control" for purposes of a distribution under Code Section 409A, then any payment of an amount that is otherwise accelerated under this Section will be delayed until the earliest time that such payment would be permissible under Code Section 409A without triggering any penalties applicable under Code Section 409A.

(d) Outside Director Awards. With respect to Awards granted to an Outside Director that are assumed or substituted for, if on the date of or following such assumption or substitution the Participant's status as a Director or a director of the successor corporation, as applicable, is terminated other than upon a voluntary resignation by the Participant (unless such resignation is at the request of the acquirer), then the Outside Director will fully vest in and have the right to exercise Options and/or Stock Appreciation Rights as to all of the Shares underlying such

Award, including those Shares which would not otherwise be vested or exercisable, all restrictions on Restricted Stock and Restricted Stock Units will lapse, and, with respect to Awards with performance-based vesting, all performance goals or other vesting criteria will be deemed achieved at one hundred percent (100%) of target levels and all other terms and conditions met, unless specifically provided otherwise under the applicable Award Agreement or other written agreement between the Participant and the Company or any of its Subsidiaries or Parents, as applicable.

15. Tax.

(a) Withholding Requirements. Prior to the delivery of any Shares or cash pursuant to an Award (or exercise thereof) or such earlier time as any tax withholding obligations are due, the Company will have the power and the right to deduct or withhold, or require a Participant to remit to the Company, an amount sufficient to satisfy federal, state, local, foreign or other taxes (including the Participant's FICA obligation) required to be withheld with respect to such Award (or exercise thereof).

(b) Withholding Arrangements. The Administrator, in its sole discretion and pursuant to such procedures as it may specify from time to time, may permit a Participant to satisfy such tax withholding obligation, in whole or in part by (without limitation) (a) paying cash, check or other cash equivalents, (b) electing to have the Company withhold otherwise deliverable cash or Shares having a fair market value equal to the minimum statutory amount required to be withheld or such greater amount as the Administrator may determine if such amount would not have adverse accounting consequences, as the Administrator determines in its sole discretion, (c) delivering to the Company already-owned Shares having a fair market value equal to the minimum statutory amount required to be withheld or such greater amount as the Administrator may determine, in each case, provided the delivery of such Shares will not result in any adverse accounting consequences, as the Administrator determines in its sole discretion, (d) selling a sufficient number of Shares otherwise deliverable to the Participant through such means as the Administrator may determine in its sole discretion (whether through a broker or otherwise) equal to the amount required to be withheld, or (e) any combination of the foregoing methods of payment. The fair market value of the Shares to be withheld or delivered will be determined as of the date that the taxes are required to be withheld.

(c) Compliance With Code Section 409A. Awards will be designed and operated in such a manner that they are either exempt from the application of, or comply with, the requirements of Code Section 409A such that the grant, payment, settlement or deferral will not be subject to the additional tax or interest applicable under Code Section 409A, except as otherwise determined in the sole discretion of the Administrator. The Plan and each Award Agreement under the Plan is intended to meet the requirements of Code Section 409A and will be construed and interpreted in accordance with such intent, except as otherwise determined in the sole discretion of the Administrator. To the extent that an Award or payment, or the settlement or deferral thereof, is subject to Code Section 409A the Award will be granted, paid, settled or deferred in a manner that will meet the requirements of Code Section 409A, such that the grant, payment, settlement or deferral will not be subject to the additional tax or interest applicable under Code Section 409A. In no event will the Company have any obligation under the terms of this Plan to reimburse a Participant for any taxes or other costs that may be imposed on Participant as a result of Section 409A.

16. No Effect on Employment or Service. Neither the Plan nor any Award will confer upon a Participant any right with respect to continuing the Participant's relationship as a Service Provider with the Company or its Subsidiaries or Parents, as applicable, nor will they interfere in any way with the Participant's right or the right of the Company and its Subsidiaries or Parents, as applicable, to terminate such relationship at any time, with or without cause, to the extent permitted by Applicable Laws.

17. Date of Grant. The date of grant of an Award will be, for all purposes, the date on which the Administrator makes the determination granting such Award, or such other later date as is determined by the Administrator. Notice of the determination will be provided to each Participant within a reasonable time after the date of such grant.

18. Term of Plan. Subject to Section 22 of the Plan, the Plan will become effective upon the later to occur of (i) its adoption by the Board or (ii) the business day immediately prior to the Registration Date. It will continue in effect for a term of ten (10) years from the date adopted by the Board, unless terminated earlier under Section 19 of the Plan.

19. Amendment and Termination of the Plan.

(a) Amendment and Termination. The Administrator may at any time amend, alter, suspend or terminate the Plan.

(b) Stockholder Approval. The Company will obtain stockholder approval of any Plan amendment to the extent necessary and desirable to comply with Applicable Laws.

(c) Effect of Amendment or Termination. No amendment, alteration, suspension or termination of the Plan will impair the rights of any Participant, unless mutually agreed otherwise between the Participant and the Administrator, which agreement must be in writing and signed by the Participant and the Company. Termination of the Plan will not affect the Administrator's ability to exercise the powers granted to it hereunder with respect to Awards granted under the Plan prior to the date of such termination.

20. Conditions Upon Issuance of Shares.

(a) Legal Compliance. Shares will not be issued pursuant to the exercise of an Award unless the exercise of such Award and the issuance and delivery of such Shares will comply with Applicable Laws and will be further subject to the approval of counsel for the Company with respect to such compliance.

(b) Investment Representations. As a condition to the exercise of an Award, the Company may require the person exercising such Award to represent and warrant at the time of any such exercise that the Shares are being purchased only for investment and without any present intention to sell or distribute such Shares if, in the opinion of counsel for the Company, such a representation is required.

21. Inability to Obtain Authority. The inability of the Company to obtain authority from any regulatory body having jurisdiction or to complete or comply with the requirements of any registration or other qualification of the Shares under any state, federal or foreign law or under the rules and regulations of the Securities and Exchange Commission, the stock exchange on which Shares of the same class are then listed, or any other governmental or regulatory body, which authority, registration, qualification or rule compliance is deemed by the Company's counsel to be necessary or advisable for the issuance and sale of any Shares hereunder, will relieve the Company of any liability in respect of the failure to issue or sell such Shares as to which such requisite authority, registration, qualification or rule compliance will not have been obtained.

22. Stockholder Approval. The Plan will be subject to approval by the stockholders of the Company within twelve (12) months after the date the Plan is adopted by the Board. Such stockholder approval will be obtained in the manner and to the degree required under Applicable Laws.

23. Forfeiture Events. The Administrator may specify in an Award Agreement that the Participant's rights, payments, and benefits with respect to an Award will be subject to the reduction, cancellation, forfeiture, or recoupment upon the occurrence of certain specified events, in addition to any otherwise applicable vesting or performance conditions of an Award. Notwithstanding any provisions to the contrary under this Plan, an Award shall be subject to the Company's clawback policy as may be established and/or amended from time to time (the "Clawback Policy"). The Administrator may require a Participant to forfeit, return or reimburse the Company all or a portion of the Award and any amounts paid thereunder pursuant to the terms of the Clawback Policy or as necessary or appropriate to comply with Applicable Laws.

DENALI THERAPEUTICS INC.
2017 EQUITY INCENTIVE PLAN
RESTRICTED STOCK AWARD AGREEMENT

NOTICE OF GRANT OF RESTRICTED STOCK

Unless otherwise defined herein, the terms defined in the Denali Therapeutics Inc. 2017 Equity Incentive Plan (the "Plan") will have the same defined meanings in this Restricted Stock Award Agreement, which includes the Notice of Grant of Restricted Stock (the "Notice of Grant"), Terms and Conditions of Restricted Stock Grant, attached hereto as Exhibit A, and all appendices and exhibits attached thereto (the "Award Agreement").

Participant Name:
Address:

The undersigned Participant has been granted the right to receive an Award of Shares of Restricted Stock, subject to the terms and conditions of the Plan and this Award Agreement, as follows:

Grant Number:

Date of Grant:

Vesting Commencement Date:

Number of Shares of Restricted Stock:

Vesting Schedule:

Subject to any acceleration provisions contained in the Plan or set forth below, the Shares of Restricted Stock will vest and the Company's right to reacquire the Restricted Stock will lapse in accordance with the following schedule:

[*Insert Vesting Schedule, e.g.:* Twenty-five percent (25%) of the Shares of Restricted Stock shall vest on the one (1) year anniversary of the Vesting Commencement Date, and twenty five percent (25%) of the Shares of Restricted Stock will vest each year thereafter on the same day as the Vesting Commencement Date, subject to Participant continuing to be a Service Provider through each such date.]

By Participant's signature and the signature of the representative of Denali Therapeutics Inc. (the "Company") below, Participant and the Company agree that this Award of Restricted Stock is granted under and governed by the terms and conditions of the Plan and this Award Agreement, including the Terms and Conditions of Restricted Stock Grant, attached hereto as Exhibit A, all of which are made a part of this document. Participant acknowledges receipt of a copy of the Plan. Participant has reviewed the Plan and this Award Agreement in their entirety, has had an opportunity to obtain the advice of counsel prior to executing this Award Agreement and fully understands all provisions of the Plan and this Award Agreement. Participant hereby agrees to accept as binding, conclusive and final all decisions or interpretations of the Administrator upon any questions relating to the Plan and Award Agreement. Participant further agrees to notify the Company upon any change in the residence address indicated below.

PARTICIPANT

Signature

«Name»
Print Name

Address:

«Address»

DENALI THERAPEUTICS INC.

Signature

Print Name

Title

EXHIBIT A

TERMS AND CONDITIONS OF RESTRICTED STOCK GRANT

1. Grant of Shares of Restricted Stock. The Company hereby grants to the individual (the "Participant") named in the Notice of Grant of Restricted Stock of this Award Agreement (the "Notice of Grant") under the Plan an Award of Shares of Restricted Stock, subject to all of the terms and conditions in this Award Agreement and the Plan, which is incorporated herein by reference. Subject to Section 19(c) of the Plan, in the event of a conflict between the terms and conditions of the Plan and this Award Agreement, the terms and conditions of the Plan shall prevail.

2. Vesting Schedule. Except as provided in Section 3 and subject to Sections 4 and 7, the Shares of Restricted Stock awarded by this Award Agreement will vest in accordance with the vesting schedule set forth in the Notice of Grant. Shares of Restricted Stock scheduled to vest on a certain date or upon the occurrence of a certain condition will not vest in accordance with any of the provisions of this Award Agreement, unless Participant will have been continuously a Service Provider from the Date of Grant until the date such vesting occurs.

3. Administrator Discretion. The Administrator, in its discretion, may accelerate the vesting of the balance, or some lesser portion of the balance, of the unvested Shares of Restricted Stock subject to this Award Agreement at any time, subject to the terms of the Plan. If so accelerated, such Shares of Restricted Stock will be considered as having vested as of the date specified by the Administrator.

4. Forfeiture Upon Termination as a Service Provider. Notwithstanding any contrary provision of this Award Agreement, the balance of the Shares of Restricted Stock that have not vested as of the time of Participant's termination as a Service Provider for any or no reason will be forfeited and automatically transferred to and reacquired by the Company at no cost to the Company upon the date of such termination and Participant will have no further rights thereunder. Participant will not be entitled to a refund of the price paid for the Shares of Restricted Stock, if any, returned to the Company pursuant to this Section 4. Participant hereby appoints the Escrow Agent with full power of substitution, as Participant's true and lawful attorney-in-fact with irrevocable power and authority in the name and on behalf of Participant to take any action and execute all documents and instruments, including, without limitation, stock powers which may be necessary to transfer the certificate or certificates evidencing such unvested Shares to the Company upon such termination of service.

5. Tax Consequences. Participant has reviewed with his or her own tax advisors the U.S. federal, state, local and non-U.S. tax consequences of this investment and the transactions contemplated by this Award Agreement. With respect to such matters, Participant relies solely on such advisors and not on any statements or representations of the Company or any of its agents, written or oral. Participant understands that Participant (and not the Company) shall be responsible for Participant's own tax liability that may arise as a result of this investment or the transactions contemplated by this Award Agreement.

6. Death of Participant. Any distribution or delivery to be made to Participant under this Award Agreement will, if Participant is then deceased, be made to Participant's designated beneficiary, or if no beneficiary survives Participant, the administrator or executor of Participant's estate. Any such transferee must furnish the Company with (a) written notice of his or her status as transferee, and (b) evidence satisfactory to the Company to establish the validity of the transfer and compliance with any laws or regulations pertaining to said transfer.

7. Tax Obligations

(a) Responsibility for Taxes. Participant acknowledges that, regardless of any action taken by the Company or, if different, Participant's employer (the "Employer") or Parent or Subsidiary to which Participant is providing services (together, the Company, the Employer and/or Parent or Subsidiary to which Participant is providing services, the "Service Recipient"), the ultimate liability for any tax and/or social insurance liability obligations and requirements in connection with the Shares of Restricted Stock, including, without limitation, (i) all federal, state, and local taxes (including the Participant's Federal Insurance Contributions Act (FICA) obligation) that are required to be withheld by the Company or the Employer or other payment of tax-related items related to Participant's participation in the Plan and legally applicable to Participant, (ii) the Participant's and, to the extent required by the Company (or Service Recipient), the Company's (or Service Recipient's) fringe benefit tax liability, if any, associated with the grant, vesting or release from escrow of the Shares of Restricted Stock, the filing of an 83(b) election with respect to the Shares of Restricted Stock, or the sale of Shares, and (iii) any other Company (or Service Recipient) taxes the responsibility for which the Participant has, or has agreed to bear, with respect to the Shares of Restricted Stock (or exercise thereof or issuance of Shares thereunder) (collectively, the "Tax Obligations"), is and remains Participant's responsibility and may exceed the amount actually withheld by the Company or the Service Recipient. Participant further acknowledges that the Company and/or the Service Recipient (A) make no representations or undertakings regarding the treatment of any Tax Obligations in connection with any aspect of the Shares of Restricted Stock, including, but not limited to, the grant, vesting or release from escrow of the Shares of Restricted Stock, the filing of an 83(b) election with respect to the Shares of Restricted Stock, the subsequent sale of Shares acquired pursuant to this Award Agreement and the receipt of any dividends or other distributions, and (B) do not commit to and are under no obligation to structure the terms of the grant or any aspect of the Award of Restricted Stock to reduce or eliminate Participant's liability for Tax Obligations or achieve any particular tax result. Further, if Participant is subject to Tax Obligations in more than one jurisdiction between the Date of Grant and the date of any relevant taxable or tax withholding event, as applicable, Participant acknowledges that the Company and/or the Service Recipient (or former employer, as applicable) may be required to withhold or account for Tax Obligations in more than one jurisdiction. If Participant fails to make satisfactory arrangements for the payment of any required Tax Obligations hereunder at the time of the applicable taxable event, Participant acknowledges and agrees that the Company may refuse to issue or deliver the Shares. Participant understands that Section 83 of the Internal Revenue Code of 1986, as amended (the "Code"), taxes as ordinary income the difference between the purchase price, if any, for the Shares and the Fair Market Value of the Shares as of each vesting date. If Participant is a U.S. taxpayer, Participant understands that Participant may elect, for purposes of U.S. tax law, to be taxed at the time the Shares are granted rather than when such Shares vest by filing an election under Section 83(b) of the Code (the "83(b) Election") with the IRS within thirty (30) days from the date of grant of the Restricted Stock Award.

(b) Tax Withholding and Default Method of Tax Withholding. Notwithstanding any contrary provision of this Award Agreement, no certificate representing the Shares of Restricted Stock may be released from the escrow established pursuant to Section 14, unless and until satisfactory arrangements (as determined by the Administrator) will have been made by Participant with respect to the payment of all Tax Obligations. When Shares of Restricted Stock are vested, Participant generally will recognize immediate U.S. taxable income if Participant is a U.S. taxpayer. If Participant is a non-U.S. taxpayer, Participant will be subject to applicable taxes in his or her jurisdiction. The minimum amount of Tax Obligations which the Company determines must be withheld with respect to this Award ("Tax Withholding Obligation") will be satisfied by Shares being sold on Participant's behalf at the prevailing market price pursuant to such procedures as the Company may specify from time to time, including through a broker-assisted arrangement (it being understood that the Shares to be sold must have vested pursuant to the terms of this Award Agreement and the Plan). The proceeds from the sale will be used to satisfy Participant's Tax Withholding Obligation arising with respect to this Award. In addition to Shares sold to satisfy the Tax Withholding Obligation, additional Shares will be sold to satisfy any associated broker or other fees. Only whole Shares will be sold to satisfy any Tax Withholding Obligation. Any proceeds from the sale of Shares in excess of the Tax Withholding Obligation and any associated broker or other fees will be paid to Participant in accordance with procedures the Company may specify from time to time. **By accepting this Award, Participant expressly consents to the sale of Shares to cover the Tax Withholding Obligations (and any associated broker or other fees and agrees and acknowledges that Participant may not satisfy them by any means other than such sale of Shares, unless required to do so by the Administrator or pursuant to the Administrator's express written consent.**

(c) Administrator Discretion. If the Administrator determines that Participant cannot satisfy Participant's Tax Withholding Obligation through the default procedure described in Section 7(b) or the Administrator otherwise determines it is in the best interests of the Company for Participant to satisfy Participant's Tax Withholding Obligation by a method other than through the default procedure described in Section 7(b), it may permit or require Participant to satisfy Participant's Tax Withholding Obligation, in whole or in part (without limitation), if permissible by applicable local law, by (i) paying cash, (ii) electing to have the Company withhold otherwise deliverable Shares having a value equal to the minimum amount statutorily required to be withheld (or such greater amount as Participant may elect if permitted by the Administrator, if such greater amount would not result in adverse financial accounting consequences), (iii) withholding the amount of such Tax Withholding Obligation from Participant's wages or other cash compensation paid to Participant by the Company and/or the Service Recipient, (iv) delivering to the Company Shares that Participant owns and that have vested with a Fair Market Value equal to the amount required to be withheld (or such greater amount as Participant may elect if permitted by the Administrator, if such greater amount would not result in adverse financial accounting consequences), or (v) such other means as the Administrator deems appropriate. To the extent determined appropriate by the Company in its discretion, it will have the right (but not the obligation) to satisfy any Tax Obligations by reducing the number of Shares otherwise deliverable to Participant.

(d) Company's Obligation to Release Shares. For clarification purposes, in no event will the Company release Shares from the escrow established pursuant to Section 14 unless and until arrangements satisfactory to the Administrator have been made for the payment of Participant's Tax Withholding Obligation. If Participant fails to make satisfactory arrangements for

the payment of such Tax Withholding Obligations hereunder at the time any applicable Shares of Restricted Stock otherwise are scheduled to vest pursuant to Sections 2 or 3, at the time Participant files a timely 83(b) Election with the IRS, or Participant's Tax Withholding Obligations otherwise become due, Participant will permanently forfeit such Shares of Restricted Stock to which Participant's Tax Withholding Obligation relates and any right to receive Shares thereunder and such Restricted Stock Units will be returned to the Company at no cost to the Company. Participant acknowledges and agrees that the Company may refuse to issue or deliver the Shares if such Tax Obligations are not delivered at the time they are due.

8. Rights as Stockholder. Neither Participant nor any person claiming under or through Participant will have any of the rights or privileges of a stockholder of the Company in respect of any Shares deliverable hereunder unless and until certificates representing such Shares (which may be in book entry form) will have been issued, recorded on the records of the Company or its transfer agents or registrars, and delivered to Participant (including through electronic delivery to a brokerage account) or the Escrow Agent. After such issuance, recordation and delivery, Participant will have all the rights of a stockholder of the Company with respect to voting such Shares and receipt of dividends and distributions on such Shares. Except as provided in Section 14(f), after such issuance, recordation and delivery, Participant will have all the rights of a stockholder of the Company with respect to voting such Shares and receipt of dividends and distributions on such Shares.

9. No Guarantee of Continued Service. PARTICIPANT ACKNOWLEDGES AND AGREES THAT THE VESTING OF THE SHARES OF RESTRICTED STOCK PURSUANT TO THE VESTING SCHEDULE HEREOF IS EARNED ONLY BY CONTINUING AS A SERVICE PROVIDER, WHICH UNLESS PROVIDED OTHERWISE UNDER APPLICABLE LAW IS AT THE WILL OF THE COMPANY (OR THE SERVICE RECIPIENT), AND NOT THROUGH THE ACT OF BEING HIRED, BEING GRANTED THIS RESTRICTED STOCK AWARD OR ACQUIRING SHARES HEREUNDER. PARTICIPANT FURTHER ACKNOWLEDGES AND AGREES THAT THIS AWARD AGREEMENT, THE TRANSACTIONS CONTEMPLATED HEREUNDER AND THE VESTING SCHEDULE SET FORTH HEREIN DO NOT CONSTITUTE AN EXPRESS OR IMPLIED PROMISE OF CONTINUED ENGAGEMENT AS A SERVICE PROVIDER FOR THE VESTING PERIOD, FOR ANY PERIOD, OR AT ALL, AND SHALL NOT INTERFERE IN ANY WAY WITH PARTICIPANT'S RIGHT OR THE RIGHT OF THE COMPANY (OR THE SERVICE RECIPIENT) TO TERMINATE PARTICIPANT'S RELATIONSHIP AS A SERVICE PROVIDER, SUBJECT TO APPLICABLE LAW, WHICH TERMINATION, UNLESS PROVIDED OTHERWISE UNDER APPLICABLE LAW, MAY BE AT ANY TIME, WITH OR WITHOUT CAUSE.

10. Grant is Not Transferable. Except for the escrow described in Section 14 or transfer of the Shares to the Company or its assignees contemplated by this Award Agreement, and except to the limited extent provided in Section 6, the unvested Shares subject to this Award Agreement and the rights and privileges conferred hereby will not be transferred, assigned, pledged or hypothecated in any way (whether by operation of law or otherwise) and will not be subject to sale under execution, attachment or similar process until such Shares shall have vested in accordance with the provisions of this Award Agreement. Upon any attempt to transfer, assign, pledge, hypothecate or otherwise dispose of the unvested Shares subject to this Award Agreement, or any right or privilege conferred hereby, or upon any attempted sale under any execution, attachment or similar process, the then-unvested Shares of Restricted Stock will thereupon be forfeited at no cost to the Company and Participant will have no further rights thereunder.

11. Nature of Grant. In accepting the grant, Participant acknowledges, understands and agrees that:

(a) the grant of the Shares of Restricted Stock is voluntary and occasional and does not create any contractual or other right to receive future grants of Shares of Restricted Stock, or benefits in lieu of Shares of Restricted Stock, even if Shares of Restricted Stock have been granted in the past;

(b) all decisions with respect to future grants of Restricted Stock or other grants, if any, will be at the sole discretion of the Company;

(c) Participant is voluntarily participating in the Plan;

(d) the Shares of Restricted Stock are not intended to replace any pension rights or compensation;

(e) the Shares of Restricted Stock, and the income and value of same, are not part of normal or expected compensation for purposes of calculating any severance, resignation, termination, redundancy, dismissal, end-of-service payments, bonuses, long-service awards, pension or retirement or welfare benefits or similar payments;

(f) the future value of the underlying Shares is unknown, indeterminable and cannot be predicted;

(g) for purposes of the Shares of Restricted Stock, Participant's status as a Service Provider will be considered terminated as of the date Participant is no longer actively providing services to the Company or any Parent or Subsidiary (regardless of the reason for such termination and whether or not later to be found invalid or in breach of employment laws in the jurisdiction where Participant is a Service Provider or the terms of Participant's employment or service agreement, if any), and unless otherwise expressly provided in this Award Agreement (including by reference in the Notice of Grant to other arrangements or contracts) or determined by the Administrator, Participant's right to vest in the Shares of Restricted Stock under the Plan, if any, will terminate as of such date and will not be extended by any notice period (e.g., Participant's period of service would not include any contractual notice period or any period of "garden leave" or similar period mandated under employment laws in the jurisdiction where Participant is a Service Provider or the terms of Participant's employment or service agreement, if any, unless Participant is providing bona fide services during such time); the Administrator shall have the exclusive discretion to determine when Participant is no longer actively providing services for purposes of the Restricted Stock Award (including whether Participant may still be considered to be providing services while on a leave of absence and consistent with local law);

(h) unless otherwise provided in the Plan or by the Company in its discretion, the Shares of Restricted Stock and the benefits evidenced by this Award Agreement do not create any entitlement to have the Shares of Restricted Stock or any such benefits transferred to, or assumed by, another company nor be exchanged, cashed out or substituted for, in connection with any corporate transaction affecting the Shares; and

(i) the following provisions apply only if Participant is providing services outside the United States:

(i) the Shares of Restricted Stock are not part of normal or expected compensation or salary for any purpose;

(ii) Participant acknowledges and agrees that none of the Company, the Employer or any Parent or Subsidiary shall be liable for any foreign exchange rate fluctuation between Participant's local currency and the United States Dollar that may affect the value of the Shares of Restricted Stock or the subsequent sale of any Shares; and

(iii) no claim or entitlement to compensation or damages shall arise from forfeiture of the Restricted Stock resulting from the termination of Participant's status as a Service Provider (for any reason whatsoever whether or not later found to be invalid or in breach of employment laws in the jurisdiction where Participant is a Service Provider or the terms of Participant's employment or service agreement, if any), and in consideration of the grant of the Restricted Stock to which Participant is otherwise not entitled, Participant irrevocably agrees never to institute any claim against the Company, any Parent or Subsidiary or the Service Recipient, waives his or her ability, if any, to bring any such claim, and releases the Company, any Parent or Subsidiary and the Service Recipient from any such claim; if, notwithstanding the foregoing, any such claim is allowed by a court of competent jurisdiction, then, by participating in the Plan, Participant shall be deemed irrevocably to have agreed not to pursue such claim and agrees to execute any and all documents necessary to request dismissal or withdrawal of such claim.

12. No Advice Regarding Grant. The Company is not providing any tax, legal or financial advice, nor is the Company making any recommendations regarding Participant's participation in the Plan, or Participant's acquisition or sale of the underlying Shares. Participant is hereby advised to consult with his or her own personal tax, legal and financial advisors regarding his or her participation in the Plan before taking any action related to the Plan.

13. Data Privacy. Participant hereby explicitly and unambiguously consents to the collection, use and transfer, in electronic or other form, of Participant's personal data as described in this Award Agreement and any other Restricted Stock grant materials by and among, as applicable, the Employer, or other Service Recipient the Company and any Parent or Subsidiary for the exclusive purpose of implementing, administering and managing Participant's participation in the Plan.

Participant understands that the Company and the Service Recipient may hold certain personal information about Participant, including, but not limited to, Participant's name, home address and telephone number, date of birth, social insurance number or other identification number, salary, nationality, job title, any Shares or directorships held in the Company, details of all Shares of Restricted Stock or any other entitlement to Shares awarded, canceled, exercised, vested, unvested or outstanding in Participant's favor ("Data"), for the exclusive purpose of implementing, administering and managing the Plan.

Participant understands that Data will be transferred to a stock plan service provider as may be selected by the Company in the future, which is assisting the Company with the implementation, administration and management of the Plan. Participant understands that the recipients of the Data may be located in the United States or elsewhere, and that the recipients' country of operation (e.g., the United States) may have different data privacy laws and protections than Participant's country. Participant understands that if he or she resides outside the United States, he or she may request a list with the names and addresses of any potential recipients of the Data by contacting his or her local human resources representative. Participant authorizes the Company, any stock plan service provider selected by the Company and any other possible recipients which may assist the Company (presently or in the future) with implementing, administering and managing the Plan to receive, possess, use, retain and transfer the Data, in electronic or other form, for the sole purpose of implementing, administering and managing his or her participation in the Plan. Participant understands that Data will be held only as long as is necessary to implement, administer and manage Participant's participation in the Plan. Participant understands if he or she resides outside the United States, he or she may, at any time, view Data, request additional information about the storage and processing of Data, require any necessary amendments to Data or refuse or withdraw the consents herein, in any case without cost, by contacting in writing his or her local human resources representative. Further, Participant understands that he or she is providing the consents herein on a purely voluntary basis. If Participant does not consent, or if Participant later seeks to revoke his or her consent, his or her status as a Service Provider and career with the Service Recipient will not be adversely affected; the only adverse consequence of refusing or withdrawing Participant's consent is that the Company would not be able to grant Participant Restricted Stock or other equity awards or administer or maintain such awards. Therefore, Participant understands that refusing or withdrawing his or her consent may affect Participant's ability to participate in the Plan. For more information on the consequences of Participant's refusal to consent or withdrawal of consent, Participant understands that he or she may contact his or her local human resources representative.

14. Escrow of Shares.

(a) All Shares of Restricted Stock will, upon execution of this Award Agreement, be delivered and deposited with an escrow holder designated by the Company (the "Escrow Holder"). The Shares of Restricted Stock will be held by the Escrow Holder until such time as the Shares of Restricted Stock vest or the date Participant ceases to be a Service Provider.

(b) The Escrow Holder will not be liable for any act it may do or omit to do with respect to holding the Shares of Restricted Stock in escrow and while acting in good faith and in the exercise of its judgment.

(c) Upon Participant's termination as a Service Provider for any reason, the Escrow Holder, upon receipt of written notice of such termination, will take all steps necessary to accomplish the transfer of the unvested Shares of Restricted Stock to the Company. Participant hereby appoints the Escrow Holder with full power of substitution, as Participant's true and lawful attorney-in-fact with irrevocable power and authority in the name and on behalf of Participant to take any action and execute all documents and instruments, including, without limitation, stock powers which may be necessary to transfer the certificate or certificates evidencing such unvested Shares of Restricted Stock to the Company upon such termination.

(d) The Escrow Holder will take all steps necessary to accomplish the transfer of Shares of Restricted Stock to Participant after they vest following Participant's request that the Escrow Holder do so.

(e) Subject to the terms hereof, Participant shall have all the rights of a stockholder with respect to such Shares while they are held in escrow, including without limitation, the right to vote the Shares and receive any cash dividends declared thereon.

(f) In the event of any dividend or other distribution (whether in the form of cash, Shares, other securities, or other property), recapitalization, stock split, reverse stock split, reorganization, merger, consolidation, split-up, spin-off, combination, repurchase, or exchange of Shares or other securities of the Company, or other change in the corporate structure of the Company affecting the Shares, the Shares of Restricted Stock will be increased, reduced or otherwise changed, and by virtue of any such change Participant will in his or her capacity as owner of unvested Shares of Restricted Stock be entitled to new or additional or different shares of stock, cash or securities (other than rights or warrants to purchase securities); such new or additional or different shares, cash or securities will thereupon be considered to be unvested Shares of Restricted Stock and will be subject to all of the conditions and restrictions which were applicable to the unvested Shares of Restricted Stock pursuant to this Award Agreement. If Participant receives rights or warrants with respect to any unvested Shares of Restricted Stock, such rights or warrants may be held or exercised by Participant, provided that until such exercise any such rights or warrants and after such exercise any shares or other securities acquired by the exercise of such rights or warrants will be considered to be unvested Shares of Restricted Stock and will be subject to all of the conditions and restrictions which were applicable to the unvested Shares of Restricted Stock pursuant to this Award Agreement. The Administrator in its absolute discretion at any time may accelerate the vesting of all or any portion of such new or additional shares of stock, cash or securities, rights or warrants to purchase securities or shares or other securities acquired by the exercise of such rights or warrants.

(g) The Company may instruct the transfer agent for its Common Stock to place a legend on the certificates representing the Restricted Stock or otherwise note its records as to the restrictions on transfer set forth in this Award Agreement.

15. Address for Notices. Any notice to be given to the Company under the terms of this Award Agreement will be addressed to the Company at Denali Therapeutics Inc., 151 Oyster Point Blvd., South San Francisco, CA 94080, or at such other address as the Company may hereafter designate in writing.

16. Electronic Delivery and Acceptance. The Company may, in its sole discretion, decide to deliver any documents related to the Shares of Restricted Stock awarded under the Plan or future Shares of Restricted Stock that may be awarded under the Plan by electronic means or request Participant's consent to participate in the Plan by electronic means. Participant hereby consents to receive such documents by electronic delivery and agrees to participate in the Plan through any on-line or electronic system established and maintained by the Company or a third party designated by the Company.

17. No Waiver. Either party's failure to enforce any provision or provisions of this Award Agreement shall not in any way be construed as a waiver of any such provision or provisions, nor prevent that party from thereafter enforcing each and every other provision of this Award Agreement. The rights granted both parties herein are cumulative and shall not constitute a waiver of either party's right to assert all other legal remedies available to it under the circumstances.

18. Successors and Assigns. The Company may assign any of its rights under this Award Agreement to single or multiple assignees, and this Award Agreement shall inure to the benefit of the successors and assigns of the Company. Subject to the restrictions on transfer herein set forth, this Award Agreement shall be binding upon Participant and his or her heirs, executors, administrators, successors and assigns. The rights and obligations of Participant under this Award Agreement may only be assigned with the prior written consent of the Company.

19. Additional Conditions to Issuance of Stock. If at any time the Company will determine, in its discretion, that the listing, registration, qualification or rule compliance of the Shares upon any securities exchange or under any state, federal or non-U.S. law, the tax code and related regulations or under the rulings or regulations of the United States Securities and Exchange Commission or any other governmental regulatory body or the clearance, consent or approval of the United States Securities and Exchange Commission or any other governmental regulatory authority is necessary or desirable as a condition to the issuance of Shares to Participant (or his or her estate) or the Escrow Holder hereunder, such issuance will not occur unless and until such listing, registration, qualification, rule compliance, clearance, consent or approval will have been completed, effected or obtained free of any conditions not acceptable to the Company. Subject to the terms of the Award Agreement and the Plan, the Company shall not be required to issue any certificate or certificates for Shares hereunder prior to the lapse of such reasonable period of time following the Date of Grant of the Shares of Restricted Stock as the Administrator may establish from time to time for reasons of administrative convenience.

20. Language. If Participant has received this Award Agreement or any other document related to the Plan translated into a language other than English and if the meaning of the translated version is different than the English version, the English version will control.

21. Interpretation. The Administrator will have the power to interpret the Plan and this Award Agreement and to adopt such rules for the administration, interpretation and application of the Plan as are consistent therewith and to interpret or revoke any such rules (including, but not limited to, the determination of whether or not any Shares of Restricted Stock have vested). All actions taken and all interpretations and determinations made by the Administrator in good faith will be final and binding upon Participant, the Company and all other interested persons. Neither the Administrator nor any person acting on behalf of the Administrator will be personally liable for any action, determination or interpretation made in good faith with respect to the Plan or this Award Agreement.

22. Captions. Captions provided herein are for convenience only and are not to serve as a basis for interpretation or construction of this Award Agreement.

23. Amendment, Suspension or Termination of the Plan. By accepting this Award, Participant expressly warrants that he or she has received an Award of Restricted Stock under the Plan, and has received, read and understood a description of the Plan. Participant understands that the Plan is discretionary in nature and may be amended, suspended or terminated by the Company at any time.

24. Modifications to the Award Agreement. This Award Agreement constitutes the entire understanding of the parties on the subjects covered. Participant expressly warrants that he or she is not accepting this Award Agreement in reliance on any promises, representations, or inducements other than those contained herein. Modifications to this Award Agreement or the Plan can be made only in an express written contract executed by a duly authorized officer of the Company. Notwithstanding anything to the contrary in the Plan or this Award Agreement, the Company reserves the right to revise this Award Agreement as it deems necessary or advisable, in its sole discretion and without the consent of Participant, to comply with Section 409A of the Internal Revenue Code of 1986, as amended and any final Treasury Regulations and Internal Revenue Service guidance thereunder, as each may be amended from time to time (together, "Section 409A") or to otherwise avoid imposition of any additional tax or income recognition under Section 409A in connection to this Award of Shares of Restricted Stock.

25. Governing Law; Venue; Severability. This Award Agreement and the Shares of Restricted Stock are governed by the internal substantive laws, but not the choice of law rules, of California. For purposes of litigating any dispute that arises under this Restricted Stock Award or this Award Agreement, the parties hereby submit to and consent to the jurisdiction of the State of California, and agree that such litigation will be conducted in the courts of San Mateo County, California, or the federal courts for the United States for the Northern District of California, and no other courts, where this Award Agreement is made and/or to be performed. In the event that any provision hereof becomes or is declared by a court of competent jurisdiction to be illegal, unenforceable or void, this Award Agreement shall continue in full force and effect.

26. Entire Agreement. The Plan is incorporated herein by reference. The Plan and this Award Agreement (including the appendices and exhibits referenced herein) constitute the entire agreement of the parties with respect to the subject matter hereof and supersede in their entirety all prior undertakings and agreements of the Company and Participant with respect to the subject matter hereof, and may not be modified adversely to the Participant's interest except by means of a writing signed by the Company and Participant.

27. Country Addendum. Notwithstanding any provisions in this Award Agreement, the Restricted Stock grant shall be subject to any special terms and conditions set forth in the appendix (if any) to this Award Agreement for Participant's country. Moreover, if Participant relocates to one of the countries included in the Country Addendum (if any), the special terms and conditions for such country will apply to Participant, to the extent the Company determines that the application of such terms and conditions is necessary or advisable for legal or administrative reasons. The Country Addendum constitutes part of this Award Agreement.

DENALI THERAPEUTICS INC.
2017 EQUITY INCENTIVE PLAN
STOCK OPTION AGREEMENT

Unless otherwise defined herein, the terms defined in the Denali Therapeutics Inc. 2017 Equity Incentive Plan (the "Plan") will have the same defined meanings in this Stock Option Agreement including the Notice of Stock Option Grant (the "Notice of Grant"), the Terms and Conditions of Stock Option Grant, and the exhibits attached thereto (all together, the "Option Agreement").

NOTICE OF STOCK OPTION GRANT

Participant Name:

Address:

The undersigned Participant has been granted an Option to purchase Common Stock of Denali Therapeutics Inc. (the "Company"), subject to the terms and conditions of the Plan and this Option Agreement, as follows:

Grant Number:	
Date of Grant:	
Vesting Commencement Date:	
Number of Shares Granted:	
Exercise Price per Share:	$
Total Exercise Price:	$
Type of Option:	___ Incentive Stock Option
	___ Nonstatutory Stock Option
Term/Expiration Date:	

Vesting Schedule:

Subject to accelerated vesting as set forth below or in the Plan, this Option will be exercisable, in whole or in part, in accordance with the following schedule:

[*Insert Vesting Schedule, e.g.:* Twenty-five percent (25%) of the Shares subject to the Option shall vest on the one (1) year anniversary of the Vesting Commencement Date, and one forty-eighth (1/48th) of the Shares subject to the Option shall vest each month thereafter on the same day of the month as the Vesting Commencement Date (and if there is no corresponding day, on the last day of the month), subject to Participant continuing to be a Service Provider through each such date.]

Termination Period:

This Option will be exercisable for [three (3) months] after Participant ceases to be a Service Provider, unless such termination is due to Participant's death or Disability, in which case this Option will be exercisable for [twelve (12) months] after Participant ceases to be a Service Provider. Notwithstanding the foregoing sentence, in no event may this Option be exercised after the Term/Expiration Date as provided above and may be subject to earlier termination as provided in Section 14 of the Plan.

Participant acknowledges receipt of a copy of the Plan and represents that he or she is familiar with the terms and provisions thereof, and hereby accepts this Option Agreement subject to all of the terms and provisions thereof. Participant has reviewed the Plan and this Option Agreement in their entirety, has had an opportunity to obtain the advice of counsel prior to executing this Option Agreement and fully understands all provisions of this Option and the Option Agreement. Participant hereby agrees to accept as binding, conclusive and final all decisions or interpretations of the Administrator upon any questions arising under the Plan or this Option Agreement. Participant further agrees to notify the Company upon any change in the residence address indicated below.

PARTICIPANT	DENALI THERAPEUTICS INC.
_____	_____
Signature	Signature
_____	_____
Print Name	Print Name
	_____
	Title
Address:	
_____	
_____	

EXHIBIT A

TERMS AND CONDITIONS OF STOCK OPTION GRANT

1. Grant of Option. The Company hereby grants to the individual (the "Participant") named in the Notice of Stock Option Grant of this Option Agreement (the "Notice of Grant") an option (the "Option") to purchase the number of Shares, as set forth in the Notice of Grant, at the exercise price per Share set forth in the Notice of Grant (the "Exercise Price"), subject to all of the terms and conditions in this Option Agreement and the Plan, which is incorporated herein by reference. Subject to Section 19(c) of the Plan, in the event of a conflict between the terms and conditions of the Plan and the terms and conditions of this Option Agreement, the terms and conditions of the Plan will prevail.

(a) For U.S. taxpayers, the Option will be designated as either an Incentive Stock Option ("ISO") or a Nonstatutory Stock Option ("NSO"). If designated in the Notice of Grant as an ISO, this Option is intended to qualify as an ISO under Section 422 of the Internal Revenue Code of 1986, as amended (the "Code"). However, if this Option is intended to be an ISO, to the extent that it exceeds the $100,000 rule of Code Section 422(d) it will be treated as an NSO. Further, if for any reason this Option (or portion thereof) will not qualify as an ISO, then, to the extent of such nonqualification, such Option (or portion thereof) shall be regarded as a NSO granted under the Plan. In no event will the Administrator, the Company or any Parent or Subsidiary or any of their respective employees or directors have any liability to Participant (or any other person) due to the failure of the Option to qualify for any reason as an ISO.

(b) For non-U.S. taxpayers, the Option will be designated as an NSO.

2. Vesting Schedule. Except as provided in Section 3, the Option awarded by this Option Agreement will vest in accordance with the vesting provisions set forth in the Notice of Grant. Shares scheduled to vest on a certain date or upon the occurrence of a certain condition will not vest in Participant in accordance with any of the provisions of this Option Agreement, unless Participant will have been continuously a Service Provider from the Date of Grant until the date such vesting occurs.

3. Administrator Discretion. The Administrator, in its discretion, may accelerate the vesting of the balance, or some lesser portion of the balance, of the unvested Option at any time, subject to the terms of the Plan. If so accelerated, such Option will be considered as having vested as of the date specified by the Administrator.

4. Exercise of Option.

(a) Right to Exercise. This Option may be exercised only within the term set out in the Notice of Grant, and may be exercised during such term only in accordance with the Plan and the terms of this Option Agreement.

(b) Method of Exercise. This Option is exercisable by delivery of an exercise notice (the "Exercise Notice") in the form attached as Exhibit A or in a manner and pursuant to such procedures as the Administrator may determine, which will state the election to exercise the Option, the number of Shares in respect of which the Option is being exercised (the "Exercised Shares"), and such other representations and agreements as may be required by the Company pursuant to the provisions of the Plan. The Exercise Notice will be completed by Participant and delivered to the Company. The Exercise Notice will be accompanied by payment of the aggregate Exercise Price as to all Exercised Shares together and of any Tax Obligations (as defined in Section 6(a)). This Option will be deemed to be exercised upon receipt by the Company of such fully executed Exercise Notice accompanied by the aggregate Exercise Price.

5. Method of Payment. Payment of the aggregate Exercise Price will be by any of the following, or a combination thereof, at the election of Participant:

(a) cash in U.S. dollars;

(b) check designated in U.S. dollars;

(c) consideration received by the Company under a formal cashless exercise program adopted by the Company in connection with the Plan; or

(d) if Participant is a U.S. employee, surrender of other Shares which have a Fair Market Value on the date of surrender equal to the aggregate Exercise Price of the Exercised Shares and that are owned free and clear of any liens, claims, encumbrances, or security interests, provided that accepting such Shares, in the sole discretion of the Administrator, will not result in any adverse accounting consequences to the Company.

6. Tax Obligations.

(a) Participant acknowledges that, regardless of any action taken by the Company or, if different, Participant's employer (the "Employer") or Parent or Subsidiary to which Participant is providing services (together, the Company, Employer and/or Parent or Subsidiary to which the Participant is providing services, the "Service Recipient"), the ultimate liability for any tax and/or social insurance liability obligations and requirements in connection with the Option, including, without limitation, (i) all federal, state, and local taxes (including the Participant's Federal Insurance Contributions Act (FICA) obligation) that are required to be withheld by the Company or the Service Recipient or other payment of tax-related items related to Participant's participation in the Plan and legally applicable to Participant, (ii) the Participant's and, to the extent required by the Company (or Service Recipient), the Company's (or Service Recipient's) fringe benefit tax liability, if any, associated with the grant, vesting, or exercise of the Option or sale of Shares, and (iii) any other Company (or Service Recipient) taxes the responsibility for which the Participant has, or has agreed to bear, with respect to the Option (or exercise thereof or issuance of Shares thereunder) (collectively, the "Tax Obligations"), is and remains Participant's responsibility and may exceed the amount actually withheld by the Company or the Service Recipient. Participant further acknowledges that the Company and/or the Service Recipient (A) make no representations or undertakings regarding the treatment of any Tax Obligations in connection with any aspect of the

Option, including, but not limited to, the grant, vesting or exercise of the Option, the subsequent sale of Shares acquired pursuant to such exercise and the receipt of any dividends or other distributions, and (B) do not commit to and are under no obligation to structure the terms of the grant or any aspect of the Option to reduce or eliminate Participant's liability for Tax Obligations or achieve any particular tax result. Further, if Participant is subject to Tax Obligations in more than one jurisdiction between the Date of Grant and the date of any relevant taxable or tax withholding event, as applicable, Participant acknowledges that the Company and/or the Service Recipient (or former employer, as applicable) may be required to withhold or account for Tax Obligations in more than one jurisdiction. If Participant fails to make satisfactory arrangements for the payment of any required Tax Obligations hereunder at the time of the applicable taxable event, Participant acknowledges and agrees that the Company may refuse to issue or deliver the Shares.

(b) Tax Withholding. When the Option is exercised, Participant generally will recognize immediate U.S. taxable income if Participant is a U.S. taxpayer. If Participant is a non-U.S. taxpayer, Participant will be subject to applicable taxes in his or her jurisdiction. Pursuant to such procedures as the Administrator may specify from time to time, the Company and/or Service Recipient shall withhold the amount required to be withheld for the payment of Tax Obligations. The Administrator, in its sole discretion and pursuant to such procedures as it may specify from time to time, may permit Participant to satisfy such Tax Obligations, in whole or in part (without limitation), if permissible by applicable local law, by (i) paying cash, (ii) electing to have the Company withhold otherwise deliverable Shares having a fair market value equal to the minimum amount that is necessary to meet the withholding requirement for such Tax Obligations (or such greater amount as Participant may elect if permitted by the Administrator, if such greater amount would not result in adverse financial accounting consequences), (iii) withholding the amount of such Tax Obligations from Participant's wages or other cash compensation paid to Participant by the Company and/or the Service Recipient, (iv) delivering to the Company already vested and owned Shares having a fair market value equal to such Tax Obligations, or (v) selling a sufficient number of such Shares otherwise deliverable to Participant through such means as the Company may determine in its sole discretion (whether through a broker or otherwise) equal to the minimum amount that is necessary to meet the withholding requirement for such Tax Obligations (or such greater amount as Participant may elect if permitted by the Administrator, if such greater amount would not result in adverse financial accounting consequences). To the extent determined appropriate by the Company in its discretion, it will have the right (but not the obligation) to satisfy any Tax Obligations by reducing the number of Shares otherwise deliverable to Participant. Further, if Participant is subject to tax in more than one jurisdiction between the Date of Grant and a date of any relevant taxable or tax withholding event, as applicable, Participant acknowledges and agrees that the Company and/or the Service Recipient (and/or former employer, as applicable) may be required to withhold or account for tax in more than one jurisdiction. If Participant fails to make satisfactory arrangements for the payment of any required Tax Obligations hereunder at the time of the Option exercise, Participant acknowledges and agrees that the Company may refuse to honor the exercise and refuse to deliver the Shares if such amounts are not delivered at the time of exercise.

(c) Notice of Disqualifying Disposition of ISO Shares. If the Option granted to Participant herein is an ISO, and if Participant sells or otherwise disposes of any of the Shares acquired pursuant to the ISO on or before the later of (i) the date two (2) years after the Date of Grant, or (ii) the date one (1) year after the date of exercise, Participant will immediately notify the Company in writing of such disposition. Participant agrees that Participant may be subject to income tax withholding by the Company on the compensation income recognized by Participant.

(d) Code Section 409A. Under Code Section 409A, a stock right (such as the Option) that vests after December 31, 2004 (or that vested on or prior to such date but which was materially modified after October 3, 2004) that was granted with a per share exercise price that is determined by the Internal Revenue Service (the "IRS") to be less than the fair market value of an underlying share on the date of grant (a "discount option") may be considered "deferred compensation." A stock right that is a "discount option" may result in (i) income recognition by the recipient of the stock right prior to the exercise of the stock right, (ii) an additional twenty percent (20%) federal income tax, and (iii) potential penalty and interest charges. The "discount option" may also result in additional state income, penalty and interest tax to the recipient of the stock right. Participant acknowledges that the Company cannot and has not guaranteed that the IRS will agree that the per Share exercise price of this Option equals or exceeds the fair market value of a Share on the date of grant in a later examination. Participant agrees that if the IRS determines that the Option was granted with a per Share exercise price that was less than the fair market value of a Share on the date of grant, Participant shall be solely responsible for Participant's costs related to such a determination.

7. Rights as Stockholder. Neither Participant nor any person claiming under or through Participant will have any of the rights or privileges of a stockholder of the Company in respect of any Shares deliverable hereunder unless and until certificates representing such Shares (which may be in book entry form) will have been issued, recorded on the records of the Company or its transfer agents or registrars, and delivered to Participant (including through electronic delivery to a brokerage account). After such issuance, recordation and delivery, Participant will have all the rights of a stockholder of the Company with respect to voting such Shares and receipt of dividends and distributions on such Shares.

8. No Guarantee of Continued Service. PARTICIPANT ACKNOWLEDGES AND AGREES THAT THE VESTING OF SHARES PURSUANT TO THE VESTING SCHEDULE HEREOF IS EARNED ONLY BY CONTINUING AS A SERVICE PROVIDER, WHICH UNLESS PROVIDED OTHERWISE UNDER APPLICABLE LAW IS AT THE WILL OF THE COMPANY (OR THE SERVICE RECIPIENT) AND NOT THROUGH THE ACT OF BEING HIRED, BEING GRANTED THIS OPTION OR ACQUIRING SHARES HEREUNDER. PARTICIPANT FURTHER ACKNOWLEDGES AND AGREES THAT THIS OPTION AGREEMENT, THE TRANSACTIONS CONTEMPLATED HEREUNDER AND THE VESTING SCHEDULE SET FORTH HEREIN DO NOT CONSTITUTE AN EXPRESS OR IMPLIED PROMISE OF CONTINUED ENGAGEMENT AS A SERVICE PROVIDER FOR THE VESTING PERIOD, FOR ANY PERIOD, OR AT ALL, AND WILL NOT INTERFERE IN ANY WAY WITH PARTICIPANT'S RIGHT OR THE RIGHT OF THE COMPANY (OR THE SERVICE RECIPIENT) TO TERMINATE PARTICIPANT'S RELATIONSHIP AS A SERVICE PROVIDER, SUBJECT TO APPLICABLE LAW, WHICH TERMINATION, UNLESS PROVIDED OTHERWISE UNDER APPLICABLE LAW, MAY BE AT ANY TIME, WITH OR WITHOUT CAUSE.

9. Nature of Grant. In accepting the Option, Participant acknowledges, understands and agrees that:

(a) the grant of the Option is voluntary and occasional and does not create any contractual or other right to receive future grants of options, or benefits in lieu of options, even if options have been granted in the past;

(b) all decisions with respect to future option or other grants, if any, will be at the sole discretion of the Company;

(c) Participant is voluntarily participating in the Plan;

(d) the Option and any Shares acquired under the Plan are not intended to replace any pension rights or compensation;

(e) the Option and Shares acquired under the Plan and the income and value of same, are not part of normal or expected compensation for purposes of calculating any severance, resignation, termination, redundancy, dismissal, end-of-service payments, bonuses, long-service awards, pension or retirement or welfare benefits or similar payments;

(f) the future value of the Shares underlying the Option is unknown, indeterminable, and cannot be predicted with certainty;

(g) if the underlying Shares do not increase in value, the Option will have no value;

(h) if Participant exercises the Option and acquires Shares, the value of such Shares may increase or decrease in value, even below the Exercise Price;

(i) for purposes of the Option, Participant's engagement as a Service Provider will be considered terminated as of the date Participant is no longer actively providing services to the Company or any Parent or Subsidiary (regardless of the reason for such termination and whether or not later found to be invalid or in breach of employment laws in the jurisdiction where Participant is a Service Provider or the terms of Participant's employment or service agreement, if any), and unless otherwise expressly provided in this Option Agreement (including by reference in the Notice of Grant to other arrangements or contracts) or determined by the Administrator, (i) Participant's right to vest in the Option under the Plan, if any, will terminate as of such date and will not be extended by any notice period (*e.g.*, Participant's period of service would not include any contractual notice period or any period of "garden leave" or similar period mandated under employment laws in the jurisdiction where Participant is a Service Provider or Participant's employment or service agreement, if any, unless Participant is providing bona fide services during such time); and (ii) the period (if any) during which Participant may exercise the Option after such termination of Participant's engagement as a Service Provider will commence on the date Participant ceases to actively provide services and will not be extended by any notice period mandated under employment laws in the jurisdiction where Participant is employed or terms of Participant's engagement agreement, if any; the Administrator shall have the exclusive discretion to determine when Participant is no longer actively providing services for purposes of his or her Option grant (including whether Participant may still be considered to be providing services while on a leave of absence and consistent with local law);

(j) unless otherwise provided in the Plan or by the Company in its discretion, the Option and the benefits evidenced by this Option Agreement do not create any entitlement to have the Option or any such benefits transferred to, or assumed by, another company nor to be exchanged, cashed out or substituted for, in connection with any corporate transaction affecting the Shares; and

(k) the following provisions apply only if Participant is providing services outside the United States:

(i) the Option and the Shares subject to the Option are not part of normal or expected compensation or salary for any purpose;

(ii) Participant acknowledges and agrees that none of the Company, the Service Recipient, or any Parent or Subsidiary shall be liable for any foreign exchange rate fluctuation between Participant's local currency and the United States Dollar that may affect the value of the Option or of any amounts due to Participant pursuant to the exercise of the Option or the subsequent sale of any Shares acquired upon exercise; and

(iii) no claim or entitlement to compensation or damages shall arise from forfeiture of the Option resulting from the termination of Participant's engagement as a Service Provider (for any reason whatsoever, whether or not later found to be invalid or in breach of employment laws in the jurisdiction where Participant is a Service Provider or the terms of Participant's employment or service agreement, if any), and in consideration of the grant of the Option to which Participant is otherwise not entitled, Participant irrevocably agrees never to institute any claim against the Company, any Parent, any Subsidiary or the Service Recipient, waives his or her ability, if any, to bring any such claim, and releases the Company, any Parent or Subsidiary and the Service Recipient from any such claim; if, notwithstanding the foregoing, any such claim is allowed by a court of competent jurisdiction, then, by participating in the Plan, Participant shall be deemed irrevocably to have agreed not to pursue such claim and agrees to execute any and all documents necessary to request dismissal or withdrawal of such claim.

10. No Advice Regarding Grant. The Company is not providing any tax, legal or financial advice, nor is the Company making any recommendations regarding Participant's participation in the Plan, or Participant's acquisition or sale of the underlying Shares. Participant is hereby advised to consult with his or her own personal tax, legal and financial advisors regarding his or her participation in the Plan before taking any action related to the Plan.

11. **Data Privacy**. ***Participant hereby explicitly and unambiguously consents to the collection, use and transfer, in electronic or other form, of Participant's personal data as described in this Option Agreement and any other Option grant materials by and among, as applicable, the Employer or other Service Recipient, the Company and any Parent or Subsidiary for the exclusive purpose of implementing, administering and managing Participant's participation in the Plan.***

Participant understands that the Company and the Employer may hold certain personal information about Participant, including, but not limited to, Participant's name, home address and telephone number, date of birth, social insurance number or other identification number, salary, nationality, job title, any Shares or directorships held in the Company, details of all Options or any other entitlement to Shares awarded, canceled, exercised, vested, unvested or outstanding in Participant's favor ("Data"), for the exclusive purpose of implementing, administering and managing the Plan.

Participant understands that Data will be transferred to a stock plan service provider as may be selected by the Company in the future, which is assisting the Company with the implementation, administration and management of the Plan. Participant understands that the recipients of the Data may be located in the United States or elsewhere, and that the recipient's country of operation (e.g., the United States) may have different data privacy laws and protections than Participant's country. Participant understands that if he or she resides outside the United States, he or she may request a list with the names and addresses of any potential recipients of the Data by contacting his or her local human resources representative. Participant authorizes the Company and any other possible recipients which may assist the Company (presently or in the future) with implementing, administering and managing the Plan to receive, possess, use, retain and transfer the Data, in electronic or other form, for the sole purposes of implementing, administering and managing Participant's participation in the Plan. Participant understands that Data will be held only as long as is necessary to implement, administer and manage Participant's participation in the Plan. Participant understands that if he or she resides outside the United States, he or she may, at any time, view Data, request additional information about the storage and processing of Data, require any necessary amendments to Data or refuse or withdraw the consents herein, in any case without cost, by contacting in writing his or her local human resources representative. Further, Participant understands that he or she is providing the consents herein on a purely voluntary basis. If Participant does not consent, or if Participant later seeks to revoke his or her consent, his or her engagement as a Service Provider and career with the Employer will not be adversely affected; the only adverse consequence of refusing or withdrawing Participant's consent is that the Company would not be able to grant Participant Options or other equity awards or administer or maintain such awards. Therefore, Participant understands that refusing or withdrawing his or her consent may affect Participant's ability to participate in the Plan. For more information on the consequences of Participant's refusal to consent or withdrawal of consent, Participant understands that he or she may contact his or her local human resources representative.

12. Address for Notices. Any notice to be given to the Company under the terms of this Option Agreement will be addressed to the Company at Denali Therapeutics Inc., 151 Oyster Point Blvd., South San Francisco, CA 94080, or at such other address as the Company may hereafter designate in writing.

13. Non-Transferability of Option. This Option may not be transferred in any manner otherwise than by will or by the laws of descent or distribution and may be exercised during the lifetime of Participant only by Participant.

14. Successors and Assigns. The Company may assign any of its rights under this Option Agreement to single or multiple assignees, and this Option Agreement shall inure to the benefit of the successors and assigns of the Company. Subject to the restrictions on transfer herein set forth, this Option Agreement shall be binding upon Participant and his or her heirs, executors, administrators, successors and assigns. The rights and obligations of Participant under this Option Agreement may only be assigned with the prior written consent of the Company.

15. Additional Conditions to Issuance of Stock. If at any time the Company will determine, in its discretion, that the listing, registration, qualification or rule compliance of the Shares upon any securities exchange or under any state, federal or non-U.S. law, the tax code and related regulations or under the rulings or regulations of the United States Securities and Exchange Commission or any other governmental regulatory body or the clearance, consent or approval of the United States Securities and Exchange Commission or any other governmental regulatory authority is necessary or desirable as a condition to the purchase by, or issuance of Shares, to Participant (or his or her estate) hereunder, such purchase or issuance will not occur unless and until such listing, registration, qualification, rule compliance, clearance, consent or approval will have been completed, effected or obtained free of any conditions not acceptable to the Company. Subject to the terms of the Option Agreement and the Plan, the Company shall not be required to issue any certificate or certificates for Shares hereunder prior to the lapse of such reasonable period of time following the date of exercise of the Option as the Administrator may establish from time to time for reasons of administrative convenience.

16. Language. If Participant has received this Option Agreement or any other document related to the Plan translated into a language other than English and if the meaning of the translated version is different than the English version, the English version will control.

17. Interpretation. The Administrator will have the power to interpret the Plan and this Option Agreement and to adopt such rules for the administration, interpretation and application of the Plan as are consistent therewith and to interpret or revoke any such rules (including, but not limited to, the determination of whether or not any Shares subject to the Option have vested). All actions taken and all interpretations and determinations made by the Administrator in good faith will be final and binding upon Participant, the Company and all other interested persons. Neither the Administrator nor any person acting on behalf of the Administrator will be personally liable for any action, determination or interpretation made in good faith with respect to the Plan or this Option Agreement.

18. Electronic Delivery and Acceptance. The Company may, in its sole discretion, decide to deliver any documents related to the Option awarded under the Plan or future options that may be awarded under the Plan by electronic means or request Participant’s consent to participate in the Plan by electronic means. Participant hereby consents to receive such documents by electronic delivery and agrees to participate in the Plan through any on-line or electronic system established and maintained by the Company or a third party designated by the Company.

19. Captions. Captions provided herein are for convenience only and are not to serve as a basis for interpretation or construction of this Option Agreement.

20. Agreement Severable. In the event that any provision in this Option Agreement will be held invalid or unenforceable, such provision will be severable from, and such invalidity or unenforceability will not be construed to have any effect on, the remaining provisions of this Option Agreement.

21. Amendment, Suspension or Termination of the Plan. By accepting this Option, Participant expressly warrants that he or she has received an Option under the Plan, and has received, read and understood a description of the Plan. Participant understands that the Plan is discretionary in nature and may be amended, suspended or terminated by the Company at any time.

22. Governing Law and Venue. This Option Agreement will be governed by the laws of California, without giving effect to the conflict of law principles thereof. For purposes of litigating any dispute that arises under this Option or this Option Agreement, the parties hereby submit to and consent to the jurisdiction of the State of California, and agree that such litigation will be conducted in the courts of San Mateo County, California, or the federal courts for the United States for the Northern District of California, and no other courts, where this Option is made and/or to be performed.

23. Country Addendum. Notwithstanding any provisions in this Option Agreement, this Option shall be subject to any special terms and conditions set forth in the appendix (if any) to this Option Agreement for Participant's country (the "Country Addendum"). Moreover, if Participant relocates to one of the countries included in the Country Addendum (if any), the special terms and conditions for such country will apply to Participant, to the extent the Company determines that the application of such terms and conditions is necessary or advisable for legal or administrative reasons. The Country Addendum constitutes part of this Option Agreement.

24. Modifications to the Agreement. This Option Agreement constitutes the entire understanding of the parties on the subjects covered. Participant expressly warrants that he or she is not accepting this Option Agreement in reliance on any promises, representations, or inducements other than those contained herein. Modifications to this Option Agreement or the Plan can be made only in an express written contract executed by a duly authorized officer of the Company. Notwithstanding anything to the contrary in the Plan or this Option Agreement, the Company reserves the right to revise this Option Agreement as it deems necessary or advisable, in its sole discretion and without the consent of Participant, to comply with Code Section 409A or to otherwise avoid imposition of any additional tax or income recognition under Section 409A of the Code in connection with the Option.

25. No Waiver. Either party's failure to enforce any provision or provisions of this Option Agreement shall not in any way be construed as a waiver of any such provision or provisions, nor prevent that party from thereafter enforcing each and every other provision of this Option Agreement. The rights granted both parties herein are cumulative and shall not constitute a waiver of either party's right to assert all other legal remedies available to it under the circumstances.

26. Tax Consequences. Participant has reviewed with its own tax advisors the U.S. federal, state, local and non-U.S. tax consequences of this investment and the transactions contemplated by this Option Agreement. With respect to such matters, Participant relies solely on such advisors and not on any statements or representations of the Company or any of its agents, written or oral. Participant understands that Participant (and not the Company) shall be responsible for Participant's own tax liability that may arise as a result of this investment or the transactions contemplated by this Option Agreement.

EXHIBIT B

DENALI THERAPEUTICS INC.

2017 EQUITY INCENTIVE PLAN

EXERCISE NOTICE

Denali Therapeutics Inc.
151 Oyster Point Blvd.
South San Francisco, CA 94080

Attention: Stock Administration

1. Exercise of Option. Effective as of today, , , the undersigned ("Purchaser") hereby elects to purchase shares (the "Shares") of the Common Stock of Denali Therapeutics Inc. (the "Company") under and pursuant to the 2017 Equity Incentive Plan (the "Plan") and the Stock Option Agreement, dated and including the Notice of Grant, the Terms and Conditions of Stock Option Grant, and exhibits attached thereto (the "Option Agreement"). The purchase price for the Shares will be $, as required by the Option Agreement.

2. Delivery of Payment. Purchaser herewith delivers to the Company the full purchase price of the Shares and any Tax Obligations (as defined in Section 6(a) of the Option Agreement) to be paid in connection with the exercise of the Option.

3. Representations of Purchaser. Purchaser acknowledges that Purchaser has received, read and understood the Plan and the Option Agreement and agrees to abide by and be bound by their terms and conditions.

4. Rights as Stockholder. Until the issuance (as evidenced by the appropriate entry on the books of the Company or of a duly authorized transfer agent of the Company) of the Shares, no right to vote or receive dividends or any other rights as a stockholder will exist with respect to the Shares subject to the Option, notwithstanding the exercise of the Option. The Shares so acquired will be issued to Purchaser as soon as practicable after exercise of the Option. No adjustment will be made for a dividend or other right for which the record date is prior to the date of issuance, except as provided in Section 14 of the Plan.

5. Tax Consultation. Purchaser understands that Purchaser may suffer adverse tax consequences as a result of Purchaser's purchase or disposition of the Shares. Purchaser represents that Purchaser has consulted with any tax consultants Purchaser deems advisable in connection with the purchase or disposition of the Shares and that Purchaser is not relying on the Company for any tax advice.

6. Entire Agreement; Governing Law. The Plan and Option Agreement are incorporated herein by reference. This Exercise Notice, the Plan and the Option Agreement constitute the entire agreement of the parties with respect to the subject matter hereof and supersede in their entirety all prior undertakings and agreements of the Company and Purchaser with respect to the subject matter hereof, and may not be modified adversely to the Purchaser's interest except by means of a writing signed by the Company and Purchaser. This Option Agreement is governed by the internal substantive laws, but not the choice of law rules, of California.

Submitted by:

PURCHASER

Signature

Print Name

Address:

Accepted by:

DENALI THERAPEUTICS INC.

Signature

Print Name

Title

Date Received

DENALI THERAPEUTICS INC.
2017 EQUITY INCENTIVE PLAN
STOCK OPTION AGREEMENT
COUNTRY ADDENDUM

Terms and Conditions

This Appendix includes additional terms and conditions that govern the Stock Options (Options) granted to Participant under the Plan if he or she resides in one of the countries listed below. Certain capitalized terms used but not defined in this Appendix have the meanings set forth in the Plan and/or the main body of the Award Agreement.

Notifications

This Appendix also includes information regarding exchange controls and certain other issues of which Participant should be aware with respect to his or her participation in the Plan. The information is based on the securities, exchange control and other laws in effect in the respective countries as of October 2016. Such laws are often complex and change frequently. As a result, the Company strongly recommends that Participant not rely on the information in this Appendix as the only source of information relating to the consequences of Participant's participation in the Plan because the information may be out of date at the time Participant exercises the Options or sells the Shares acquired under the Plan.

In addition, the information contained herein is general in nature and may not apply to Participant's particular situation and the Company is not in a position to assure Participant of any particular result. Accordingly, Participant is advised to seek appropriate professional advice as to how the relevant laws of Participant's country may apply to his or her situation.

Finally, if Participant is a citizen or resident of a country other than the one in which Participant is currently working or transfers to another country after the grant of the Stock Options, or is considered a resident of another country for local law purposes, the information contained herein may not be applicable to Participant in the same manner. In addition, the Company shall, in its discretion, determine to what extent the terms and conditions contained herein shall apply to Participant under these circumstances.

[JURISDICTION-SPECIFIC COUNTRY ADDENDA TO BE INSERTED IF/AS APPROPRIATE]

DENALI THERAPEUTICS INC.
2017 EQUITY INCENTIVE PLAN
RESTRICTED STOCK UNIT AGREEMENT

NOTICE OF RESTRICTED STOCK UNIT GRANT

Unless otherwise defined herein, the terms defined in the Denali Therapeutics Inc. 2017 Equity Incentive Plan (the "Plan") will have the same defined meanings in this Restricted Stock Unit Agreement which includes the Notice of Restricted Stock Unit Grant (the "Notice of Grant"), Terms and Conditions of Restricted Stock Unit Grant, attached hereto as Exhibit A, and all appendices and exhibits attached thereto (the "Award Agreement").

Participant Name:
Address:

The undersigned Participant has been granted the right to receive an Award of Restricted Stock Units, subject to the terms and conditions of the Plan and this Award Agreement, as follows:

Grant Number:

Date of Grant:

Vesting Commencement Date:

Number of Restricted Stock Units:

Vesting Schedule:

Subject to any acceleration provisions contained in the Plan or set forth below, the Restricted Stock Units will vest in accordance with the following schedule:

[*Insert Vesting Schedule, e.g.:* Twenty-five percent (25%) of the Restricted Stock Units will vest on the one (1) year anniversary of the Vesting Commencement Date, and twenty-five percent (25%) of the Restricted Stock Units will vest each year thereafter on the same day as the Vesting Commencement Date, subject to Participant continuing to be a Service Provider through each such date.**]**

In the event Participant ceases to be a Service Provider for any or no reason before Participant vests in the Restricted Stock Units, the Restricted Stock Units and Participant's right to acquire any Shares hereunder will immediately terminate.

By Participant's signature and the signature of the representative of Denali Therapeutics Inc. (the "Company") below, Participant and the Company agree that this Award of Restricted Stock Units is granted under and governed by the terms and conditions of the Plan and this Award Agreement, including the Terms and Conditions of Restricted Stock Unit Grant, attached hereto as Exhibit A, all of which are made a part of this document. Participant acknowledges receipt of a copy of the Plan. Participant has reviewed the Plan and this Award Agreement in their entirety, has had

an opportunity to obtain the advice of counsel prior to executing this Award Agreement and fully understands all provisions of the Plan and this Award Agreement. Participant hereby agrees to accept as binding, conclusive and final all decisions or interpretations of the Administrator upon any questions relating to the Plan and Award Agreement. Participant further agrees to notify the Company upon any change in the residence address indicated below.

PARTICIPANT:	DENALI THERAPEUTICS INC.
Signature	Signature
«Name»	
Print Name	Print Name
	Title

Address:

«Address»

EXHIBIT A

TERMS AND CONDITIONS OF RESTRICTED STOCK UNIT GRANT

1. Grant of Restricted Stock Units. The Company hereby grants to the individual (the "Participant") named in the Notice of Grant of Restricted Stock Units of this Award Agreement (the "Notice of Grant") under the Plan an Award of Restricted Stock Units, subject to all of the terms and conditions in this Award Agreement and the Plan, which is incorporated herein by reference. Subject to Section 19(c) of the Plan, in the event of a conflict between the terms and conditions of the Plan and this Award Agreement, the terms and conditions of the Plan shall prevail.

2. Company's Obligation to Pay. Each Restricted Stock Unit represents the right to receive a Share on the date it vests. Unless and until the Restricted Stock Units will have vested in the manner set forth in Section 3 or 4, Participant will have no right to payment of any such Restricted Stock Units. Prior to actual payment of any vested Restricted Stock Units, such Restricted Stock Unit will represent an unsecured obligation of the Company, payable (if at all) only from the general assets of the Company.

3. Vesting Schedule. Except as provided in Section 4, and subject to Section 5, the Restricted Stock Units awarded by this Award Agreement will vest in accordance with the vesting schedule set forth in the Notice of Grant, subject to Participant continuing to be a Service Provider through each applicable vesting date.

4. Payment after Vesting.

(a) General Rule. Subject to Section 8, any Restricted Stock Units that vest will be paid to Participant (or in the event of Participant's death, to his or her properly designated beneficiary or estate) in whole Shares. Subject to the provisions of Section 4(b), such vested Restricted Stock Units shall be paid in whole Shares as soon as practicable after vesting, but in each such case within sixty (60) days following the vesting date. In no event will Participant be permitted, directly or indirectly, to specify the taxable year of payment of any Restricted Stock Units payable under this Award Agreement.

(b) Acceleration.

(i) Discretionary Acceleration. The Administrator, in its discretion, may accelerate the vesting of the balance, or some lesser portion of the balance, of the unvested Restricted Stock Units at any time, subject to the terms of the Plan. If so accelerated, such Restricted Stock Units will be considered as having vested as of the date specified by the Administrator. If Participant is a U.S. taxpayer, the payment of Shares vesting pursuant to this Section 4(b) shall in all cases be paid at a time or in a manner that is exempt from, or complies with, Section 409A. The prior sentence may be superseded in a future agreement or amendment to this Award Agreement only by direct and specific reference to such sentence.

(ii) Notwithstanding anything in the Plan or this Award Agreement or any other agreement (whether entered into before, on or after the Date of Grant), if the vesting of the balance, or some lesser portion of the balance, of the Restricted Stock Units is accelerated in connection with Participant's termination as a Service Provider (provided that such termination is a "separation from service" within the meaning of Section 409A, as determined by the Company), other than due to Participant's death, and if (x) Participant is a U.S. taxpayer and a "specified employee" within the meaning of Section 409A at the time of such termination as a Service Provider and (y) the payment of such accelerated Restricted Stock Units will result in the imposition of additional tax under Section 409A if paid to Participant on or within the six (6) month period following Participant's termination as a Service Provider, then the payment of such accelerated Restricted Stock Units will not be made until the date six (6) months and one (1) day following the date of Participant's termination as a Service Provider, unless Participant dies following his or her termination as a Service Provider, in which case, the Restricted Stock Units will be paid in Shares to Participant's estate as soon as practicable following his or her death.

(c) Section 409A. It is the intent of this Award Agreement that it and all payments and benefits to U.S. taxpayers hereunder be exempt from, or comply with, the requirements of Section 409A so that none of the Restricted Stock Units provided under this Award Agreement or Shares issuable thereunder will be subject to the additional tax imposed under Section 409A, and any ambiguities herein will be interpreted to be so exempt or so comply. Each payment payable under this Award Agreement is intended to constitute a separate payment for purposes of Treasury Regulation Section 1.409A-2(b)(2). However, in no event will the Company reimburse Participant, or be otherwise responsible for, any taxes or costs that may be imposed on Participant as a result of Section 409A. For purposes of this Award Agreement, "Section 409A" means Section 409A of the Code, and any final Treasury Regulations and Internal Revenue Service guidance thereunder, as each may be amended from time to time.

5. Forfeiture Upon Termination as a Service Provider. Notwithstanding any contrary provision of this Award Agreement, if Participant ceases to be a Service Provider for any or no reason, the then-unvested Restricted Stock Units awarded by this Award Agreement will thereupon be forfeited at no cost to the Company and Participant will have no further rights thereunder.

6. Tax Consequences. Participant has reviewed with his or her own tax advisors the U.S. federal, state, local and non-U.S. tax consequences of this investment and the transactions contemplated by this Award Agreement. With respect to such matters, Participant relies solely on such advisors and not on any statements or representations of the Company or any of its agents, written or oral. Participant understands that Participant (and not the Company) shall be responsible for Participant's own tax liability that may arise as a result of this investment or the transactions contemplated by this Award Agreement.

7. Death of Participant. Any distribution or delivery to be made to Participant under this Award Agreement will, if Participant is then deceased, be made to Participant's designated beneficiary, or if no beneficiary survives Participant, the administrator or executor of Participant's estate. Any such transferee must furnish the Company with (a) written notice of his or her status as transferee, and (b) evidence satisfactory to the Company to establish the validity of the transfer and compliance with any laws or regulations pertaining to said transfer.

8. Tax Obligations

(a) Responsibility for Taxes. Participant acknowledges that, regardless of any action taken by the Company or, if different, Participant's employer (the "Employer") or Parent or Subsidiary to which Participant is providing services (together, the Company, Employer and/or Parent or Subsidiary to which the Participant is providing services, the "Service Recipient"), the ultimate liability for any tax and/or social insurance liability obligations and requirements in connection with the Restricted Stock Units, including, without limitation, (i) all federal, state, and local taxes (including the Participant's Federal Insurance Contributions Act (FICA) obligation) that are required to be withheld by the Company or the Employer or other payment of tax-related items related to Participant's participation in the Plan and legally applicable to Participant, (ii) the Participant's and, to the extent required by the Company (or Service Recipient), the Company's (or Service Recipient's) fringe benefit tax liability, if any, associated with the grant, vesting, or settlement of the Restricted Stock Units or sale of Shares, and (iii) any other Company (or Service Recipient) taxes the responsibility for which the Participant has, or has agreed to bear, with respect to the Restricted Stock Units (or settlement thereof or issuance of Shares thereunder) (collectively, the "Tax Obligations"), is and remains Participant's responsibility and may exceed the amount actually withheld by the Company or the Service Recipient. Participant further acknowledges that the Company and/or the Service Recipient (A) make no representations or undertakings regarding the treatment of any Tax Obligations in connection with any aspect of the Restricted Stock Units, including, but not limited to, the grant, vesting or settlement of the Restricted Stock Units, the subsequent sale of Shares acquired pursuant to such settlement and the receipt of any dividends or other distributions, and (B) do not commit to and are under no obligation to structure the terms of the grant or any aspect of the Restricted Stock Units to reduce or eliminate Participant's liability for Tax Obligations or achieve any particular tax result. Further, if Participant is subject to Tax Obligations in more than one jurisdiction between the Date of Grant and the date of any relevant taxable or tax withholding event, as applicable, Participant acknowledges that the Company and/or the Service Recipient (or former employer, as applicable) may be required to withhold or account for Tax Obligations in more than one jurisdiction. If Participant fails to make satisfactory arrangements for the payment of any required Tax Obligations hereunder at the time of the applicable taxable event, Participant acknowledges and agrees that the Company may refuse to issue or deliver the Shares.

(b) Tax Withholding and Default Method of Tax Withholding. When Shares are issued as payment for vested Restricted Stock Units, Participant generally will recognize immediate U.S. taxable income if Participant is a U.S. taxpayer. If Participant is a non-U.S. taxpayer, Participant will be subject to applicable taxes in his or her jurisdiction. The minimum amount of Tax Obligations which the Company determines must be withheld with respect to this Award ("Tax Withholding Obligation") will be satisfied by Shares being sold on Participant's behalf at the prevailing market price pursuant to such procedures as the Company may specify from time to time, including through a broker-assisted arrangement (it being understood that the Shares to be sold must have vested pursuant to the terms of this Award Agreement and the Plan). The proceeds from the sale will be used to satisfy Participant's Tax Withholding Obligation arising with respect to this Award. In addition to Shares sold to satisfy the Tax Withholding Obligation, additional Shares will be sold to satisfy any associated broker or other fees. Only whole Shares will be sold to satisfy any Tax Withholding Obligation. Any proceeds from the sale of Shares in excess of the Tax Withholding Obligation and any associated broker or other fees will be paid to Participant in accordance with procedures the Company may specify from time to time. **By accepting this**

Award, Participant expressly consents to the sale of Shares to cover the Tax Withholding Obligations (and any associated broker or other fees and agrees and acknowledges that Participant may not satisfy them by any means other than such sale of Shares, unless required to do so by the Administrator or pursuant to the Administrator's express written consent.

(c) Administrator Discretion. If the Administrator determines that Participant cannot satisfy Participant's Tax Withholding Obligation through the default procedure described in Section 8(b) or the Administrator otherwise determines it is in the best interests of the Company for Participant to satisfy Participant's Tax Withholding Obligation by a method other than through the default procedure described in Section 8(b), it may permit or require Participant to satisfy Participant's Tax Withholding Obligation, in whole or in part (without limitation), if permissible by applicable local law, by (i) paying cash, (ii) electing to have the Company withhold otherwise deliverable Shares having a value equal to the minimum amount statutorily required to be withheld (or such greater amount as Participant may elect if permitted by the Administrator, if such greater amount would not result in adverse financial accounting consequences), (iii) withholding the amount of such Tax Withholding Obligation from Participant's wages or other cash compensation paid to Participant by the Company and/or the Service Recipient, (iv) delivering to the Company Shares that Participant owns and that have vested with a Fair Market Value equal to the amount required to be withheld (or such greater amount as Participant may elect if permitted by the Administrator, if such greater amount would not result in adverse financial accounting consequences), or (v) such other means as the Administrator deems appropriate. To the extent determined appropriate by the Company in its discretion, it will have the right (but not the obligation) to satisfy any Tax Obligations by reducing the number of Shares otherwise deliverable to Participant.

(d) Company's Obligation to Deliver Shares. For clarification purposes, in no event will the Company issue Participant any Shares unless and until arrangements satisfactory to the Administrator have been made for the payment of Participant's Tax Withholding Obligation. If Participant fails to make satisfactory arrangements for the payment of such Tax Withholding Obligations hereunder at the time any applicable Restricted Stock Units otherwise are scheduled to vest pursuant to Sections 3 or 4 or Participant's Tax Withholding Obligations otherwise become due, Participant will permanently forfeit such Restricted Stock Units to which Participant's Tax Withholding Obligation relates and any right to receive Shares thereunder and such Restricted Stock Units will be returned to the Company at no cost to the Company. Participant acknowledges and agrees that the Company may refuse to issue or deliver the Shares if such Tax Obligations are not delivered at the time they are due.

9. Rights as Stockholder. Neither Participant nor any person claiming under or through Participant will have any of the rights or privileges of a stockholder of the Company in respect of any Shares deliverable hereunder unless and until certificates representing such Shares (which may be in book entry form) will have been issued, recorded on the records of the Company or its transfer agents or registrars, and delivered to Participant (including through electronic delivery to a brokerage account). After such issuance, recordation and delivery, Participant will have all the rights of a stockholder of the Company with respect to voting such Shares and receipt of dividends and distributions on such Shares.

10. No Guarantee of Continued Service. PARTICIPANT ACKNOWLEDGES AND AGREES THAT THE VESTING OF THE RESTRICTED STOCK UNITS PURSUANT TO THE VESTING SCHEDULE HEREOF IS EARNED ONLY BY CONTINUING AS A SERVICE PROVIDER, WHICH UNLESS PROVIDED OTHERWISE UNDER APPLICABLE LAW IS AT THE WILL OF THE COMPANY (OR THE SERVICE RECIPIENT) AND NOT THROUGH THE ACT OF BEING HIRED, BEING GRANTED THIS RESTRICTED STOCK UNIT AWARD OR ACQUIRING SHARES HEREUNDER. PARTICIPANT FURTHER ACKNOWLEDGES AND AGREES THAT THIS AWARD AGREEMENT, THE TRANSACTIONS CONTEMPLATED HEREUNDER AND THE VESTING SCHEDULE SET FORTH HEREIN DO NOT CONSTITUTE AN EXPRESS OR IMPLIED PROMISE OF CONTINUED ENGAGEMENT AS A SERVICE PROVIDER FOR THE VESTING PERIOD, FOR ANY PERIOD, OR AT ALL, AND SHALL NOT INTERFERE IN ANY WAY WITH PARTICIPANT'S RIGHT OR THE RIGHT OF THE COMPANY (OR THE SERVICE RECIPIENT) TO TERMINATE PARTICIPANT'S RELATIONSHIP AS A SERVICE PROVIDER, SUBJECT TO APPLICABLE LAW, WHICH TERMINATION, UNLESS PROVIDED OTHERWISE UNDER APPLICABLE LAW, MAY BE AT ANY TIME, WITH OR WITHOUT CAUSE.

11. Grant is Not Transferable. Except to the limited extent provided in Section 7, this grant and the rights and privileges conferred hereby will not be transferred, assigned, pledged or hypothecated in any way (whether by operation of law or otherwise) and will not be subject to sale under execution, attachment or similar process. Upon any attempt to transfer, assign, pledge, hypothecate or otherwise dispose of this grant, or any right or privilege conferred hereby, or upon any attempted sale under any execution, attachment or similar process, this grant and the rights and privileges conferred hereby immediately will become null and void.

12. Nature of Grant. In accepting the grant, Participant acknowledges, understands and agrees that:

(a) the grant of the Restricted Stock Units is voluntary and occasional and does not create any contractual or other right to receive future grants of Restricted Stock Units, or benefits in lieu of Restricted Stock Units, even if Restricted Stock Units have been granted in the past;

(b) all decisions with respect to future Restricted Stock Units or other grants, if any, will be at the sole discretion of the Company;

(c) Participant is voluntarily participating in the Plan;

(d) the Restricted Stock Units and the Shares subject to the Restricted Stock Units are not intended to replace any pension rights or compensation;

(e) the Restricted Stock Units and the Shares subject to the Restricted Stock Units, and the income and value of same, are not part of normal or expected compensation for purposes of calculating any severance, resignation, termination, redundancy, dismissal, end-of-service payments, bonuses, long-service awards, pension or retirement or welfare benefits or similar payments;

(f) the future value of the underlying Shares is unknown, indeterminable and cannot be predicted;

(g) for purposes of the Restricted Stock Units, Participant's status as a Service Provider will be considered terminated as of the date Participant is no longer actively providing services to the Company or any Parent or Subsidiary (regardless of the reason for such termination and whether or not later to be found invalid or in breach of employment laws in the jurisdiction where Participant is a Service Provider or the terms of Participant's employment or service agreement, if any), and unless otherwise expressly provided in this Award Agreement (including by reference in the Notice of Grant to other arrangements or contracts) or determined by the Administrator, Participant's right to vest in the Restricted Stock Units under the Plan, if any, will terminate as of such date and will not be extended by any notice period (e.g., Participant's period of service would not include any contractual notice period or any period of "garden leave" or similar period mandated under employment laws in the jurisdiction where Participant is a Service Provider or the terms of Participant's employment or service agreement, if any, unless Participant is providing bona fide services during such time); the Administrator shall have the exclusive discretion to determine when Participant is no longer actively providing services for purposes of the Restricted Stock Units grant (including whether Participant may still be considered to be providing services while on a leave of absence and consistent with local law);

(h) unless otherwise provided in the Plan or by the Company in its discretion, the Restricted Stock Units and the benefits evidenced by this Award Agreement do not create any entitlement to have the Restricted Stock Units or any such benefits transferred to, or assumed by, another company nor be exchanged, cashed out or substituted for, in connection with any corporate transaction affecting the Shares; and

(i) the following provisions apply only if Participant is providing services outside the United States:

(i) the Restricted Stock Units and the Shares subject to the Restricted Stock Units are not part of normal or expected compensation or salary for any purpose;

(ii) Participant acknowledges and agrees that none of the Company, the Employer or any Parent or Subsidiary shall be liable for any foreign exchange rate fluctuation between Participant's local currency and the United States Dollar that may affect the value of the Restricted Stock Units or of any amounts due to Participant pursuant to the settlement of the Restricted Stock Units or the subsequent sale of any Shares acquired upon settlement; and

(iii) no claim or entitlement to compensation or damages shall arise from forfeiture of the Restricted Stock Units resulting from the termination of Participant's status as a Service Provider (for any reason whatsoever whether or not later found to be invalid or in breach of employment laws in the jurisdiction where Participant is a Service Provider or the terms of Participant's employment or service agreement, if any), and in consideration of the grant of the Restricted Stock Units to which Participant is otherwise not entitled, Participant irrevocably agrees never to institute any claim against the Company, any Parent or Subsidiary or the Service Recipient, waives his or her ability, if any, to bring any such claim, and releases the Company, any Parent or Subsidiary and the Service Recipient from any such claim; if, notwithstanding the foregoing, any such claim is allowed by a court of competent jurisdiction, then, by participating in the Plan, Participant shall be deemed irrevocably to have agreed not to pursue such claim and agrees to execute any and all documents necessary to request dismissal or withdrawal of such claim.

13. No Advice Regarding Grant. The Company is not providing any tax, legal or financial advice, nor is the Company making any recommendations regarding Participant's participation in the Plan, or Participant's acquisition or sale of the underlying Shares. Participant is hereby advised to consult with his or her own personal tax, legal and financial advisors regarding his or her participation in the Plan before taking any action related to the Plan.

14. ***Data Privacy. Participant hereby explicitly and unambiguously consents to the collection, use and transfer, in electronic or other form, of Participant's personal data as described in this Award Agreement and any other Restricted Stock Unit grant materials by and among, as applicable, the Employer, or other Service Recipient the Company and any Parent or Subsidiary for the exclusive purpose of implementing, administering and managing Participant's participation in the Plan.***

Participant understands that the Company and the Service Recipient may hold certain personal information about Participant, including, but not limited to, Participant's name, home address and telephone number, date of birth, social insurance number or other identification number, salary, nationality, job title, any Shares or directorships held in the Company, details of all Restricted Stock Units or any other entitlement to Shares awarded, canceled, exercised, vested, unvested or outstanding in Participant's favor ("Data"), for the exclusive purpose of implementing, administering and managing the Plan.

Participant understands that Data will be transferred to a stock plan service provider as may be selected by the Company in the future, which is assisting the Company with the implementation, administration and management of the Plan. Participant understands that the recipients of the Data may be located in the United States or elsewhere, and that the recipients' country of operation (e.g., the United States) may have different data privacy laws and protections than Participant's country. Participant understands that if he or she resides outside the United States, he or she may request a list with the names and addresses of any potential recipients of the Data by contacting his or her local human resources representative. Participant authorizes the Company, any stock plan service provider selected by the Company and any other possible recipients which may assist the Company (presently or in the future) with implementing, administering and managing the Plan to receive, possess, use, retain and transfer the Data, in electronic or other form, for the sole purpose of implementing, administering and managing his or her participation in the Plan. Participant understands that Data will be held only as long as is necessary to implement, administer and manage Participant's participation in the Plan. Participant understands if he or she resides outside the United States, he or she may, at any time, view Data, request additional information about the storage and processing of Data, require any necessary amendments to Data or refuse or withdraw the consents herein, in any case without cost, by contacting in writing his or her local human resources representative. Further, Participant understands that he or she is providing the consents herein on a purely voluntary basis. If Participant does not consent, or if Participant later seeks to revoke his or her consent, his or her status as a Service Provider and career with the Service Recipient will not be adversely affected; the only adverse consequence of refusing or withdrawing Participant's consent is that the Company would not be able to grant Participant Restricted Stock Units or other equity awards or administer or maintain such awards. Therefore, Participant understands that refusing or withdrawing his or her consent may affect Participant's ability to participate in the Plan. For more information on the consequences of Participant's refusal to consent or withdrawal of consent, Participant understands that he or she may contact his or her local human resources representative.

15. Address for Notices. Any notice to be given to the Company under the terms of this Award Agreement will be addressed to the Company at Denali Therapeutics Inc., 151 Oyster Point Blvd., South San Francisco, CA 94080, or at such other address as the Company may hereafter designate in writing.

16. Electronic Delivery and Acceptance. The Company may, in its sole discretion, decide to deliver any documents related to the Restricted Stock Units awarded under the Plan or future Restricted Stock Units that may be awarded under the Plan by electronic means or request Participant's consent to participate in the Plan by electronic means. Participant hereby consents to receive such documents by electronic delivery and agrees to participate in the Plan through any on-line or electronic system established and maintained by the Company or a third party designated by the Company.

17. No Waiver. Either party's failure to enforce any provision or provisions of this Award Agreement shall not in any way be construed as a waiver of any such provision or provisions, nor prevent that party from thereafter enforcing each and every other provision of this Award Agreement. The rights granted both parties herein are cumulative and shall not constitute a waiver of either party's right to assert all other legal remedies available to it under the circumstances.

18. Successors and Assigns. The Company may assign any of its rights under this Award Agreement to single or multiple assignees, and this Award Agreement shall inure to the benefit of the successors and assigns of the Company. Subject to the restrictions on transfer herein set forth, this Award Agreement shall be binding upon Participant and his or her heirs, executors, administrators, successors and assigns. The rights and obligations of Participant under this Award Agreement may only be assigned with the prior written consent of the Company.

19. Additional Conditions to Issuance of Stock. If at any time the Company will determine, in its discretion, that the listing, registration, qualification or rule compliance of the Shares upon any securities exchange or under any state, federal or non-U.S. law, the tax code and related regulations or under the rulings or regulations of the United States Securities and Exchange Commission or any other governmental regulatory body or the clearance, consent or approval of the United States Securities and Exchange Commission or any other governmental regulatory authority is necessary or desirable as a condition to the issuance of Shares to Participant (or his or her estate) hereunder, such issuance will not occur unless and until such listing, registration, qualification, rule compliance, clearance, consent or approval will have been completed, effected or obtained free of any conditions not acceptable to the Company. Subject to the terms of the Award Agreement and the Plan, the Company shall not be required to issue any certificate or certificates for Shares hereunder prior to the lapse of such reasonable period of time following the date of vesting of the Restricted Stock Units as the Administrator may establish from time to time for reasons of administrative convenience.

20. Language. If Participant has received this Award Agreement or any other document related to the Plan translated into a language other than English and if the meaning of the translated version is different than the English version, the English version will control.

21. Interpretation. The Administrator will have the power to interpret the Plan and this Award Agreement and to adopt such rules for the administration, interpretation and application of the Plan as are consistent therewith and to interpret or revoke any such rules (including, but not limited to, the determination of whether or not any Restricted Stock Units have vested). All actions taken and all interpretations and determinations made by the Administrator in good faith will be final and binding upon Participant, the Company and all other interested persons. Neither the Administrator nor any person acting on behalf of the Administrator will be personally liable for any action, determination or interpretation made in good faith with respect to the Plan or this Award Agreement.

22. Captions. Captions provided herein are for convenience only and are not to serve as a basis for interpretation or construction of this Award Agreement.

23. Amendment, Suspension or Termination of the Plan. By accepting this Award, Participant expressly warrants that he or she has received an Award of Restricted Stock Units under the Plan, and has received, read and understood a description of the Plan. Participant understands that the Plan is discretionary in nature and may be amended, suspended or terminated by the Company at any time.

24. Modifications to the Award Agreement. This Award Agreement constitutes the entire understanding of the parties on the subjects covered. Participant expressly warrants that he or she is not accepting this Award Agreement in reliance on any promises, representations, or inducements other than those contained herein. Modifications to this Award Agreement or the Plan can be made only in an express written contract executed by a duly authorized officer of the Company. Notwithstanding anything to the contrary in the Plan or this Award Agreement, the Company reserves the right to revise this Award Agreement as it deems necessary or advisable, in its sole discretion and without the consent of Participant, to comply with Section 409A or to otherwise avoid imposition of any additional tax or income recognition under Section 409A in connection to this Award of Restricted Stock Units.

25. Governing Law; Venue; Severability. This Award Agreement and the Restricted Stock Units are governed by the internal substantive laws, but not the choice of law rules, of California. For purposes of litigating any dispute that arises under these Restricted Stock Units or this Award Agreement, the parties hereby submit to and consent to the jurisdiction of the State of California, and agree that such litigation will be conducted in the courts of San Mateo County, California, or the federal courts for the United States for the Northern District of California, and no other courts, where this Award Agreement is made and/or to be performed. In the event that any provision hereof becomes or is declared by a court of competent jurisdiction to be illegal, unenforceable or void, this Award Agreement shall continue in full force and effect.

26. Entire Agreement. The Plan is incorporated herein by reference. The Plan and this Award Agreement (including the appendices and exhibits referenced herein) constitute the entire agreement of the parties with respect to the subject matter hereof and supersede in their entirety all prior undertakings and agreements of the Company and Participant with respect to the subject matter hereof, and may not be modified adversely to the Participant’s interest except by means of a writing signed by the Company and Participant.

27. Country Addendum. Notwithstanding any provisions in this Award Agreement, the Restricted Stock Unit grant shall be subject to any special terms and conditions set forth in the appendix (if any) to this Award Agreement for Participant's country. Moreover, if Participant relocates to one of the countries included in the Country Addendum (if any), the special terms and conditions for such country will apply to Participant, to the extent the Company determines that the application of such terms and conditions is necessary or advisable for legal or administrative reasons. The Country Addendum constitutes part of this Award Agreement.

Exhibit 10.4

DENALI THERAPEUTICS INC.

2017 EMPLOYEE STOCK PURCHASE PLAN

1. Purpose. The purpose of the Plan is to provide employees of the Company and its Designated Companies with an opportunity to purchase Common Stock through accumulated Contributions. The Company intends for the Plan to have two components: a component that is intended to qualify as an "employee stock purchase plan" under Section 423 of the Code (the "423 Component") and a component that is not intended to qualify as an "employee stock purchase plan" under Section 423 of the Code (the "Non-423 Component"). The provisions of the 423 Component, accordingly, will be construed so as to extend and limit Plan participation in a uniform and nondiscriminatory basis consistent with the requirements of Section 423 of the Code. In addition, this Plan authorizes the grant of an option to purchase shares of Common Stock under the Non-423 Component that does not qualify as an "employee stock purchase plan" under Section 423 of the Code; an option granted under the Non-423 Component will provide for substantially the same benefits as an option granted under the 423 Component, except that a Non-423 Component option may include features necessary to comply with applicable non-U.S. laws pursuant to rules, procedures or sub-plans adopted by the Administrator. Except as otherwise provided herein or by the Administrator, the Non-423 Component will operate and be administered in the same manner as the 423 Component.

2. Definitions.

(a) "Administrator" means the Board or any Committee designated by the Board to administer the Plan pursuant to Section 14.

(b) "Affiliate" means any entity, other than a Subsidiary, in which the Company has an equity or other ownership interest.

(c) "Applicable Laws" means the requirements relating to the administration of equity-based awards, including but not limited to the related issuance of shares of Common Stock, under U.S. state corporate laws, U.S. federal and state securities laws, the Code, any stock exchange or quotation system on which the Common Stock is listed or quoted and the applicable laws of any non-U.S. country or jurisdiction where options are, or will be, granted under the Plan.

(d) "Board" means the Board of Directors of the Company.

(e) "Change in Control" means the occurrence of any of the following events:

(i) A change in the ownership of the Company which occurs on the date that any one person, or more than one person acting as a group ("Person"), acquires ownership of the stock of the Company that, together with the stock held by such Person, constitutes more than fifty percent (50%) of the total voting power of the stock of the Company; provided, however, that for purposes of this subsection, the acquisition of additional stock by any one Person, who is considered to own more than fifty percent (50%) of the total voting power of the stock of the Company will not be considered a Change in Control.

Further, if the stockholders of the Company immediately before such change in ownership continue to retain immediately after the change in ownership, in substantially the same proportions as their ownership of shares of the Company's voting stock immediately prior to the change in ownership, direct or indirect beneficial ownership of fifty percent (50%) or more of the total voting power of the stock of the Company or of the ultimate parent entity of the Company, such event shall not be considered a Change in Control under this subsection (i). For this purpose, indirect beneficial ownership shall include, without limitation, an interest resulting from ownership of the voting securities of one or more corporations or other business entities which own the Company, as the case may be, either directly or through one or more subsidiary corporations or other business entities; or

(ii) A change in the effective control of the Company which occurs on the date that a majority of members of the Board is replaced during any twelve (12) month period by Directors whose appointment or election is not endorsed by a majority of the members of the Board prior to the date of the appointment or election. For purposes of this subsection (ii), if any Person is considered to be in effective control of the Company, the acquisition of additional control of the Company by the same Person will not be considered a Change in Control; or

(iii) A change in the ownership of a substantial portion of the Company's assets which occurs on the date that any Person acquires (or has acquired during the twelve (12) month period ending on the date of the most recent acquisition by such person or persons) assets from the Company that have a total gross fair market value equal to or more than fifty percent (50%) of the total gross fair market value of all of the assets of the Company immediately prior to such acquisition or acquisitions; provided, however, that for purposes of this subsection (iii), the following will not constitute a change in the ownership of a substantial portion of the Company's assets: (A) a transfer to an entity that is controlled by the Company's stockholders immediately after the transfer, or (B) a transfer of assets by the Company to: (1) a stockholder of the Company (immediately before the asset transfer) in exchange for or with respect to the Company's stock, (2) an entity, fifty percent (50%) or more of the total value or voting power of which is owned, directly or indirectly, by the Company, (3) a Person, that owns, directly or indirectly, fifty percent (50%) or more of the total value or voting power of all the outstanding stock of the Company, or (4) an entity, at least fifty percent (50%) of the total value or voting power of which is owned, directly or indirectly, by a Person described in this subsection (iii)(B)(3). For purposes of this subsection (iii), gross fair market value means the value of the assets of the Company, or the value of the assets being disposed of, determined without regard to any liabilities associated with such assets.

For purposes of this definition, persons will be considered to be acting as a group if they are owners of a corporation that enters into a merger, consolidation, purchase or acquisition of stock, or similar business transaction with the Company.

Notwithstanding the foregoing, a transaction will not be deemed a Change in Control unless the transaction qualifies as a change in control event within the meaning of Section 409A.

Further and for the avoidance of doubt, a transaction will not constitute a Change in Control if: (i) its sole purpose is to change the state of the Company's incorporation, or (ii) its sole purpose is to create a holding company that will be owned in substantially the same proportions by the persons who held the Company's securities immediately before such transaction.

(f) "Code" means the U.S. Internal Revenue Code of 1986, as amended. Reference to a specific section of the Code or U.S. Treasury Regulation thereunder will include such section or regulation, any valid regulation or other official applicable guidance promulgated under such section, and any comparable provision of any future legislation or regulation amending, supplementing or superseding such section or regulation.

(g) "Committee" means a committee of the Board appointed in accordance with Section 14 hereof.

(h) "Common Stock" means the common stock of the Company.

(i) "Company" means Denali Therapeutics Inc., a Delaware corporation, or any successor thereto.

(j) "Compensation" means an Eligible Employee's base straight time gross earnings, payments for overtime and shift premium, but exclusive of payments for commissions, incentive compensation, equity compensation, bonuses and other similar compensation. The Administrator, in its discretion, may, on a uniform and nondiscriminatory basis, establish a different definition of Compensation for a subsequent Offering Period.

(k) "Contributions" means the payroll deductions and other additional payments that the Company may permit to be made by a Participant to fund the exercise of options granted pursuant to the Plan.

(l) "Designated Company" means any Subsidiary or Affiliate that has been designated by the Administrator from time to time in its sole discretion as eligible to participate in the Plan. For purposes of the 423 Component, only the Company and its Subsidiaries may be Designated Companies, provided, however that at any given time, a Subsidiary that is a Designated Company under the 423 Component shall not be a Designated Company under the Non-423 Component.

(m) "Director" means a member of the Board.

(n) "Eligible Employee" means any individual who is a common law employee providing services to the Company or a Designated Company and is customarily employed for at least twenty (20) hours per week and more than five (5) months in any calendar year by the Employer, or any lesser number of hours per week and/or number of months in any calendar year established by the Administrator (if required under Applicable Law) for purposes of any separate Offering or for Participants in the Non-423 Component. For purposes of the Plan, the employment relationship will be treated as continuing intact while the individual is on sick leave or other leave of absence that the Employer approves or is legally protected under Applicable Laws with respect to the Participant's participation in the Plan. Where the period of leave exceeds three (3) months and the individual's right to reemployment is not guaranteed either by statute or by contract, the employment relationship will be deemed to have terminated three (3)

months and one (1) day following the commencement of such leave. The Administrator, in its discretion, from time to time may, prior to an Enrollment Date for all options to be granted on such Enrollment Date in an Offering, determine (for each Offering under the 423 Component, on a uniform and nondiscriminatory basis or as otherwise permitted by U.S. Treasury Regulation Section 1.423-2) that the definition of Eligible Employee will or will not include an individual if he or she: (i) has not completed at least two (2) years of service since his or her last hire date (or such lesser period of time as may be determined by the Administrator in its discretion), (ii) customarily works not more than twenty (20) hours per week (or such lesser period of time as may be determined by the Administrator in its discretion), (iii) customarily works not more than five (5) months per calendar year (or such lesser period of time as may be determined by the Administrator in its discretion), (iv) is a highly compensated employee within the meaning of Section 414(q) of the Code, or (v) is a highly compensated employee within the meaning of Section 414(q) of the Code with compensation above a certain level or is an officer or subject to the disclosure requirements of Section 16(a) of the Exchange Act, provided the exclusion is applied with respect to each Offering under the 423 Component in an identical manner to all highly compensated individuals of the Employer whose Employees are participating in that Offering. Each exclusion shall be applied with respect to an Offering under the 423 Component in a manner complying with U.S. Treasury Regulation Section 1.423-2(e)(2)(ii). Such exclusions may be applied with respect to an Offering under the Non- 423 Component without regard to the limitations of U.S. Treasury Regulation Section 1.423-2.

(o) "Employer" means the employer of the applicable Eligible Employee(s).

(p) "Enrollment Date" means the first Trading Day of each Offering Period.

(q) "Exchange Act" means the U.S. Securities Exchange Act of 1934, as amended, including the rules and regulations promulgated thereunder.

(r) "Exercise Date" means the first Trading Day on or after May 31 and November 30 of each Purchase Period. Notwithstanding the foregoing, the first Exercise Date under the Plan will be the first Trading Day on or after May 31, 2018. Notwithstanding the foregoing, in the event that an Offering Period is terminated prior to its expiration pursuant to Section 19, the Administrator, in its sole discretion, may determine that such Offering Period will terminate without options being exercised on the Exercise Date(s) that otherwise would have occurred during such Offering Period.

(s) "Fair Market Value" means, as of any date and unless the Administrator determines otherwise, the value of Common Stock determined as follows:

(i) If the Common Stock is listed on any established stock exchange or a national market system, including without limitation the NASDAQ Global Select Market, the NASDAQ Global Market, the NASDAQ Capital Market of The NASDAQ Stock Market or the New York Stock Exchange, its Fair Market Value will be the closing sales price for such stock as quoted on such exchange or system on the date of determination (or the closing bid, if no sales were reported), as reported in *The Wall Street Journal* or such other source as the Administrator deems reliable;

(ii) If the Common Stock is regularly quoted by a recognized securities dealer but selling prices are not reported, its Fair Market Value will be the mean between the high bid and low asked prices for the Common Stock on the date of determination (or if no bids and asks were reported on that date, as applicable, on the last Trading Day such bids and asks were reported), as reported in *The Wall Street Journal* or such other source as the Administrator deems reliable;

(iii) In the absence of an established market for the Common Stock, the Fair Market Value thereof will be determined in good faith by the Administrator; or

(iv) For purposes of the Enrollment Date of the first Offering Period under the Plan, the Fair Market Value will be the initial price to the public as set forth in the final prospectus included within the registration statement on Form S-1 filed with the Securities and Exchange Commission for the initial public offering of the Common Stock (the "Registration Statement").

(t) "Fiscal Year" means the fiscal year of the Company.

(u) "New Exercise Date" means a new Exercise Date if the Administrator shortens any Offering Period then in progress.

(v) "Offering" means an offer under the Plan of an option that may be exercised during an Offering Period as further described in Section 4. For purposes of the Plan, the Administrator may designate separate Offerings under the Plan (the terms of which need not be identical) in which Eligible Employees of one or more Employers will participate, even if the dates of the applicable Offering Periods of each such Offering are identical and the provisions of the Plan will separately apply to each Offering. To the extent permitted by U.S. Treasury Regulation Section 1.423-2(a)(1), the terms of each Offering need not be identical provided that the terms of the Plan and an Offering together satisfy U.S. Treasury Regulation Section 1.423-2(a)(2) and (a)(3).

(w) "Offering Periods" means the overlapping, consecutive periods of approximately twelve (12) months during which an option granted pursuant to the Plan may be exercised, (i) commencing on the first Trading Day on or after May 31 and November 30 of each year and terminating on the first Trading Day on or after May 31 and November 30, approximately twelve (12) months later; provided, however, that the first Offering Period under the Plan will commence with the first Trading Day on or after the date on which the Securities and Exchange Commission declares the Company's Registration Statement effective and will end on the first Trading Day on or after November 30, 2018, and provided, further, that the second Offering Period under the Plan will commence on the first Trading Day on or after November 30, 2018, subject to Section 29. The duration and timing of Offering Periods may be changed pursuant to Sections 4 and 20.

(x) "Parent" means a "parent corporation," whether now or hereafter existing, as defined in Section 424(e) of the Code.

(y) "Participant" means an Eligible Employee that participates in the Plan.

(z) "Plan" means this Denali Therapeutics Inc. 2017 Employee Stock Purchase Plan.

(aa) "Purchase Period" means the period during an Offering Period and during which shares of Common Stock may be purchased on a Participant's behalf in accordance with the terms of the Plan. Unless the Administrator provides otherwise, Purchase Periods will be the approximately six (6) month period commencing after one Exercise Date and ending with the next Exercise Date, except that the first Purchase Period of any Offering Period will commence on the Enrollment Date and end with the next Exercise Date.

(bb) "Purchase Price" means an amount equal to eighty-five percent (85%) of the Fair Market Value of a share of Common Stock on the Enrollment Date or on the Exercise Date, whichever is lower; provided however, that the Purchase Price may be determined for subsequent Offering Periods by the Administrator subject to compliance with Section 423 of the Code (or any successor rule or provision or any other Applicable Law, regulation or stock exchange rule) or pursuant to Section 19.

(cc) "Registration Date" means the effective date of the first registration statement that is filed by the Company and declared effective pursuant to Section 12(b) of the Exchange Act, with respect to any class of the Company's securities.

(dd) "Section 409A" means Section 409A of the Code and the regulations and guidance thereunder, as may be amended or modified from time to time.

(ee) "Subsidiary" means a "subsidiary corporation," whether now or hereafter existing, as defined in Section 424(f) of the Code.

(ff) "Trading Day" means a day on which the national stock exchange upon which the Common Stock is listed is open for trading.

(gg) "U.S. Treasury Regulations" means the Treasury regulations of the Code. Reference to a specific Treasury Regulation or Section of the Code shall include such Treasury Regulation or Section, any valid regulation promulgated under such Section, and any comparable provision of any future legislation or regulation amending, supplementing or superseding such Section or regulation.

3. Eligibility.

(a) First Offering Period. Any individual who is an Eligible Employee immediately prior to the first Offering Period will be automatically enrolled in the first Offering Period.

(b) Subsequent Offering Periods. Any Eligible Employee on a given Enrollment Date subsequent to the first Offering Period will be eligible to participate in the Plan, subject to the requirements of Section 5.

(c) Non-U.S. Employees. Eligible Employees who are citizens or residents of a non-U.S. jurisdiction (without regard to whether they also are citizens or residents of the United States or resident aliens (within the meaning of Section 7701(b)(1)(A) of the Code)) may be excluded from participation in the Plan or an Offering if the participation of such Eligible Employees is prohibited under the laws of the applicable jurisdiction or if complying with the laws of the applicable jurisdiction would cause the Plan or an Offering to violate Section 423 of the Code. In the case of the Non-423 Component, an Eligible Employee may be excluded from participation in the Plan or an Offering if the Administrator has determined that participation of such Eligible Employee is not advisable or practicable.

(d) Limitations. Any provisions of the Plan to the contrary notwithstanding, no Eligible Employee will be granted an option under the Plan (i) to the extent that, immediately after the grant, such Eligible Employee (or any other person whose stock would be attributed to such Eligible Employee pursuant to Section 424(d) of the Code) would own capital stock of the Company or any Parent or Subsidiary of the Company and/or hold outstanding options to purchase such stock possessing five percent (5%) or more of the total combined voting power or value of all classes of the capital stock of the Company or of any Parent or Subsidiary of the Company, or (ii) to the extent that his or her rights to purchase stock under all employee stock purchase plans (as defined in Section 423 of the Code) of the Company or any Parent or Subsidiary of the Company accrues at a rate, which exceeds twenty-five thousand dollars ($25,000) worth of stock (determined at the Fair Market Value of the stock at the time such option is granted) for each calendar year in which such option is outstanding at any time, as determined in accordance with Section 423 of the Code and the regulations thereunder.

4. Offering Periods. The Plan will be implemented by consecutive, overlapping Offering Periods with a new Offering Period commencing on the first Trading Day on or after May 31 and November 30 each year, or on such other date as the Administrator will determine; provided, however, that the first Offering Period under the Plan will commence with the first Trading Day on or after the date upon which the Company's Registration Statement is declared effective by the Securities and Exchange Commission and end on the first Trading Day on or after November 30, 2018, and provided, further, that the second Offering Period under the Plan will commence on the first Trading Day on or after November 30, 2018, subject to Section 29. The Administrator will have the power to change the duration of Offering Periods (including the commencement dates thereof) with respect to future Offerings without stockholder approval if such change is announced prior to the scheduled beginning of the first Offering Period to be affected thereafter; provided, however, that no Offering Period may last more than twenty-seven (27) months.

5. Participation.

(a) First Offering Period. An Eligible Employee will be entitled to continue to participate in the first Offering Period pursuant to Section 3(a) only if such individual submits a subscription agreement authorizing Contributions in a form determined by the Administrator (which may be similar to the form attached hereto as Exhibit A) to the Company's designated plan administrator (i) no earlier than the effective date of the Form S-8 registration statement with respect to the issuance of Common Stock under this Plan and (ii) with respect to the first Offering Period, no later than ten (10) business days following the effective date of such Form S-8 registration statement or such other date as the Administrator may determine (the "Enrollment Window"). An Eligible Employee's failure to submit the subscription agreement during the Enrollment Window will result in the automatic termination of such individual's participation in the first Offering Period.

(b) Subsequent Offering Periods. An Eligible Employee may participate in the Plan pursuant to Section 3(b) by (i) submitting to the Company's stock administration office (or its designee), a properly completed subscription agreement authorizing Contributions in the form provided by the Administrator for such purpose, or (ii) following an electronic or other enrollment procedure determined by the Administrator, in either case, on or before a date determined by the Administrator prior to an applicable Enrollment Date.

6. Contributions.

(a) At the time a Participant enrolls in the Plan pursuant to Section 5, he or she will elect to have Contributions (in the form of payroll deductions or otherwise, to the extent permitted by the Administrator) made on each pay day during the Offering Period in an amount not exceeding fifteen percent (15%) of the Compensation, which he or she receives on each pay day during the Offering Period; provided, however, that should a pay day occur on an Exercise Date, a Participant will have any Contributions made on such day applied to his or her account under the then-current Purchase Period or Offering Period. The Administrator, in its sole discretion, may permit all Participants in a specified Offering to contribute amounts to the Plan through payment by cash, check or other means set forth in the subscription agreement prior to each Exercise Date of each Purchase Period. A Participant's subscription agreement will remain in effect for successive Offering Periods unless terminated as provided in Section 10 hereof.

(b) In the event Contributions are made in the form of payroll deductions, such payroll deductions for a Participant will commence on the first pay day following the Enrollment Date and will end on the last pay day on or prior to the last Exercise Date of such Offering Period to which such authorization is applicable, unless sooner terminated by the Participant as provided in Section 10 hereof; provided, however, that for the first Offering Period, payroll deductions will commence on the first pay day on or following the end of the Enrollment Window.

(c) All Contributions made for a Participant will be credited to his or her account under the Plan and Contributions will be made in whole percentages of his or her Compensation only. A Participant may not make any additional payments into such account.

(d) A Participant may discontinue his or her participation in the Plan as provided under Section 10. Until and unless determined otherwise by the Administrator, in its sole discretion, for an Offering Period, a Participant may decrease (including to zero (0%)) the rate of his or her Contributions (but not increase the rate) during the Offering Period by (i) properly completing and submitting to the Company's stock administration office (or its designee), a new subscription agreement authorizing the change in Contribution rate in the form provided by the Administrator for such purpose, or (ii) following an electronic or other procedure prescribed by the Administrator, in either case, on or before a date determined by the Administrator prior to an applicable Exercise Date. If a Participant has not followed such procedures to change the rate of Contributions, the rate of his or her Contributions will continue at the originally elected rate throughout the Purchase Period and Offering Period and future Purchase Periods and Offering Periods (unless the Participant's participation is terminated as provided in Sections 10 or 11). The Administrator may, in its sole discretion, limit or amend the nature and/or number of Contribution rate changes (including

to permit, prohibit and/or limit increases and/or decreases to rate changes) that may be made by Participants during any Purchase Period or Offering Period, and may establish such other conditions or limitations as it deems appropriate for Plan administration. Any change in Contribution rate made pursuant to this Section 6(d) will be effective as of the first full payroll period following five (5) business days after the date on which the change is made by the Participant (unless the Administrator, in its sole discretion, elects to process a given change in Contribution rate more quickly).

(e) Notwithstanding the foregoing, to the extent necessary to comply with Section 423(b)(8) of the Code and Section 3(d) (which generally limit participation in an Offering Period pursuant to certain Applicable Laws), a Participant's Contributions may be decreased to zero percent (0%) by the Administrator at any time during a an Offering Period (or a Purchase Period, as applicable). Subject to Section 423(b)(8) of the Code and Section 3(d) hereof, Contributions will recommence at the rate originally elected by the Participant effective as of the beginning of the first Offering Period (or Purchase Period, as applicable) scheduled to end in the following calendar year, unless terminated by the Participant as provided in Section 10.

(f) Notwithstanding any provisions to the contrary in the Plan, the Administrator may allow Participants to participate in the Plan via cash contributions instead of payroll deductions if (i) payroll deductions are not permitted or advisable under Applicable Law, (ii) the Administrator determines that cash contributions are permissible for Participants participating in the 423 Component and/or (iii) the Participants are participating in the Non-423 Component.

(g) At the time the option is exercised, in whole or in part, or at the time some or all of the Common Stock issued under the Plan is disposed of (or at any other time that a taxable event related to the Plan occurs), the Participant must make adequate provision for the Company's or Employer's federal, state, local or any other tax liability payable to any authority including taxes imposed by jurisdictions outside of the U.S., national insurance, social security or other tax withholding obligations, if any, which arise upon the exercise of the option or the disposition of the Common Stock (or any other time that a taxable event related to the Plan occurs). At any time, the Company or the Employer may, but will not be obligated to, withhold from the Participant's compensation the amount necessary for the Company or the Employer to meet applicable withholding obligations, including any withholding required to make available to the Company or the Employer any tax deductions or benefits attributable to the sale or early disposition of Common Stock by the Eligible Employee. In addition, the Company or the Employer may, but will not be obligated to, withhold from the proceeds of the sale of Common Stock or any other method of withholding the Company or the Employer deems appropriate to the extent permitted by U.S. Treasury Regulation Section 1.423-2(f).

7. Grant of Option. On the Enrollment Date of each Offering Period, each Eligible Employee participating in such Offering Period will be granted an option to purchase on each Exercise Date during such Offering Period (at the applicable Purchase Price) up to a number of shares of Common Stock determined by dividing such Eligible Employee's Contributions accumulated prior to such Exercise Date and retained in the Eligible Employee's account as of the Exercise Date by the applicable Purchase Price; provided that in no event will an Eligible Employee be permitted to purchase during each Purchase Period more than 2,000

shares of Common Stock (subject to any adjustment pursuant to Section 18) and provided further that such purchase will be subject to the limitations set forth in Sections 3(d) and 13 and in the subscription agreement. The Eligible Employee may accept the grant of such option (i) with respect to the first Offering Period by submitting a properly completed subscription agreement in accordance with the requirements of Section 5 on or before the last day of the Enrollment Window, and (ii) with respect to any subsequent Offering Period under the Plan, by electing to participate in the Plan in accordance with the requirements of Section 5. The Administrator may, for future Offering Periods, increase or decrease, in its absolute discretion, the maximum number of shares of Common Stock that an Eligible Employee may purchase during each Purchase Period or Offering Period, as applicable. Exercise of the option will occur as provided in Section 8, unless the Participant has withdrawn pursuant to Section 10. The option will expire on the last day of the Offering Period.

8. Exercise of Option.

(a) Unless a Participant withdraws from the Plan as provided in Section 10, his or her option for the purchase of shares of Common Stock will be exercised automatically on the Exercise Date, and the maximum number of full shares subject to the option will be purchased for such Participant at the applicable Purchase Price with the accumulated Contributions from his or her account. No fractional shares of Common Stock will be purchased; any Contributions accumulated in a Participant's account, which are not sufficient to purchase a full share will be retained in the Participant's account for the subsequent Purchase Period or Offering Period, as applicable, subject to earlier withdrawal by the Participant as provided in Section 10. Any other funds left over in a Participant's account after the Exercise Date will be returned to the Participant. During a Participant's lifetime, a Participant's option to purchase shares of Common Stock hereunder is exercisable only by him or her.

(b) If the Administrator determines that, on a given Exercise Date, the number of shares of Common Stock with respect to which options are to be exercised may exceed (i) the number of shares of Common Stock that were available for sale under the Plan on the Enrollment Date of the applicable Offering Period, or (ii) the number of shares of Common Stock available for sale under the Plan on such Exercise Date, the Administrator may in its sole discretion (x) provide that the Company will make a pro rata allocation of the shares of Common Stock available for purchase on such Enrollment Date or Exercise Date, as applicable, in as uniform a manner as will be practicable and as it will determine in its sole discretion to be equitable among all Participants exercising options to purchase Common Stock on such Exercise Date, and continue all Offering Periods then in effect or (y) provide that the Company will make a pro rata allocation of the shares of Common Stock available for purchase on such Enrollment Date or Exercise Date, as applicable, in as uniform a manner as will be practicable and as it will determine in its sole discretion to be equitable among all participants exercising options to purchase Common Stock on such Exercise Date, and terminate any or all Offering Periods then in effect pursuant to Section 19. The Company may make a pro rata allocation of the shares of Common Stock available on the Enrollment Date of any applicable Offering Period pursuant to the preceding sentence, notwithstanding any authorization of additional shares of Common Stock for issuance under the Plan by the Company's stockholders subsequent to such Enrollment Date.

9. Delivery. As soon as reasonably practicable after each Exercise Date on which a purchase of shares of Common Stock occurs, the Company will arrange the delivery to each Participant of the shares purchased upon exercise of his or her option in a form determined by the Administrator (in its sole discretion) and pursuant to rules established by the Administrator. The Company may permit or require that shares be deposited directly with a broker designated by the Company or to a trustee or designated agent of the Company, and the Company may utilize electronic or automated methods of share transfer. The Company may require that shares be retained with such broker, trustee or agent for a designated period of time and/or may establish other procedures to permit tracking of disqualifying dispositions or other dispositions of such shares. No Participant will have any voting, dividend, or other stockholder rights with respect to shares of Common Stock subject to any option granted under the Plan until such shares have been purchased and delivered to the Participant as provided in this Section 9.

10. Withdrawal.

(a) A Participant may withdraw all but not less than all the Contributions credited to his or her account and not yet used to exercise his or her option under the Plan at any time by (i) submitting to the Company's stock administration office (or its designee) a written notice of withdrawal in the form determined by the Administrator for such purpose (which may be similar to the form attached hereto as Exhibit B), or (ii) following an electronic or other withdrawal procedure determined by the Administrator. The Administrator may set forth a deadline of when a withdrawal must occur to be effective prior to a given Exercise Date in accordance with policies it may approve from time to time. All of the Participant's Contributions credited to his or her account will be paid to such Participant as soon as administratively practicable after receipt of notice of withdrawal and such Participant's option for the Offering Period will be automatically terminated, and no further Contributions for the purchase of shares will be made for such Offering Period. If a Participant withdraws from an Offering Period, Contributions will not resume at the beginning of the succeeding Offering Period, unless the Participant re-enrolls in the Plan in accordance with the provisions of Section 5.

(b) A Participant's withdrawal from an Offering Period will not have any effect upon his or her eligibility to participate in any similar plan that may hereafter be adopted by the Company or in succeeding Offering Periods that commence after the termination of the Offering Period from which the Participant withdraws.

11. Termination of Employment. Upon a Participant's ceasing to be an Eligible Employee, for any reason, he or she will be deemed to have elected to withdraw from the Plan and the Contributions credited to such Participant's account during the Offering Period but not yet used to purchase shares of Common Stock under the Plan will be returned to such Participant, or, in the case of his or her death, to the person or persons entitled thereto, and such Participant's option will be automatically terminated. Unless determined otherwise by the Administrator in a manner that, with respect to an Offering under the 423 Component, is permitted by, and compliant with, Section 423 of the Code, a Participant whose employment transfers between entities through a termination with an immediate rehire (with no break in service) by the Company or a Designated Company shall not be treated as terminated under the Plan; however, if a Participant transfers from an Offering under the 423 Component to the Non-423 Component, the exercise of

the option will be qualified under the 423 Component only to the extent it complies with Section 423 of the Code; further, no Participant shall be deemed to switch from an Offering under the Non-423 Component to an Offering under the 423 Component or vice versa unless (and then only to the extent) such switch would not cause the 423 Component or any option thereunder to fail to comply with Section 423 of the Code.

12. Interest. No interest will accrue on the Contributions of a participant in the Plan, except as may be required by Applicable Law, as determined by the Company, and if so required by the laws of a particular jurisdiction, shall, with respect to Offerings under the 423 Component, apply to all Participants in the relevant Offering, except to the extent otherwise permitted by U.S. Treasury Regulation Section 1.423-2(f).

13. Stock.

(a) Subject to adjustment upon changes in capitalization of the Company as provided in Section 18 hereof, the maximum number of shares of Common Stock that will be made available for sale under the Plan will be 1,000,000 shares of Common Stock, plus an annual increase to be added on the first day of each Fiscal Year beginning with the 2019 Fiscal Year equal to the least of (i) 2,000,000 shares of Common Stock, (ii) one percent (1%) of the outstanding shares of Common Stock on the last day of immediately preceding Fiscal Year, or (iii) an amount determined by the Administrator.

(b) Until the shares of Common Stock are issued (as evidenced by the appropriate entry on the books of the Company or of a duly authorized transfer agent of the Company), a Participant will only have the rights of an unsecured creditor with respect to such shares, and no right to vote or receive dividends or any other rights as a stockholder will exist with respect to such shares.

(c) Shares of Common Stock to be delivered to a Participant under the Plan will be registered in the name of the Participant or, if so required under Applicable Laws, in the name of the Participant and his or her spouse.

14. Administration. The Plan will be administered by the Board or a Committee appointed by the Board, which Committee will be constituted to comply with Applicable Laws. The Administrator will have full and exclusive discretionary authority to construe, interpret and apply the terms of the Plan, to delegate ministerial duties to any of the Company's employees, to designate separate Offerings under the Plan, to designate Subsidiaries and Affiliates as participating in the 423 Component or Non-423 Component, to determine eligibility, to adjudicate all disputed claims filed under the Plan and to establish such procedures that it deems necessary or advisable for the administration of the Plan (including, without limitation, to adopt such procedures, sub-plans, and appendices to the enrollment agreement as are necessary or appropriate to permit the participation in the Plan by employees who are foreign nationals or employed outside the U.S., the terms of which sub-plans and appendices may take precedence over other provisions of this Plan, with the exception of Section 13(a) hereof, but unless otherwise superseded by the terms of such sub-plan or appendix, the provisions of this Plan shall govern the operation of such sub-plan or appendix). Unless otherwise determined by the Administrator, the Eligible Employees eligible to participate in each sub-plan will participate in a separate Offering under the 423 Component, or if the terms would not qualify under the 423 Component, in the Non-423 Component, in either case unless such

designation would cause the 423 Component to violate the requirements of Section 423 of the Code. Without limiting the generality of the foregoing, the Administrator is specifically authorized to adopt rules and procedures regarding eligibility to participate, the definition of Compensation, handling of Contributions, making of Contributions to the Plan (including, without limitation, in forms other than payroll deductions), establishment of bank or trust accounts to hold Contributions, payment of interest, conversion of local currency, obligations to pay payroll tax, determination of beneficiary designation requirements, withholding procedures and handling of stock certificates that vary with applicable local requirements. The Administrator also is authorized to determine that, to the extent permitted by U.S. Treasury Regulation Section 1.423-2(f), the terms of an option granted under the Plan or an Offering to citizens or residents of a non-U.S. jurisdiction will be less favorable than the terms of options granted under the Plan or the same Offering to employees resident solely in the U.S. Every finding, decision and determination made by the Administrator will, to the full extent permitted by law, be final and binding upon all parties.

15. Transferability. Neither Contributions credited to a Participant's account nor any rights with regard to the exercise of an option or to receive shares of Common Stock under the Plan may be assigned, transferred, pledged or otherwise disposed of in any way (other than by will, the laws of descent and distribution) by the Participant. Any such attempt at assignment, transfer, pledge or other disposition will be without effect, except that the Company may treat such act as an election to withdraw funds from an Offering Period in accordance with Section 10 hereof.

16. Use of Funds. The Company may use all Contributions received or held by it under the Plan for any corporate purpose, and the Company will not be obligated to segregate such Contributions except under Offerings or for Participants in the Non-423 Component for which Applicable Laws require that Contributions to the Plan by Participants be segregated from the Company's general corporate funds and/or deposited with an independent third party, provided that, if such segregation or deposit with an independent third party is required by Applicable Laws, it will apply to all Participants in the relevant Offering under the 423 Component, except to the extent otherwise permitted by U.S. Treasury Regulation Section 1.423-2(f). Until shares of Common Stock are issued, Participants will only have the rights of an unsecured creditor with respect to such shares.

17. Reports. Individual accounts will be maintained for each Participant in the Plan. Statements of account will be given to participating Eligible Employees at least annually, which statements will set forth the amounts of Contributions, the Purchase Price, the number of shares of Common Stock purchased and the remaining cash balance, if any.

18. Adjustments, Dissolution, Liquidation, Merger or Change in Control.

(a) Adjustments. In the event that any dividend or other distribution (whether in the form of cash, Common Stock, other securities, or other property), recapitalization, stock split, reverse stock split, reorganization, merger, consolidation, split-up, spin-off, combination, repurchase, or exchange of Common Stock or other securities of the Company, or other change in the corporate structure of the Company affecting the Common Stock occurs, the Administrator, in order to prevent dilution or enlargement of the benefits or potential benefits intended to be made available under the Plan, will, in such manner as it may deem equitable, adjust the number and class of Common Stock that may be delivered under the Plan, the Purchase Price per share, class and the number of shares of Common Stock covered by each option under the Plan that has not yet been exercised, and the numerical limits of Sections 7 and 13.

(b) Dissolution or Liquidation. In the event of the proposed dissolution or liquidation of the Company, any Offering Period then in progress will be shortened by setting a New Exercise Date, and will terminate immediately prior to the consummation of such proposed dissolution or liquidation, unless provided otherwise by the Administrator. The New Exercise Date will be before the date of the Company's proposed dissolution or liquidation. The Administrator will notify each Participant in writing or electronically, prior to the New Exercise Date, that the Exercise Date for the Participant's option has been changed to the New Exercise Date and that the Participant's option will be exercised automatically on the New Exercise Date, unless prior to such date the Participant has withdrawn from the Offering Period as provided in Section 10 hereof.

(c) Merger or Change in Control. In the event of a merger or Change in Control, each outstanding option will be assumed or an equivalent option substituted by the successor corporation or a Parent or Subsidiary of the successor corporation. In the event that the successor corporation refuses to assume or substitute for the option, the Offering Period with respect to which such option relates will be shortened by setting a New Exercise Date on which such Offering Period shall end. The New Exercise Date will occur before the date of the Company's proposed merger or Change in Control. The Administrator will notify each Participant in writing or electronically prior to the New Exercise Date, that the Exercise Date for the Participant's option has been changed to the New Exercise Date and that the Participant's option will be exercised automatically on the New Exercise Date, unless prior to such date the Participant has withdrawn from the Offering Period as provided in Section 10 hereof.

19. Amendment or Termination.

(a) The Administrator, in its sole discretion, may amend, suspend, or terminate the Plan, or any part thereof, at any time and for any reason. If the Plan is terminated, the Administrator, in its discretion, may elect to terminate all outstanding Offering Periods either immediately or upon completion of the purchase of shares of Common Stock on the next Exercise Date (which may be sooner than originally scheduled, if determined by the Administrator in its discretion), or may elect to permit Offering Periods to expire in accordance with their terms (and subject to any adjustment pursuant to Section 18). If the Offering Periods are terminated prior to expiration, all amounts then credited to Participants' accounts that have not been used to purchase shares of Common Stock will be returned to the Participants (without interest thereon, except as otherwise required under Applicable Laws, as further set forth in Section 12 hereof) as soon as administratively practicable.

(b) Without stockholder consent and without limiting Section 19(a), the Administrator will be entitled to change the Offering Periods and any Purchase Periods, designate separate Offerings, limit the frequency and/or number of changes in the amount withheld during an Offering Period, establish the exchange ratio applicable to amounts withheld in a currency other than U.S. dollars, permit Contributions in excess of the amount designated by a Participant in order to adjust for delays or mistakes in the Company's

processing of properly completed Contribution elections, establish reasonable waiting and adjustment periods and/or accounting and crediting procedures to ensure that amounts applied toward the purchase of Common Stock for each Participant properly correspond with Contribution amounts, and establish such other limitations or procedures as the Administrator determines in its sole discretion advisable that are consistent with the Plan.

(c) In the event the Administrator determines that the ongoing operation of the Plan may result in unfavorable financial accounting consequences, the Administrator may, in its discretion and, to the extent necessary or desirable, modify, amend or terminate the Plan to reduce or eliminate such accounting consequence including, but not limited to:

(i) amending the Plan to conform with the safe harbor definition under the Financial Accounting Standards Board Accounting Standards Codification Topic 718 (or any successor thereto), including with respect to an Offering Period underway at the time;

(ii) altering the Purchase Price for any Offering Period or Purchase Period including an Offering Period or Purchase Period underway at the time of the change in Purchase Price;

(iii) shortening any Offering Period or Purchase Period by setting a New Exercise Date, including an Offering Period or Purchase Period underway at the time of the Administrator action;

(iv) reducing the maximum percentage of Compensation a Participant may elect to set aside as Contributions; and

(v) reducing the maximum number of shares of Common Stock a Participant may purchase during any Offering Period or Purchase Period.

Such modifications or amendments will not require stockholder approval or the consent of any Plan Participants.

20. Notices. All notices or other communications by a Participant to the Company under or in connection with the Plan will be deemed to have been duly given when received in the form and manner specified by the Company at the location, or by the person, designated by the Company for the receipt thereof.

21. Conditions Upon Issuance of Shares. Shares of Common Stock will not be issued with respect to an option unless the exercise of such option and the issuance and delivery of such shares pursuant thereto will comply with all applicable provisions of law, domestic or foreign, including, without limitation, the Securities Act of 1933, as amended, the Exchange Act, the rules and regulations promulgated thereunder, and the requirements of any stock exchange upon which the shares may then be listed, and will be further subject to the approval of counsel for the Company with respect to such compliance.

As a condition to the exercise of an option, the Company may require the person exercising such option to represent and warrant at the time of any such exercise that the shares are being purchased only for investment and without any present intention to sell or distribute such shares if, in the opinion of counsel for the Company, such a representation is required by any of the aforementioned applicable provisions of law.

22. Section 409A. The Plan is intended to be exempt from the application of Section 409A, and, to the extent not exempt, is intended to comply with Section 409A and any ambiguities herein will be interpreted to so be exempt from, or comply with, Section 409A. In furtherance of the foregoing and notwithstanding any provision in the Plan to the contrary, if the Administrator determines that an option granted under the Plan may be subject to Section 409A or that any provision in the Plan would cause an option under the Plan to be subject to Section 409A, the Administrator may amend the terms of the Plan and/or of an outstanding option granted under the Plan, or take such other action the Administrator determines is necessary or appropriate, in each case, without the Participant's consent, to exempt any outstanding option or future option that may be granted under the Plan from or to allow any such options to comply with Section 409A, but only to the extent any such amendments or action by the Administrator would not violate Section 409A. Notwithstanding the foregoing, the Company shall have no liability to a Participant or any other party if the option to purchase Common Stock under the Plan that is intended to be exempt from or compliant with Section 409A is not so exempt or compliant or for any action taken by the Administrator with respect thereto. The Company makes no representation that the option to purchase Common Stock under the Plan is compliant with Section 409A.

23. Term of Plan. The Plan will become effective upon the later to occur of (a) its adoption by the Board or (b) the business day immediately prior to the Registration Date. It will continue in effect for a term of twenty (20) years, unless sooner terminated under Section 19.

24. Stockholder Approval. The Plan will be subject to approval by the stockholders of the Company within twelve (12) months after the date the Plan is adopted by the Board. Such stockholder approval will be obtained in the manner and to the degree required under Applicable Laws.

25. Governing Law. The Plan shall be governed by, and construed in accordance with, the laws of the State of California (except its choice-of-law provisions).

26. No Right to Employment. Participation in the Plan by a Participant shall not be construed as giving a Participant the right to be retained as an employee of the Company or a Subsidiary or Affiliate, as applicable. Furthermore, the Company or a Subsidiary or Affiliate may dismiss a Participant from employment at any time, free from any liability or any claim under the Plan.

27. Severability. If any provision of the Plan is or becomes or is deemed to be invalid, illegal, or unenforceable for any reason in any jurisdiction or as to any Participant, such invalidity, illegality or unenforceability shall not affect the remaining parts of the Plan, and the Plan shall be construed and enforced as to such jurisdiction or Participant as if the invalid, illegal or unenforceable provision had not been included.

28. Compliance with Applicable Laws. The terms of this Plan are intended to comply with all Applicable Laws and will be construed accordingly.

29. Automatic Transfer to Low Price Offering Period. To the extent permitted by Applicable Laws, if the Fair Market Value of the Common Stock on any Exercise Date in an Offering Period is lower than the Fair Market Value of the Common Stock on the Enrollment Date of such Offering Period, then all Participants in such Offering Period will be automatically withdrawn from such Offering Period immediately after the exercise of their option on such Exercise Date and automatically re-enrolled in the immediately following Offering Period as of the first day thereof.

EXHIBIT A

DENALI THERAPEUTICS INC.

2017 EMPLOYEE STOCK PURCHASE PLAN

SUBSCRIPTION AGREEMENT

_____ Original Application Offering Date: _____

_____ Change in Payroll Deduction Rate

1. hereby elects to participate in the Denali Therapeutics Inc. 2017 Employee Stock Purchase Plan (the "Plan") and subscribes to purchase shares of the Company's Common Stock in accordance with this Subscription Agreement and the Plan. Any capitalized terms not specifically defined in this Subscription Agreement will have the meaning ascribed to them under the Plan.

2. I hereby authorize and consent to payroll deductions from each paycheck in the amount of % of my Compensation on each payday (from 1% to 15%; a decrease in rate may be to 0%) during the Offering Period in accordance with the Plan. (Please note that no fractional percentages are permitted.)

3. I understand that said payroll deductions will be accumulated for the purchase of shares of Common Stock at the applicable Purchase Price determined in accordance with the Plan. I understand that if I do not withdraw from an Offering Period, any accumulated payroll deductions will be used to automatically exercise my option and purchase Common Stock under the Plan. I further understand that if I am outside of the U.S., my payroll deductions will be converted to U.S. dollars at an exchange rate selected by the Company on the purchase date.

4. I have received a copy of the complete Plan and its accompanying prospectus. I understand that my participation in the Plan is in all respects subject to the terms of the Plan.

5. Shares of Common Stock purchased for me under the Plan should be issued in the name(s) of (Eligible Employee or Eligible Employee and spouse only).

6. If I am a U.S. taxpayer, I understand that if I dispose of any shares received by me pursuant to the Plan within two (2) years after the Offering Date (the first day of the Offering Period during which I purchased such shares) or one (1) year after the Exercise Date, I will be treated for federal income tax purposes as having received ordinary income at the time of such disposition in an amount equal to the excess of the fair market value of the shares at the time such shares were purchased by me over the price that I paid for the shares. I hereby agree to notify the Company in writing within thirty (30) days after the date of any disposition of my shares and I will make adequate provision for federal, state or other tax withholding obligations, if any, which arise upon the disposition of the Common Stock. The Company may, but will not be obligated to, withhold from my compensation the amount necessary to meet any applicable withholding obligation including any withholding necessary to make available to the Company any tax

deductions or benefits attributable to sale or early disposition of Common Stock by me. If I dispose of such shares at any time after the expiration of the two (2)-year and one (1)-year holding periods, I understand that I will be treated for federal income tax purposes as having received income only at the time of such disposition, and that such income will be taxed as ordinary income only to the extent of an amount equal to the lesser of (a) the excess of the fair market value of the shares at the time of such disposition over the purchase price which I paid for the shares, or (b) 15% of the fair market value of the shares on the first day of the Offering Period. The remainder of the gain, if any, recognized on such disposition will be taxed as capital gain.

7. For employees that may be subject to tax in non U.S. jurisdictions, I acknowledge and agree that, regardless of any action taken by the Company or any Subsidiary with respect to any or all income tax, social security, social insurances, National Insurance Contributions, payroll tax, fringe benefit, or other tax-related items related to my participation in the Plan and legally applicable to me including, without limitation, in connection with the grant of such options, the purchase or sale of shares of Common Stock acquired under the Plan and/or the receipt of any dividends on such shares ("Tax-Related Items"), the ultimate liability for all Tax-Related Items is and remains my responsibility and may exceed the amount actually withheld by the Company or a Subsidiary. Furthermore, I acknowledge that the Company and/or the Subsidiary (a) make no representations or undertakings regarding the treatment of any Tax-Related Items in connection with any aspect of the options under the Plan and (b) do not commit to and are under no obligation to structure the terms of the grant of options or any aspect of my participation in the Plan to reduce or eliminate my liability for Tax-Related Items or achieve any particular tax result. Further, if I have become subject to tax in more than one jurisdiction between the date of my enrollment and the date of any relevant taxable or tax withholding event, as applicable, I acknowledge that the Company and/or the Employer (or former employer, as applicable) may be required to withhold or account for Tax-Related Items in more than one jurisdiction.

Prior to the purchase of shares of Common Stock under the Plan or any other relevant taxable or tax withholding event, as applicable, I agree to make adequate arrangements satisfactory to the Company and/or the Subsidiary to satisfy all Tax-Related Items. In this regard, I authorize the Company and/or the Subsidiary, or their respective agents, at their discretion, to satisfy the obligations with regard to all Tax-Related Items by one or a combination of the following: (1) withholding from my wages or Compensation paid to me by the Company and/or the Subsidiary; or (2) withholding from proceeds of the sale of the shares of Common Stock purchased under the Plan either through a voluntary sale or through a mandatory sale arranged by the Company (on my behalf pursuant to this authorization). Depending on the withholding method, the Company may withhold or account for Tax-Related Items by considering applicable maximum applicable withholding rates, in which case I will receive a refund of any over-withheld amount in cash and will have no entitlement to the Common Stock equivalent.

Finally, I agree to pay to the Company or the Subsidiary any amount of Tax-Related Items that the Company or the Subsidiary may be required to withhold as a result of my participation in the Plan that cannot be satisfied by the means previously described. The Company may refuse to purchase shares of Common Stock under the Plan on my behalf and/or refuse to issue or deliver the shares or the proceeds of the sale of shares if I fail to comply with my obligations in connection with the Tax-Related Items.

8. By electing to participate in the Plan, I acknowledge, understand and agree that:

(a) the Plan is established voluntarily by the Company, it is discretionary in nature and it may be modified, amended, suspended or terminated by the Company at any time, to the extent provided for in the Plan;

(b) all decisions with respect to future grants under the Plan, if applicable, will be at the sole discretion of the Company;

(c) the grant of purchase rights under the Plan shall not create a right to employment or be interpreted as forming an employment or service contract with the Company, or any Subsidiary of the Company, and shall not interfere with the ability of the Company or the Subsidiary, as applicable, to terminate my employment (if any);

(d) I am voluntarily participating in the Plan;

(e) the purchase rights granted under the Plan and the shares of Common Stock underlying such purchase rights, and the income and value of same, are not intended to replace any pension rights or compensation;

(f) the purchase rights granted under the Plan and the shares of Common Stock underlying such purchase rights, and the income and value of same, are not part of my normal or expected compensation for any purpose, including, but not limited to, calculating any severance, resignation, termination, redundancy, dismissal, end-of-service payments, bonuses, long-service awards, pension or retirement benefits or similar payments;

(g) the future value of the shares of Common Stock offered under the Plan is unknown, indeterminable and cannot be predicted with certainty;

(h) the shares of Common Stock that I acquire under the Plan may increase or decrease in value, even below the Purchase Price;

(i) no claim or entitlement to compensation or damages shall arise from the forfeiture of purchase rights granted to me under the Plan as a result of the termination of my status as an eligible employee (for any reason whatsoever, and whether or not later found to be invalid or in breach of employment laws in the jurisdiction where I am employed or the terms of my employment agreement, if any) and, in consideration of the grant of purchase rights under the Plan to which I am otherwise not entitled, I irrevocably agree never to institute a claim against the Company, or any Subsidiary, waive my ability, if any, to bring such claim, and release the Company, and any Subsidiary from any such claim that may arise; if, notwithstanding the foregoing, any such claim is allowed by a court of competent jurisdiction, I shall be deemed irrevocably to have agreed to not to pursue such claim and agree to execute any and all documents necessary to request dismissal or withdrawal of such claim; and

(j) in the event of the termination of my status as an eligible employee (for any reason whatsoever, whether or not later found to be invalid or in breach of employment laws in the jurisdiction where I am employed or the terms of my employment agreement, if any), my right to participate in the Plan and any options granted to me under the Plan, if any, will terminate effective as of the date that I am no longer actively employed by the Company or one of its Designated Companies and, in any event, will not be extended by any notice period mandated under the employment laws in the jurisdiction in which I am employed or the terms of my employment agreement, if any (*e.g.*, active employment would not include a period of "garden leave" or similar period pursuant to the employment laws in the jurisdiction in which I am employed or the terms of my employment agreement, if any); the Company shall have the exclusive discretion to determine when I am no longer actively employed for purposes of my participation in the Plan (including whether I may still be considered to be actively employed while on a leave of absence).

9. I understand that the Company and the Subsidiary may collect, where permissible under applicable law certain personal information about me, including, but not limited to, my name, home address and telephone number, date of birth, social insurance number or other identification number, salary, nationality, job title, any shares of Common Stock or directorships held in the Company, details of all options granted under the Plan or any other entitlement to shares of Common Stock awarded, canceled, exercised, vested, unvested or outstanding in my favor ("Data"), for the exclusive purpose of implementing, administering and managing the Plan. I understand that Company may transfer my Data to the United States, which is not considered by the European Commission to have data protection laws equivalent to the laws in my country. I understand that the Company will transfer my Data to its designated broker, or such other stock plan service provider as may be selected by the Company in the future, which is assisting the Company with the implementation, administration and management of the Plan. I understand that the recipients of the Data may be located in the United States or elsewhere, and that a recipient's country of operation (e.g., the United States) may have different, including less stringent, data privacy laws that the European Commission or my jurisdiction does not consider to be equivalent to the protections in my country. I understand that I may request a list with the names and addresses of any potential recipients of the Data by contacting my local human resources representative. I authorize the Company, the Company's designated broker and any other possible recipients which may assist the Company with implementing, administering and managing the Plan to receive, possess, use, retain and transfer the Data, in electronic or other form, for the sole purpose of implementing, administering and managing my participation in the Plan. I understand that Data will be held only as long as is necessary to implement, administer and manage my participation in the Plan. I understand that that I may, at any time, view Data, request additional information about the storage and processing of Data, require any necessary amendments to Data or refuse or withdraw the consents herein, in any case without cost, by contacting in writing my local human resources representative. Further, I understand that I am providing the consents herein on a purely voluntary basis. If I do not consent, or if I later seek to revoke my consent, my employment status or career with the Company or the Subsidiary will not be adversely affected; the only adverse consequence of refusing or withdrawing my consent is that the Company would not be able to grant me options under the Plan or other equity awards, or administer or maintain such awards. Therefore, I understand that refusing or withdrawing my consent may affect my ability to participate in the Plan. For more information on the consequences of my refusal to consent or withdrawal of consent, I understand that I may contact my local human resources representative.

For employees outside the U.S., I understand that I have the right to access, and to request a copy of, the Data held about me. I also understand that I have the right to discontinue the collection, processing, or use of my Data, or supplement, correct, or request deletion of my Data. To exercise my rights, I may contact my local human resources representative.

I hereby explicitly and unambiguously consent to the collection, use and transfer, in electronic or other form, of my personal data as described herein and any other Plan materials by and among, as applicable, the Company and its Subsidiaries for the exclusive purpose of implementing, administering and managing my participation in the Plan. I understand that my consent will be sought and obtained for any processing or transfer of my data for any purpose other than as described in the enrollment form and any other plan materials.

10. If I have received the Subscription Agreement or any other document related to the Plan translated into a language other than English and if the meaning of the translated version is different than the English version, the English version will control, subject to applicable laws.

11. The provisions of the Subscription Agreement and these appendices are severable and if any one or more provisions are determined to be illegal or otherwise unenforceable, in whole or in part, the remaining provisions shall nevertheless be binding and enforceable.

12. Notwithstanding any provisions in this Subscription Agreement, I understand that if I am working or resident in a country other than the United States, my participation in the Plan shall also be subject to the additional terms and conditions set forth on Appendix A and any special terms and conditions for my country set forth on Appendix A. Moreover, if I relocate to one of the countries included in Appendix A, the special terms and conditions for such country will apply to me to the extent the Company determines that the application of such terms and conditions is necessary or advisable for legal or administrative reasons. Appendix A constitutes part of this Subscription Agreement and the provisions of this Subscription Agreement govern each Appendix (to the extent not superseded or supplemented by the terms and conditions set forth in the applicable Appendix).

13. I hereby agree to be bound by the terms of the Plan. The effectiveness of this Subscription Agreement is dependent upon my eligibility to participate in the Plan.

Employee's Social
Security Number
(for U.S.-based employees): _____

Employee's Address: _____

_____

_____

I UNDERSTAND THAT THIS SUBSCRIPTION AGREEMENT WILL REMAIN IN EFFECT THROUGHOUT SUCCESSIVE OFFERING PERIODS UNLESS TERMINATED BY ME.

Dated: _____

_____

Signature of Employee

EXHIBIT B

DENALI THERAPEUTICS INC.

2017 EMPLOYEE STOCK PURCHASE PLAN

NOTICE OF WITHDRAWAL

The undersigned Participant in the Offering Period of the Denali Therapeutics Inc. 2017 Employee Stock Purchase Plan that began on , (the "Offering Date") hereby notifies the Company that he or she hereby withdraws from the Offering Period. He or she hereby directs the Company to pay to the undersigned as promptly as practicable all the payroll deductions credited to his or her account with respect to such Offering Period. The undersigned understands and agrees that his or her option for such Offering Period will be automatically terminated. The undersigned understands further that no further payroll deductions will be made for the purchase of shares in the current Offering Period and the undersigned will be eligible to participate in succeeding Offering Periods only by delivering to the Company a new Subscription Agreement. Capitalized terms not otherwise defined herein will have the same meanings as such terms are defined in the Plan.

Name and Address of Participant:

_____

_____

_____

Signature:

_____

Date: _____

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the reference to our firm under the caption "Experts" and to the use of our report dated September 8, 2017 (except for the second paragraph of Note 1 and for Note 13, as to which the date is December , 2017), in Amendment No. 1 to the Registration Statement (Form S-1 No. 333-221522) and related Prospectus of Denali Therapeutics Inc. for the registration of 8,333,333 shares of its common stock.

Ernst & Young LLP

Redwood City, California

The foregoing consent is in the form that will be signed upon the effectiveness of the reverse stock split described in the second paragraph of Note 1 to the consolidated financial statements.

/s/ Ernst & Young LLP

Redwood City, California
November 27, 2017