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

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2025

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from _____ to _____

Commission File Number: 001-38311

Denali Therapeutics Inc.

(Exact name of registrant as specified in its charter)

Delaware	**46-3872213**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

161 Oyster Point Blvd.
South San Francisco, CA, 94080

(Address of principal executive offices and zip code)

(650) 866-8547
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Stock, par value $0.01 per share	DNLI	The Nasdaq Global Select Market

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☒ No ☐

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Securities Exchange Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a 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. (Check one):

Large accelerated filer	☒	Accelerated filer	☐
Non-accelerated filer	☐	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 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of the common stock held by non-affiliates of the registrant as of June 30, 2025 (the last business day of the registrant's most recently completed second fiscal quarter) was approximately $1.1 billion, based on the closing price of the registrant's common stock, as reported by the Nasdaq Global Select Market on June 30, 2025 of $13.99 per share. Shares of the registrant's common stock held by each executive officer, director and holder of 5% or more of the outstanding common stock have been excluded in that such persons may be deemed to be affiliates. This calculation does not reflect a determination that certain persons are affiliates of the registrant for any other purpose.

The number of outstanding shares of the registrant's common stock as of February 20, 2026 was 158,591,491 par value $0.01 per share, outstanding. This number does not include 28,331,779 shares of common stock issuable upon the exercise of pre-funded warrants outstanding as of February 20, 2026 (which are immediately exercisable at an exercise price of $0.01 per share of common stock, subject to beneficial ownership limitations). See Note 8 — Common Stock to the registrant's consolidated financial statements.

DOCUMENTS INCORPORATED BY REFERENCE:

Portions of the registrant's Definitive Proxy Statement relating to the registrant's 2026 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K where indicated. Such Definitive Proxy Statement will be filed with the Securities and Exchange Commission within 120 days after the end of the registrant's 2025 fiscal year ended December 31, 2025.

Denali Therapeutics Inc.
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PART I

Special Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements. All statements other than statements of historical facts contained in this report, 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 report include, but are not limited to, statements about:

- *the progress, success, cost and timing of our development activities, preclinical studies and clinical trials, and in particular the development of our blood-brain barrier (“BBB”) platform technology, programs, and biomarkers, including the initiation and completion of studies or trials and related preparatory work, enrollment in such trials, the timing of when data from clinical trials will become available, the advancement of new molecule entities into clinical development and related timing, and the filing of investigational new drug applications or clinical trial applications;*

- *the impact of preclinical 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 and potential revenue resulting from strategic collaborations with third parties 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 extent to which any dosing limitations that we have been subject to, and/or may be subject to in the future, may affect the success of our product candidates;*

- *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 and/or acquire additional intellectual property relating to our product candidates and Transport Vehicle;*

- *our ability to obtain funding for our operations, including funding necessary to develop and commercialize our current and potential future product candidates;*

- *our plans and ability to establish sales, marketing, manufacturing, 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;*
- *our plans and ability to develop our own manufacturing facilities;*
- *the pricing and reimbursement of our product candidates, if approved and commercialized;*
- *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 ability to enhance operational, financial, and information management systems;*
- *the impact of adverse economic conditions such as instability in the financial services sector, rising interest rates, rising inflation, and increased labor market competition;*
- *the impact of increased geopolitical uncertainty, the global pandemic, and related global economic disruptions and social conditions on our business; and*
- *our financial performance.*

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 report and are subject to a number of risks, uncertainties and assumptions described in the section titled “Risk Factors” and elsewhere in this report. 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 undertake no obligation to update publicly any forward-looking statements for any reason after the date of this Annual Report on Form 10-K to conform these statements to actual results or to changes in expectations.

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 report, 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.

This report 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 report 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.

ITEM 1. BUSINESS

Overview and Strategy

Our purpose is to bring the power of biotherapeutics to the whole body, including the brain, by discovering, developing, and delivering medicines for people living with serious diseases.

Historically, the blood-brain barrier has been a major challenge to the development of medicines for diseases of the central nervous system. While the blood-brain barrier protects the brain and is essential for our survival, it also prevents the delivery of medicines to the brain in sufficient quantities to have therapeutic effect. We have invented, developed, and validated a proprietary technology, called the TransportVehicle™ ("TV"), to address the blood-brain barrier challenge and enable a new class of barrier-crossing therapeutics. The TV has a modular design enabling delivery of large molecules, i.e., enzymes, oligonucleotides, and antibodies, to all tissues of the body, including the brain, by crossing the blood-brain barrier after systemic administration. Over the last few decades, large molecule biotherapeutics have enabled medical breakthroughs in treating a wide array of serious diseases, but with very limited success in central nervous system diseases. Now, with the invention and validation of our TV technology, we are leading the field in delivering on the potential of biotherapeutics to transform the lives of individuals with neurodegenerative diseases, lysosomal storage disorders, and other serious diseases.

We are building a broad portfolio of therapeutic candidates by investing in our TV franchises, i.e., Enzyme TV ("ETV"), Oligonucleotide TV ("OTV"), and Antibody TV ("ATV"), to advance programs for rare diseases, such as lysosomal storage diseases, and common diseases, such as Alzheimer's disease and Parkinson's disease. Our most advanced TV-enabled program is tividenofusp alfa (DNL310, ETV:IDS) for the potential treatment of mucopolysaccharidosis II ("MPS II", or Hunter syndrome). The biologics license application ("BLA") for tividenofusp alfa is under priority review for accelerated approval by the U.S. Food and Drug Administration ("FDA"), and we have established commercial readiness in anticipation of the Prescription Drug User Fee Act (PDUFA) target action date of April 5, 2026. Our TV-enabled clinical development portfolio also includes DNL126 (ETV:SGSH) for mucopolysaccharidosis IIIA (“MPS IIIA”, or Sanfilippo syndrome type A), DNL593 (PTV:PGRN) for frontotemporal dementia-granulin (“FTD-*GRN*”), DNL628 (OTV:MAPT) for Alzheimer’s disease, and DNL952 (ETV:GAA) for Pompe disease. We believe the combination of a clinically-validated delivery platform and a maturing therapeutic portfolio will position us for long-term success in our goal to deliver barrier-crossing, targeted, and effective medicines.

Key elements of our strategy include:

1) **Discover:** Advance a new class of barrier-crossing therapeutics by leveraging our TV platforms and deep expertise in blood-brain barrier biology to enhance the delivery of biotherapeutics to the brain and throughout the body.

2) **Develop:** Accelerate and expand a broad portfolio of TV-based product candidates to fully unlock the potential of barrier-crossing therapeutics, applying patient-informed development and driving biomarker-guided regulatory approvals.

3) **Deliver:** Launch initial products targeting rare lysosomal storage diseases as a strategic foundation for expansion into common neurodegenerative conditions and other serious diseases, while building integrated capabilities for long-term growth and profitability.

Our “D3X3” strategy reflects our next phase of execution and is anchored in our “Discover, Develop, Deliver” (D3) framework, with three-year objectives (X3) across our portfolio, as we transition from platform validation to delivery and scalable growth. Our goals are to (i) deliver two growing commercial brands, tividenofusp alfa (ETV:IDS) for Hunter syndrome and DNL126 (ETV:SGSH) for Sanfilippo syndrome type A, establishing the foundation for a durable rare disease franchise; (ii) achieve five clinical proof-of-concept readouts across our portfolio, including programs in Alzheimer’s disease (ATV:Abeta and OTV:MAPT), FTD-*GRN* (PTV:PGRN), Pompe disease (ETV:GAA), and Parkinson’s disease (LRRK2 inhibitor); and (iii) advance four to six additional TV-enabled programs into the clinic (**Figure 1)**. We believe disciplined and efficient execution against these objectives will demonstrate the breadth and scalability of our TV platform, position us to deliver sustainable long-term growth, and advance our mission to unlock the full potential of biotherapeutics with the goal of transforming the lives of people living with serious diseases.

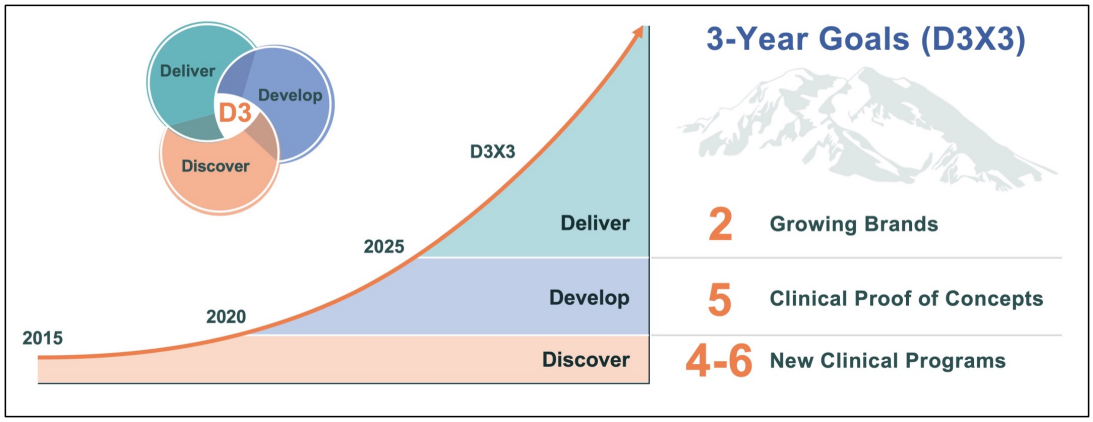

Figure 1: **Denali’s D3X3 Three-Year Strategic Framework.** Illustration of Denali’s evolution over time in the context of our Discover, Develop, Deliver (D3) foundation and three-year (D3X3) objectives (2026 - 2028) to deliver two growing brands, achieve five clinical proof-of-concept readouts, and advance four to six new clinical programs as we transition from platform validation to commercial delivery and scalable growth.

We expect our first potential product launches will be with tividenofusp alfa for MPS II followed by DNL126 for MPS IIIA. MPS II and MPS IIIA belong to a group of lysosomal storage diseases, which are caused by genetic mutations that lead to single-enzyme deficiencies. Lysosomal storage diseases afflict more than 30,000 individuals worldwide. About two-thirds of these diseases affect the central nervous system; however, the current standard treatment, enzyme replacement therapy, does not address central nervous system manifestations, even for the lysosomal storage diseases where enzyme replacement therapy is available. Our ETV therapeutics are designed as next-generation enzyme replacement therapies to address both central nervous system and somatic manifestations of lysosomal storage diseases. Our BLA submission for tividenofusp alfa under the accelerated approval pathway is based on alignment with the FDA that cerebrospinal fluid ("CSF") heparan sulfate may be used as a surrogate biomarker for MPS II. Likewise, given that CSF heparan sulfate is also the primary substrate in MPS IIIA, we have aligned with the FDA on an accelerated approval path for DNL126. Together, we expect these two programs to have a combined market opportunity of over $1 billion and to be the foundation of a broad commercial franchise of ETV-enabled enzyme replacement therapies with a collective market potential of over $5 billion.

We have established commercial readiness for tividenofusp alfa including continued dialogue with advocacy groups, prescribers and payers, and building a suite of patient support services and capabilities to enable access. We have established a right-sized team in commercial and medical affairs to support tividenofusp alfa and additional ETV launches, including DNL126 (ETV:SGSH) for MPS IIIA. We include PTV:PGRN as one of our ETV franchise programs as it has a similar mechanism of action in increasing levels of deficient or missing protein to improve lysosomal function. We have an active collaboration with Takeda Pharmaceutical Company Limited ("Takeda") for the development and commercialization of TAK-594/DNL593 (PTV:PGRN) for FTD-*GRN*. We are initiating clinical development with DNL952 (ETV:GAA) for late-onset Pompe disease, expanding the reach of our TV platform into muscle disease. We intend to commercialize these product candidates, if approved, in key markets and/or leverage partnerships or distributors to ensure optimal access for patients. Launching in rare indications first gives us the opportunity to build and establish our own commercial organization so that we are poised for success in larger indications over time.

In parallel, we are advancing TV-enabled programs for common neurodegenerative diseases, such as Alzheimer’s disease and Parkinson's disease, which afflict over 40 million individuals worldwide and have a market potential of over $5 billion per indication. We have advanced DNL628 (OTV:MAPT) targeting tau into a Phase 1b clinical study for Alzheimer’s disease, and we plan to submit a regulatory application in the first half of 2026 to begin clinical testing of DNL921 (ATV:Abeta) targeting amyloid plaques. Amyloid plaques and tau tangles are pathological hallmarks of Alzheimer's disease. We are targeting both of these pathologies with our ATV and OTV platforms, respectively, aiming to deliver the next generation of anti-amyloid therapeutics and a potential first-in-class anti-tau therapeutic. Preclinical studies with ATV:Abeta have demonstrated potential for better efficacy and safety compared to a standard antibody, with superior plaque reduction and very low rates of amyloid related imaging abnormalities ("ARIA"). Likewise, preclinical studies with OTV:MAPT have demonstrated robust and sustained reductions of tau protein. For late-stage development and commercialization in common indications, such as Alzheimer's disease, we may plan to initially leverage strategic collaborations that contribute existing global infrastructure.

In addition to our development programs for neurodegenerative and lysosomal storage diseases, we have a robust discovery effort to further expand our portfolio and capture the full potential of our TV platform to enhance delivery of biotherapeutics to all tissues in the body. We are also pursuing opportunities of unmet need in other disease areas including oncology. For example, we have engineered a bispecific ATV:HER2 antibody and have demonstrated preclinically improved peripheral anti-tumor activity as well as enhanced brain uptake of the bispecific ATV:HER2 as compared to a non-ATV HER2 antibody. The data support the potential for ATV:HER2 to treat HER2-positive peripheral tumors and brain metastases and further validate the potential for TV applications in oncology.

Our therapeutic portfolio also includes BIIB122/DNL151 (LRRK2 inhibitor) for Parkinson's disease, a small molecule drug candidate that does not use the TV platform but is engineered with optimized chemical and physical properties to cross the blood-brain barrier. Denali has an active collaboration with Biogen Inc.’s subsidiaries, Biogen MA Inc. (“BIMA”) and Biogen International GmbH (“BIG”) (BIMA and BIG, collectively, “Biogen”) for the development and commercialization of BIIB122/DNL151. Biogen is conducting the global Phase 2b LUMA study, which is evaluating the ability of BIIB122 to slow disease progression as compared to placebo in participants with early-stage Parkinson's disease. A total of 650 participants were enrolled in LUMA and data are expected in mid-2026. In addition, Denali is conducting the complementary Phase 2a BEACON study in LRRK2-associated Parkinson's disease with the aim to generate biomarker and safety data to inform how LRRK2 inhibition may impact this disease.

In March 2025, we officially opened our clinical biomanufacturing facility in Salt Lake City, Utah, expanding our U.S. manufacturing capabilities and strengthening supply chain control and operational efficiency. We have begun manufacturing drug supply for clinical trials to support expansion of our TV-enabled therapeutic portfolio. We employ standard antibody manufacturing processes, including Chinese hamster ovary cell culture and Protein A affinity purification, which are compatible with existing global manufacturing infrastructure and enable efficient scale-up. We expect to continue a hybrid manufacturing strategy, utilizing both internal capabilities and external contract manufacturers for additional capacity, sterile fill-finish, and oligonucleotide synthesis, as appropriate, to support our pipeline and future commercial needs.

Collaborations and partnering are central components of our strategy to build, develop, and commercialize our portfolio of product candidates. We have numerous arrangements with biopharmaceutical companies, technology companies, academic institutions, foundations, and patient-focused data companies. Notable active arrangements include those with Biogen and Takeda as described above and Genzyme Corporation, a wholly owned subsidiary of Sanofi S.A. ("Sanofi"), for the development and commercialization of SAR443122/DNL758 (peripherally restricted small molecule RIPK1 inhibitor) in ulcerative colitis. We hold significant development and commercialization rights to all of our central nervous system programs, including the programs which are subject to our collaboration agreements with Biogen and Takeda, where we share responsibility for clinical development and share commercialization rights in the United States and China. Our costs of developing programs associated with these collaborations are largely covered through upfront payments, expected incoming milestone and royalty payments, and cost sharing. We may seek additional strategic partnering opportunities as we strive to capture the full value of our portfolio and platforms.

We are guided by the core Denali Values of trust, growth, grit and unity. Our working culture seeks to develop quality leaders, emphasize continuous growth, and promote problem-solving and invention. We strive to manage our operations in a way that is sustainable and reduces our impact on the environment, including through a Green Alternative program, which provides researchers with information on suitable alternative chemicals that have a lower environmental impact for common solvents. Additionally, several waste streams have been segregated on-site for proper disposal or recycling, such as containers, food waste, plastics, styrofoam, and glass chemical containers, to maximize recycling and composting. We also maintain an ongoing commitment to corporate governance principles, with oversight of ESG matters by Denali's Board of Directors, and strong performance orientation in our compensation program.

Our TransportVehicle™ Platform

Historically, the blood-brain barrier has been a major challenge to the development of medicines for diseases of the central nervous system. As a tightly knit layer of endothelial cells lining the vasculature of the brain, the blood-brain barrier protects the brain from threats such as harmful substances and infections by closely regulating transport of molecules from the blood into and out of the brain. While the blood-brain barrier is essential for our survival, it also prevents the delivery of medicines to the brain in sufficient quantities to have therapeutic effect. We have pioneered and are developing a new class of biotherapeutics to directly address the blood-brain barrier challenge.

We invented, developed, and continue to optimize a proprietary technology, called the TransportVehicle™ ("TV"), to deliver our large molecule biotherapeutic candidates to the brain after systemic administration. Our research has shown that the TV platform enables efficient delivery of biotherapeutics throughout the body, including the brain and other tissues that are traditionally difficult to reach. By engaging endogenous receptor-mediated transport pathways, such as the transferrin receptor ("TfR"), the TV enhances distribution beyond the vasculature, supporting uptake in the central nervous system as well as peripheral tissues such as muscle, bone, and other organs. This whole-body delivery capability allows us to address diseases with both central and systemic manifestations using a single therapeutic approach. Our TV technology is modular and enables brain delivery of several classes of biotherapeutics including enzymes, oligonucleotides, antibodies, and other proteins (**Figure 2**).

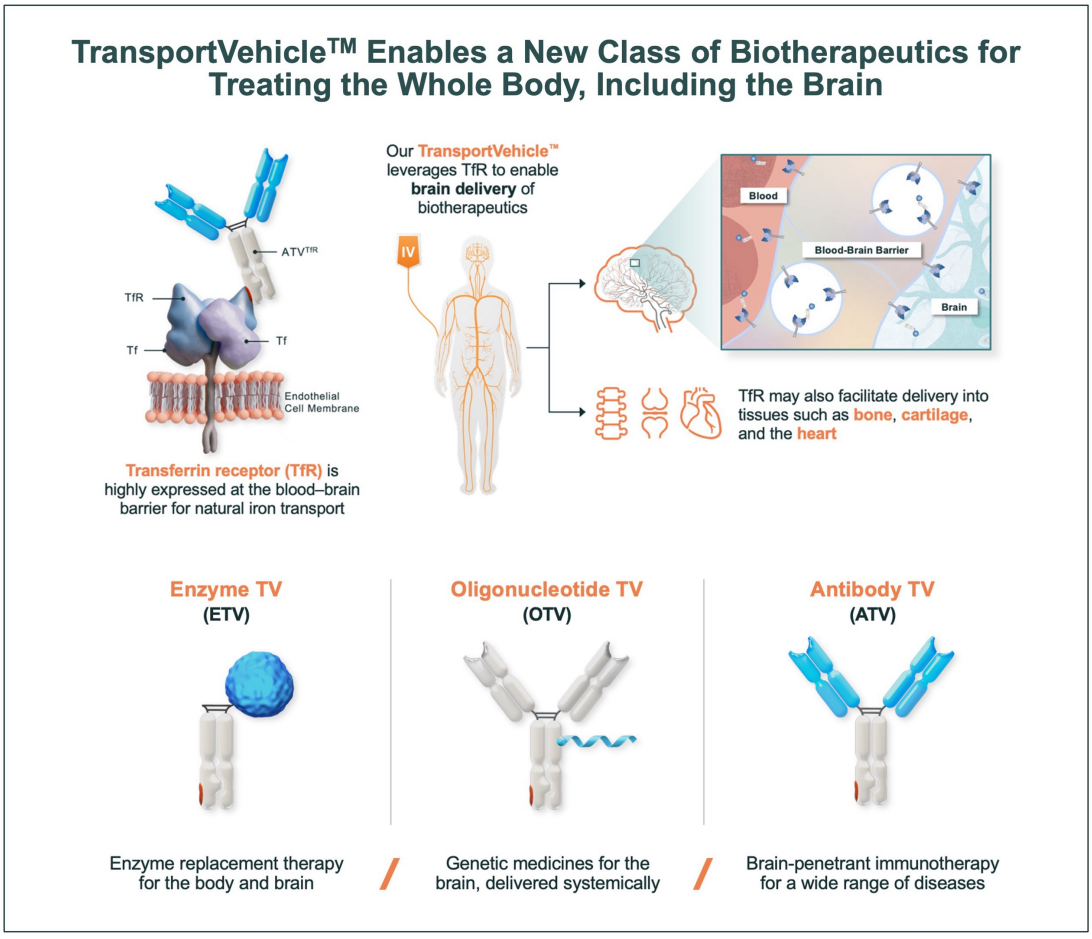

Figure 2: Engineering brain delivery. Schematic of the TV platform and modalities, designed to cross the blood-brain barrier through receptor mediated transcytosis, leveraging endogenous receptors expressed on endothelial cells of the central nervous system vasculature.

Our TV technology is differentiated from other blood-brain barrier technologies through its engineering approach, which may provide superior therapeutic efficacy, safety, and tolerability through higher stability, exposure, and biodistribution as well as the potential for lower immunogenicity of drug candidates in the brain. Compared to conventional approaches that use the Fab portion (the "arms") of a full-length antibody to bind to the targeted blood-brain barrier receptor (e.g.,TfR), we use an Fc domain (the "legs") (**Figure 3**). We have engineered the blood-brain barrier receptor binding site into one of the Fc's (monovalent binding) and we can optimize binding affinity (how tightly the Fc binds its blood-brain barrier receptor target) and epitope (where the Fc binds its blood-brain barrier receptor target) to enhance brain delivery and limit receptor degradation. Clinical and preclinical studies with several of our TV-enabled product candidates demonstrated high concentrations and broad distribution in all explored regions of the central nervous system and in key central nervous system cell types and showed improved pharmacodynamic effects compared to standard biotherapeutics.

We can also modify the amino acid sequences in the Fc to enable "conditional effector function", which is important for optimal activity of certain molecules, such as ATV:Abeta, that require immune cell activity for therapeutic effect. By toggling effector function "on or off", the loss of reticulocytes (immature red blood cells) can be avoided, potentially limiting anemia, which is a known liability associated with targeting TfR. Further, as the blood-brain barrier receptor binding site is a short amino acid sequence integrated into the Fc, the TV maintains high fidelity to the natural protein and does not require appended sequences, thereby improving stability and limiting risk of immunogenicity and infusion-related reactions ("IRRs"). In addition, Fc engineering enables modularity for the broadest utility to transport biologics including enzymes, oligonucleotides, and antibodies.

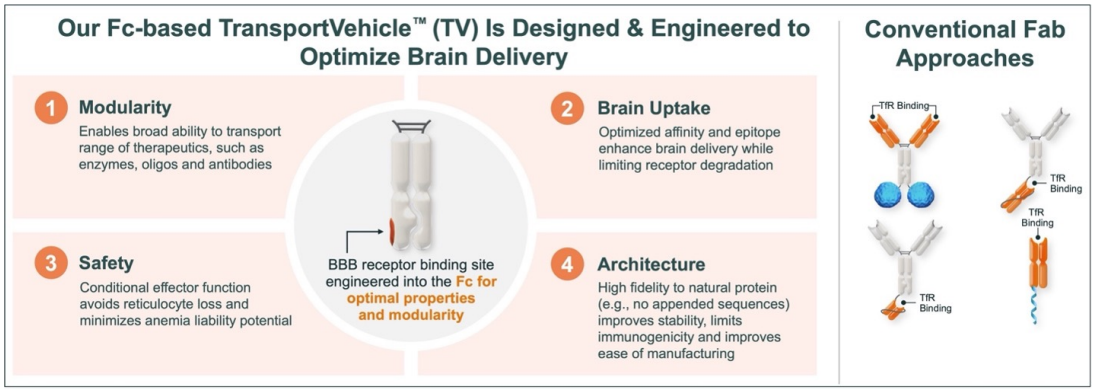

Figure 3: Denali's Fc-based TV technology is modular, designed to optimize brain delivery and safety, and is highly differentiated from conventional Fab-based approaches.

Across TV modalities, we have shown in preclinical and/or clinical studies that TV enables broader brain biodistribution, enhanced target engagement, and normalization of key disease biomarkers (**Figure 4**). More than 200 subjects have participated in clinical studies of our TV-enabled programs and more than 11,000 doses of TV-enabled therapeutics have been administered for up to over five years (as of November 3, 2025). We achieved proof of concept with safety and pharmacokinetic and pharmacodynamic data from Phase 1/2 clinical studies in patients and healthy volunteers, as well as data from several preclinical studies in mouse and nonhuman primate models. For example, we have demonstrated the ability to correct neurodegeneration observed as substantial reduction and normalization of levels of neurofilament light chain ("NfL"), a biomarker of neuronal damage, in the Phase 1/2 study of tividenofusp alfa for MPS II as well as in multiple animal models.

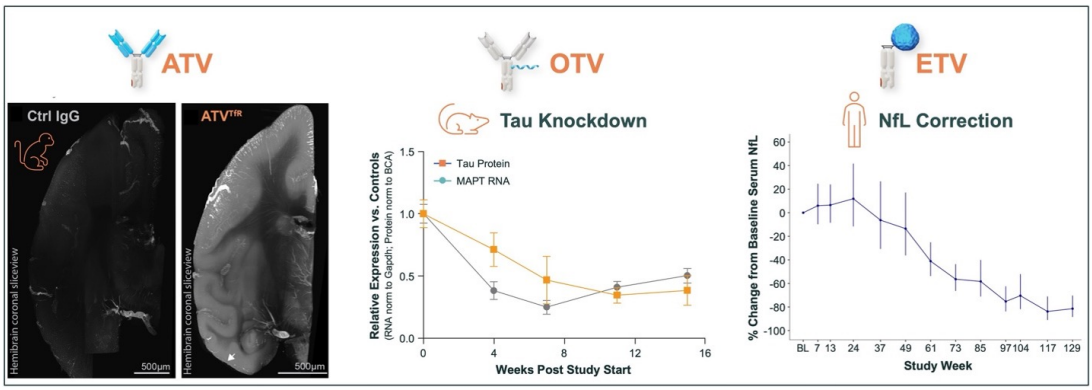

Figure 4: *Left Panel:* TV provides high and uniform deposition of ATV across the brain with systemic delivery; *Middle Panel:* TV enables sustained brain tau knockdown with OTV:MAPT systemic delivery; *Right Panel:* TV enables ETV:IDS to reduce serum NfL by >80%, achieving normal levels.

We believe that we can further expand our portfolio by targeting other blood-brain barrier receptors that may confer different properties from targeting TfR. For example, we are targeting CD98hc, an amino acid transporter highly expressed on the blood-brain barrier (**Figure 5**). Our preclinical studies have established TV^{CD98hc} as a modular brain delivery platform with favorable kinetic, biodistribution, and safety properties distinct from previously reported blood-brain barrier platforms. We believe that the distinct properties of our two TV platforms, TV^{TfR} and TV^{CD98hc} may enable selection of the optimal platform for a given drug target thereby expanding our portfolio opportunities. In addition, we have developed a dual TV platform that engages both TfR and CD98hc, combining complementary brain delivery properties and providing additional flexibility to optimize brain exposure across a range of therapeutic programs.

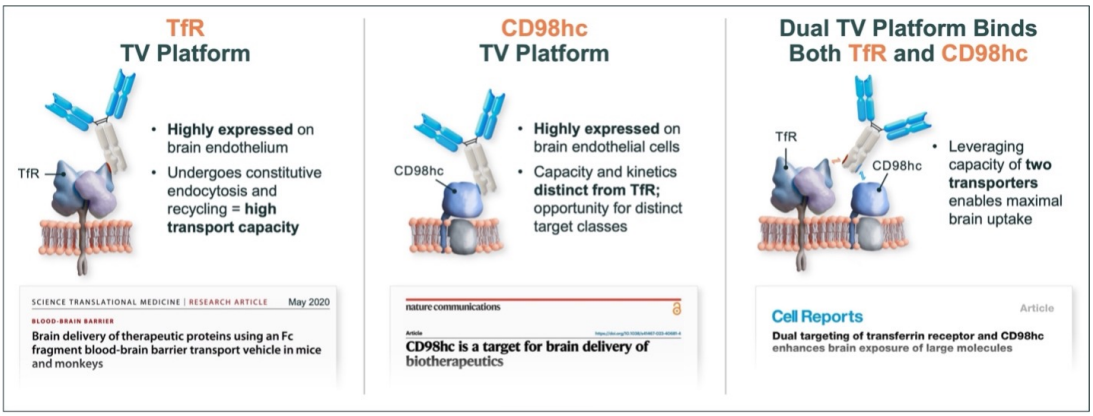

Figure 5: TV^{TfR} targets TfR and TV^{CD98hc} targets CD98hc, an amino acid transporter. Both receptors are highly expressed on the blood-brain barrier and can be utilized for brain delivery of biotherapeutics.

Our Therapeutic Portfolio

Our therapeutic portfolio (**Figure 6**) currently includes five clinical-stage TV-enabled programs and more than ten programs in preclinical development and spans a broad range of investigational therapies for neurodegenerative diseases, lysosomal storage disorders, and other serious diseases. In addition to our current clinical development portfolio, we expect to advance four to six new molecule entities (“NMEs”) into clinical development over the next three years beginning in 2026. We discuss our most advanced programs in further detail below.

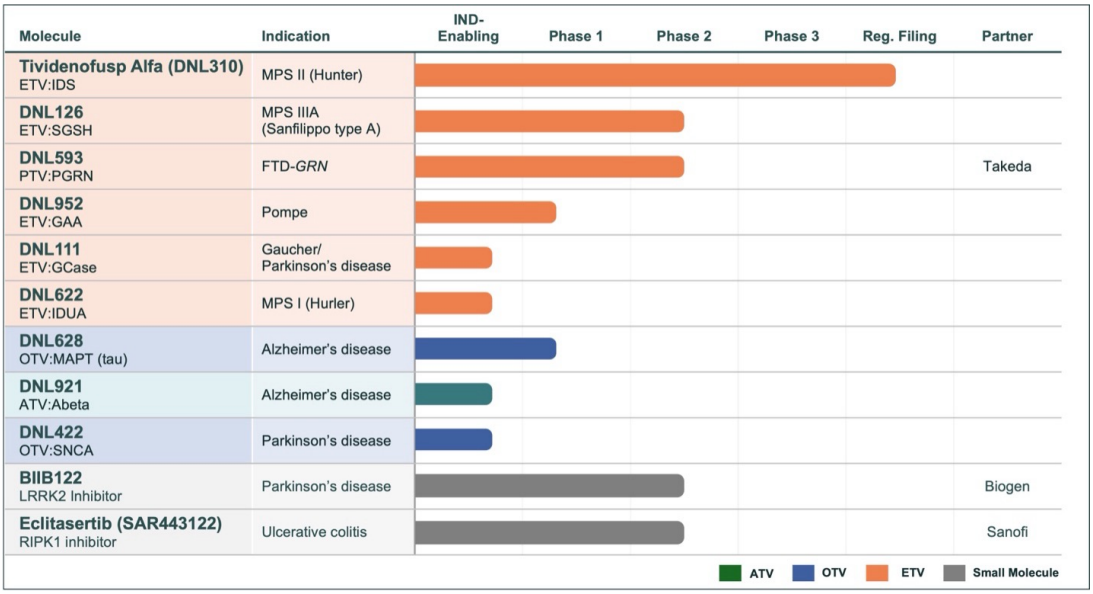

Figure 6: Our therapeutic portfolio is broad and diverse, spanning neurodegenerative diseases, lysosomal storage disorders, and other serious diseases that may be addressed by our TV platform for enabling and enhancing the delivery of biotherapeutics to target tissues.

Enzyme TransportVehicle™ Franchise

The Enzyme TransportVehicle™ ("ETV") franchise (**Figure 7**) represents our first potential commercial application of the TV platform and is designed to address significant unmet needs in lysosomal storage disorders, many of which have both central nervous system and systemic manifestations. By enabling efficient delivery of enzyme replacement therapies to the brain and throughout the body, the ETV franchise has the potential to improve upon existing standards of care that are limited by inadequate tissue distribution, and do not reach the brain in sufficient concentrations. We believe the ETV franchise offers a substantial near- and long-term commercial opportunity, supported by validated disease biology, established regulatory pathways, and the historically high success rates of approximately 80 percent of enzyme replacement therapies in rare genetic diseases.

The ETV franchise is intended to serve as the commercial and financial foundation of our business, with the anticipated launch of tividenofusp alfa for Hunter syndrome and the advancement of additional ETV programs, including DNL126 for Sanfilippo syndrome type A, DNL593 for FTD-*GRN*, and DNL952 for Pompe disease. Revenue generated from the ETV franchise is expected to support continued investment in our TV platform, enabling us to expand our pipeline across additional enzyme, antibody, and oligonucleotide-based therapeutics. Through this strategy, we aim to build a sustainable, revenue-generating rare disease business while funding the long-term development of our broader platform across neurodegenerative and other serious diseases.

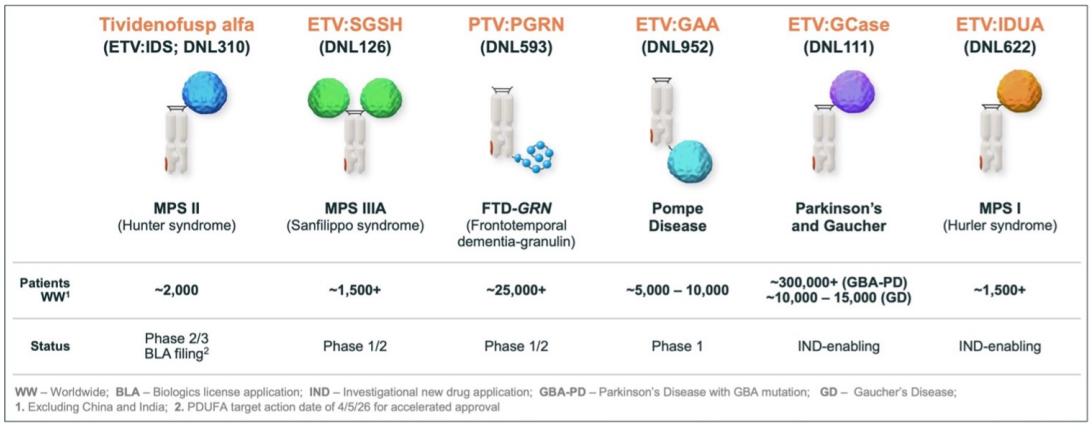

Figure 7: Our ETV franchise is intended to deliver the next generation of enzyme replacement therapies designed to treat central nervous system and somatic manifestations of lysosomal storage diseases and other serious genetic diseases.

ETV Clinical Programs

Tividenofusp alfa (DNL310, ETV:IDS) Enzyme Replacement Therapy Program for MPS II (Hunter Syndrome)

MPS II, also called Hunter syndrome, is a rare genetic disease that affects over 2,000 individuals, primarily males, in commercially accessible geographies world-wide and leads to behavioral, cognitive, and physical symptoms ultimately resulting in shortened lifespan. MPS II is caused by mutations in the iduronate-2-sulfatase ("*IDS*") gene, which leads to a deficiency of the IDS enzyme responsible for the breakdown of the glycosaminoglycans ("GAGs") heparan sulfate and dermatan sulfate in lysosomes. Symptoms often begin emerging around age two and include physical complications, including organ dysfunction, joint stiffness, hearing loss and impaired growth leading to short stature, and neurocognitive symptoms with impaired development. The disease is characterized by a buildup of GAGs in lysosomes, the part of the cell that breaks down materials, including GAGs. The current standard of care enzyme replacement therapy partially treats the physical symptoms but does not cross the blood-brain barrier, and as a result, cognitive and behavioral symptoms experienced by the majority of patients with MPS II are not addressed. Therapies that address behavioral, cognitive, and somatic manifestations of the disease are one of the greatest unmet needs for this community.

Tividenofusp alfa (DNL310, ETV:IDS), composed of the IDS enzyme fused to TV, is designed to deliver IDS into cells and tissues throughout the body, including the brain by crossing the blood-brain barrier, with the goal of addressing behavioral, cognitive, and physical manifestations of Hunter syndrome (MPS II). In March 2021, the U.S. Food and Drug Administration granted Fast Track designation to tividenofusp alfa for the treatment of patients with MPS II. In May 2022, the European Medicines Agency ("EMA") granted tividenofusp alfa Priority Medicines designation. In January, 2025, the FDA granted tividenofusp alfa Breakthrough Therapy Designation for MPS II.

In September 2024, we announced a successful Type C meeting with FDA's Center for Drug Evaluation and Research ("CDER") providing a path to filing a BLA for accelerated approval and subsequent conversion to full approval for tividenofusp alfa based on the Phase 2/3 COMPASS study for the treatment of MPS II. Agreement was reached that a reduction in CSF heparan sulfate is reasonably likely to predict clinical benefit and can be used as a surrogate endpoint to support accelerated approval for tividenofusp alfa in MPS II.

In May 2025, we announced that the BLA was submitted under the accelerated approval pathway and included preclinical and clinical data on biomarkers (CSF and urine heparan sulfate and neurofilament light ("NfL")), safety data, and clinical data including liver volume, hearing thresholds, cognition, and adaptive behavior. In July 2025, we announced that the FDA accepted the BLA submission and assigned a PDUFA target action date of January 5, 2026. In October 2025, we announced that the FDA had extended its review timeline of the BLA and assigned a new PDUFA target date of April 5, 2026. The extension followed our submission of updated clinical pharmacology data in response to an information request from the FDA as part of the standard review process and was not related to efficacy, safety or biomarkers. The FDA classified the submission as a Major Amendment (MA) to the BLA, which, per FDA regulations, extended the review by three months. No additional data were requested by the FDA in the MA letter. We believe that the updated information submitted in the amendment does not affect the clinical pharmacology or benefit-risk conclusions of the BLA.

Tividenofusp alfa received Rare Pediatric Disease Designation (“RPDD”) status for the treatment of Hunter syndrome in January 2019. In December 2025, we announced ongoing dialogue with the FDA related to the eligibility of tividenofusp alfa to receive a Rare Pediatric Disease Priority Review Voucher (“PRV”) upon approval. Because we submitted a filing of our intent to request a PRV after the initial BLA submission, based on discussions with the FDA, we may not be eligible to receive the PRV. Therefore, we are not including any potential future proceeds from the sale of a PRV in our financial planning. We continue to work with the FDA and the FDA will determine whether to award a PRV upon approval of tividenofusp alfa.

The Late Cycle Meeting with the FDA has been completed and labeling discussions are ongoing. We are building our launch plans in partnership with the MPS II community, and we are engaged in prelaunch activities, including continued dialogue with advocacy groups, prescribers and payers, and building a suite of patient support services and capabilities to enable access. We have built a right-sized team in commercial and medical affairs to support tividenofusp alfa and additional ETV product launches.

We are also conducting the global Phase 2/3 COMPASS study, which will support global approval. The Phase 2/3 COMPASS study is being conducted in North America, South America, and Europe. The participants are randomized 2:1 to receive either tividenofusp alfa or idursulfase, respectively. Cohort A includes children ages ≥2 to <6 years with neuronopathic disease; cohort B includes children and adults ages ≥6 to <26 without neuronopathic disease. Cohort A enrollment of a total of 44 participants was completed in December 2025, and Cohort B continues to enroll participants with non-neuronopathic MPS II.

We have previously reported interim analyses from the Phase 1/2 study, and, most recently, the primary analysis upon which the BLA was based was published in *The New England Journal of Medicine* in January 2026 (Muenzer et al., *NEJM*, 2026).

The primary objective of the Phase 1/2 study was safety and tolerability, and secondary objectives evaluated central nervous system and peripheral effects of tividenofusp alfa by measuring the GAG heparan sulfate (HS) in cerebrospinal fluid (CSF) and urine, adaptive behavior and liver volume. The study evaluated treatment in 47 ERT-naïve (n=15) and previously treated (n=32) study participants (aged 0.3–13 [median, 5] years), ranging from less severe to severe disease variants. Safety and tolerability data were consistent with previously reported results from this Phase 1/2 trial (**Table 1**). The most common treatment-related adverse events were infusion-related reactions, which decreased in incidence with continued use (**Figure 8A**). At baseline, 19% of the participants had anemia of grade 1 or higher. Decreases in the hemoglobin level were observed early with tividenofusp alfa treatment but generally returned to baseline values (**Figure 8B**), were clinically manageable, and did not result in discontinuation of study participation. Causes of anemia are probably multifactorial, including nutritional deficiencies, frequent phlebotomy early in the study, and possible immune effects such as the formation of antidrug antibodies.

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Event	Part 1: 24-Week Treatment Period (N=47)	Part 2: 80-Week Safety Extension (N=46)	Part 3: 157-Week Open-Label Extension (N=27)	All Periods (N=47)
	number of participants (percent)			
Adverse event†	47 (100)	41 (89)	25 (93)	47 (100)
Mild	8 (17)	3 (7)	8 (30)	2 (4)
Moderate	35 (74)	30 (65)	15 (56)	32 (68)
Severe	4 (9)	8 (17)	2 (7)	13 (28)
Serious adverse event‡	6 (13)	11 (24)	4 (15)	18 (38)
Treatment-related serious adverse event§	3 (6)	0	0	3 (6)
Adverse events of special interest¶				
Infusion-related reaction	27 (57)	15 (33)	4 (15)	29 (62)
Anemia	11 (23)	2 (4)	1 (4)	11 (23)
Adverse event leading to discontinuation of study participation	1 (2)	0	0	1 (2)
Adverse event leading to dose reduction	22 (47)	11 (24)	4 (15)	27 (57)
Adverse event leading to dose interruption	34 (72)	37 (80)	15 (56)	43 (91)
Most frequent adverse events				
Infusion-related reaction	39 (83)	26 (57)	11 (41)	41 (87)
Upper respiratory tract infection	11 (23)	20 (43)	8 (30)	28 (60)
Pyrexia	11 (23)	17 (37)	6 (22)	26 (55)
Cough	8 (17)	14 (30)	6 (22)	22 (47)
Vomiting	14 (30)	10 (22)	6 (22)	20 (43)
Diarrhea	9 (19)	10 (22)	4 (15)	19 (40)
Rash	10 (21)	8 (17)	6 (22)	19 (40)
Anemia	18 (38)	3 (7)	2 (7)	18 (38)
Covid-19	6 (13)	13 (28)	2 (7)	18 (38)
Rhinorrhea	9 (19)	8 (17)	4 (15)	18 (38)

* Shown are new adverse events that occurred after the first dose of tividenofusp alfa. Covid-19 denotes coronavirus disease 2019.
† Adverse events are listed according to maximum severity. If a participant had more than one occurrence of the same event, the highest severity was summarized.
‡ A serious adverse event was defined as an event that was fatal or life-threatening, resulted in or prolonged participant hospitalization, resulted in persistent or clinically significant disability or incapacity, was a congenital anomaly or birth defect, or was considered by the investigator to be a clinically significant medical event.
§ Serious adverse events that were considered by the investigator to be related to treatment were infusion-related reactions (in two participants) and anemia (in one participant).
¶ These events were defined as infusion-related reactions (including allergic reactions and anaphylaxis) that were graded as moderate or greater in severity and anemia that was graded as moderate or greater in severity.

Table 1: Summary of Adverse Events in Phase 1/2 study of tividenofusp alfa (Muenzer *et al*., *NEJM,* 2026)

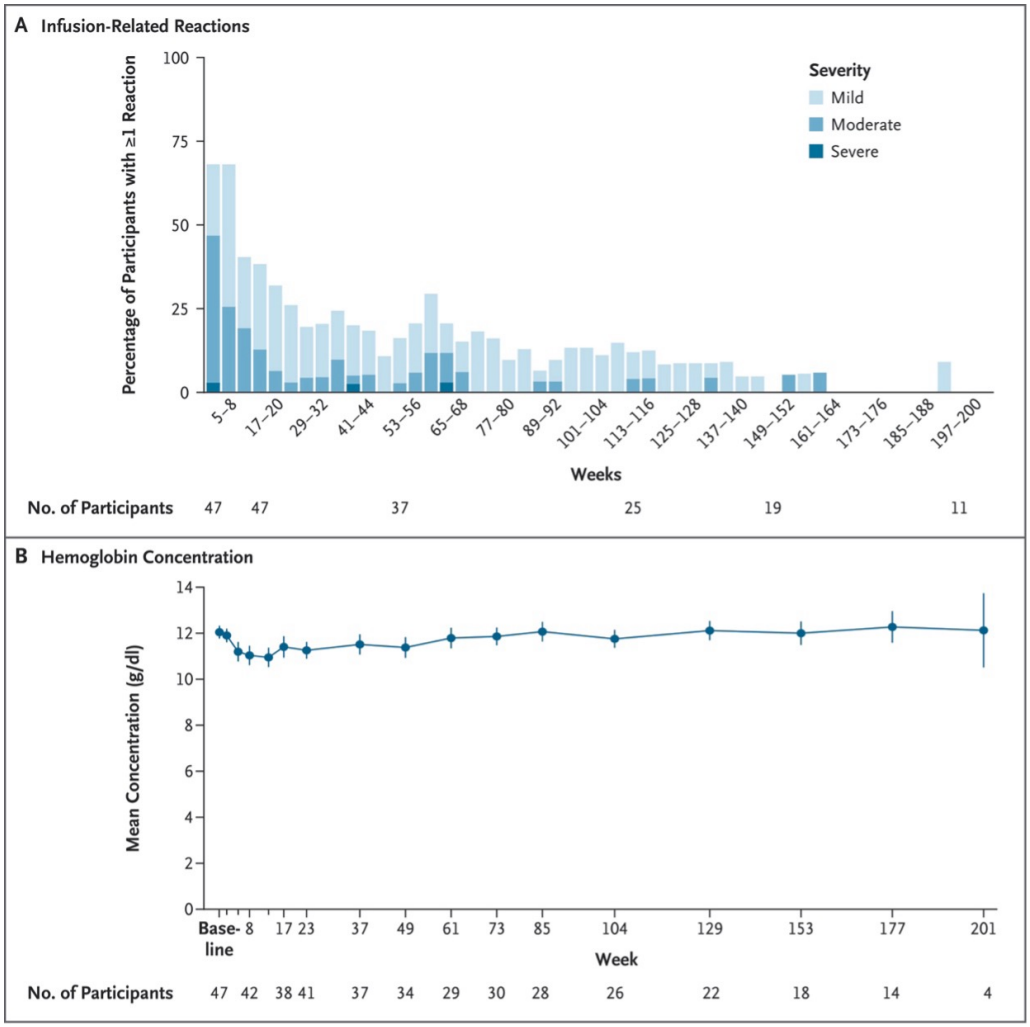

Figure 8: Infusion-Related Reactions and Hemoglobin Levels over Time. Infusion related reactions (A) decreased in frequency and severity over time and early decreases in hemoglobin levels (B) generally returned to baseline values, were clinically manageable, and did not result in discontinuation of study participation in the Phase 1/2 study of tividenofusp alfa (Muenzer *et al*., *NEJM,* 2026).

Results from key secondary endpoints included:

- Mean CSF levels of HS, the primary substrate found in high levels in the brain of individuals with MPS II, were reduced from baseline by 91% (95% CI, 90% to 92%; N=44) at Week 24 and maintained through Week 153 (92%; 95% CI, 90% to 93%; N=16). At Week 24, 93% of study participants reached levels within the range of children without MPS II (**Figure 9**).

- Mean urine HS levels were reduced by 88% (95% CI, 85% to 90%; N=40) from baseline at Week 24 and maintained through Week 153 (91%; 95% CI, 87% to 94%; N=10). At Week 24, 58% of participants reached levels in the range of children without MPS II (**Figure 9**).

- Serum neurofilament light (NfL) chain levels, a well-established biomarker of neuronal injury and an exploratory endpoint of the study, were reduced by 21% (95% CI, 5% to 35%; N=34) from baseline at Week 49. At Week 153, NfL was reduced by 76% (95% CI, 68% to 82%; N=13), and 85% of participants reached levels within the range of children without MPS II (**Figure 9**).

- Clinical results included normalization in liver volume after 24 weeks, and as shown in **Figure 10**, improvement in hearing thresholds across tested frequencies, and skill gains in most participants on measures of adaptive behavior and cognition.

2026 expected progress and milestones:

- Commercial launch pending approval with PDUFA target action date of April 5, 2026.

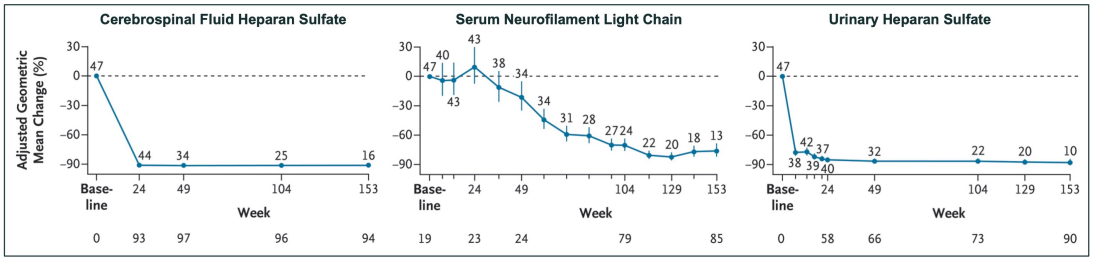

Figure 9: Treatment with tividenofusp alfa over a median duration of 2 years was associated with reductions in central nervous system and peripheral biomarkers of substrate accumulation and neuronal injury to levels within the range of unaffected children (Muenzer et al., *NEJM* 2026).

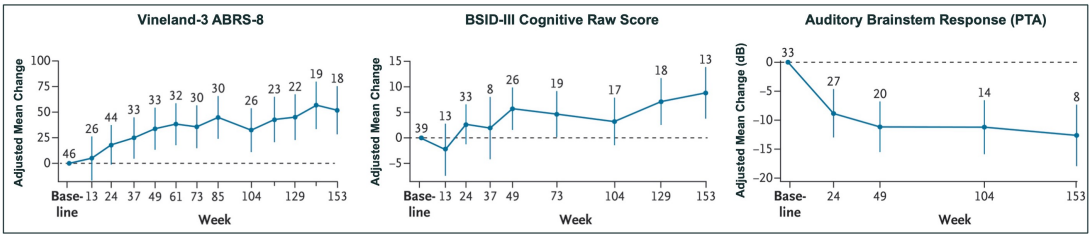

Figure 10: While on tividenofusp alfa, clinical outcomes showed skill gains relative to baseline on measures of adaptive behavior, cognition and hearing threshold improvement represented as pure tone average (PTA) (Muenzer *et al.*, *NEJM,* 2026).

DNL126 (ETV:SGSH) Program for MPS IIIA (Sanfilippo Syndrome Type A)

MPS III, also called Sanfilippo syndrome, is a rare, genetic lysosomal storage disease that causes neurodegeneration. There are four main types of MPS III, depending on the enzyme affected. Type A is caused by genetic defects that result in reduction in the activity of N-sulfoglucosamine sulfohydrolase ("SGSH"), an enzyme responsible for degrading heparan sulfate in the lysosome. There are no approved treatments for MPS IIIA.

DNL126 (ETV:SGSH) is composed of SGSH fused to TV, which is engineered to cross the blood-brain barrier via receptor mediated transcytosis into the brain and to enable broad delivery of SGSH into cells and tissues throughout the body with the goal of treating MPS IIIA. Preclinical data demonstrate that DNL126 improved lysosomal and microglial morphology, neurodegeneration, and cognitive function in adult MPS IIIA mice. Peripheral treatment with ETV:SGSH lowered substrate accumulation (heparan sulfate) in the brain and in CSF, which was correlated with improved cognitive behavioral performance in adult MPS IIIA mice.

In January 2024, we commenced dosing of participants with MPS IIIA in a multicenter, open-label, Phase 1/2 study to assess the safety, tolerability, pharmacokinetics, pharmacodynamics, and exploratory clinical efficacy of DNL126. The core study period is 25 weeks followed by an open-label extension period through 193 weeks. In June 2024, we announced that DNL126 was selected for the FDA's Support for Clinical Trials Advancing Rare disease Therapeutics ("START") program to accelerate the development of rare disease therapeutics, and collaborative engagement has commenced to support progress to a pre-BLA meeting.

In August 2025, we announced having reached alignment with the FDA's CDER that cerebrospinal fluid heparan sulfate (CSF HS) may be considered a reasonably likely surrogate endpoint to predict clinical benefit and may therefore be used to support accelerated approval of DNL126 for MPS IIIA. We also announced that additional 49-week data from the ongoing open-label Phase 1/2 study were consistent with previously announced 25-week data, demonstrating a significant reduction in CSF HS from baseline, including normalization, and a safety profile that supports continued development.

The Phase 1/2 study completed enrollment of a total of 20 participants with MPS IIIA in September 2025. In February 2026, we reported preliminary results from the Phase 1/2 study at the WORLDSymposium. Preliminary data from 14 participants enrolled at the time of the clinical data cut-off (June 4, 2025) were presented, including biomarker results from the dose-finding cohorts (n=8) and safety data from the dose-finding and efficacy cohorts (n=14). Preliminary biomarker results from dose-finding cohorts showed treatment with DNL126 resulted in a mean reduction in cerebrospinal fluid heparan sulfate (CSF HS) of 80% (95% CI: 43% to 93%) and 61% in CSF GM3 (95% CI: 36% to 76%), a biomarker of lysosomal function, from baseline at Week 49 (**Figure 11**). Normalization of CSF HS and CSF GM3 levels was observed in three and six of seven individuals, respectively, with CSF samples available at Week 49. A mean reduction in urine HS of 83% (95% CI: 77% to 87%) from baseline was observed at Week 49, and improvement in liver volume was observed as early as Week 25 (**Figure 12**). Preliminary safety data from dose finding and efficacy cohorts up to the data cutoff date, including 13 of 14 participants treated for at least 24 weeks and 8 of 14 participants treated for at least 48 weeks, demonstrated that the safety profile of DNL126 is generally consistent with established enzyme replacement therapies. The most common treatment-related adverse events in the study were infusion-related reactions (**Table 2**).

2026 expected progress and milestones:

- Report preliminary data at WORLDSymposium (*presented February 2026*).
- Initiate activities to begin the Phase 3 confirmatory study.

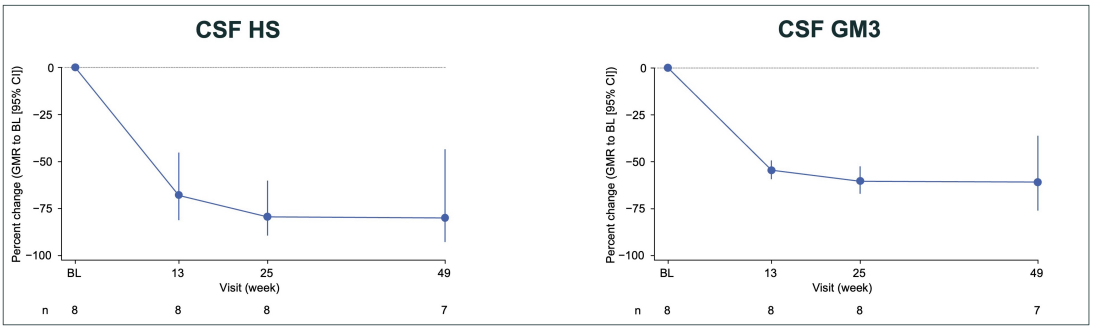

Figure 11: Robust reductions from baseline in CSF heparan sulfate and CSF GM3 with normalization of levels in 3 and 6 of 7 participants, respectively, who had CSF samples at Week 49 after treatment with DNL126.

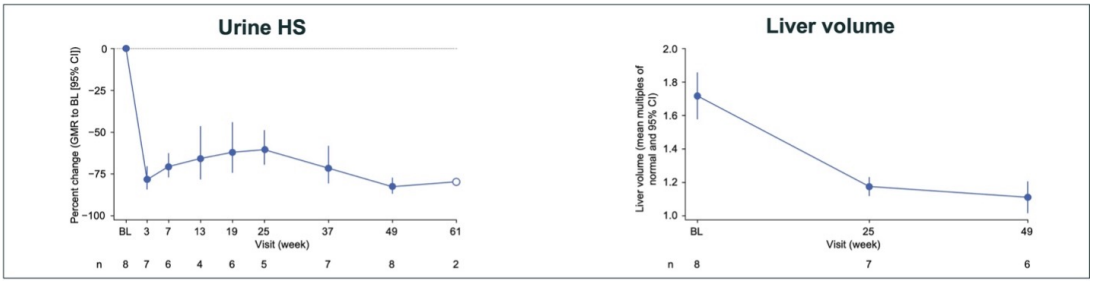

Figure 12: Substantial reductions from baseline in urine HS and liver volume at the first post-baseline time point where these endpoints were measured.

Preferred term	All cohorts (n = 14) [n (%)]
Infusion-related reaction	14 (100)
Upper respiratory infection	9 (64.3)
Vomiting	9 (64.3)
Nasal congestion	7 (50.0)
Cough	6 (42.9)
Diarrhea	5 (35.7)
Ear infection	5 (35.7)
Fall	5 (35.7)
Gastroenteritis	5 (35.7)
Irritability	5 (35.7)

Table 2: Treatment-Emergent Adverse Events (TEAEs) reported in >30% of participants (n=14) from dose-finding and efficacy cohorts as of the clinical cutoff date (June 4, 2025).

TAK-594/DNL593 (PTV:PGRN) Program for FTD-GRN

FTD is the most common form of dementia in people under 60 years of age. While the progression of symptoms varies by individual, FTD brings an inevitable decline in function together with changes in personality and social behaviors, and sometimes language and/or motor dysfunction. Mutations in the granulin ("*GRN*") gene, which encodes the progranulin ("PGRN") protein, generally result in reduced levels of PGRN and are among the most common genetic causes of FTD. It is estimated that FTD-*GRN* is 5-10% of the total FTD patient population, or more than 25,000 people worldwide. There are currently no approved medicines to stop or slow the progression of FTD or FTD-*GRN*.

TAK-594/DNL593 (PTV:PGRN) is an investigational, PGRN replacement therapy enabled by Denali's TV platform and designed to cross the blood-brain barrier and restore PGRN levels in the brain without interfering with normal PGRN transport and processing. As described in more detail in “Business - Licenses and Collaborations” below, we are collaborating with Takeda to co-develop and co-commercialize TAK-594/DNL593 (PTV:PGRN). Preclinical proof of concept demonstrates that PTV enhances uptake of recombinant PGRN by multiple cell types in the brain, including neurons and microglia, as compared to non-PTV PGRN. In addition, TAK-594/DNL593 rescued both neurodegeneration and microglial dysfunction in PGRN-deficient mice. Our improved mechanistic understanding of the role of PGRN in lysosomal function indicates that intravenous delivery of TAK-594/DNL593 followed by PTV-enhanced transport to the brain may be an effective therapeutic approach to increase PGRN levels in lysosomes.

Together with Takeda, we initiated a Phase 1/2 clinical trial of TAK-594/DNL593 for FTD-*GRN* in 2022. Results from Part A of this study evaluating TAK-594/DNL593 in healthy subjects were presented at the Alzheimer's Association International Conference in July 2023. Single doses of TAK-594/DNL593 were generally well-tolerated and resulted in substantial increases in CSF PGRN levels, suggesting that brain delivery of TAK-594/DNL593 was achieved and that TAK-594/DNL593 has the potential to address PGRN deficiency (**Figure 13)**.

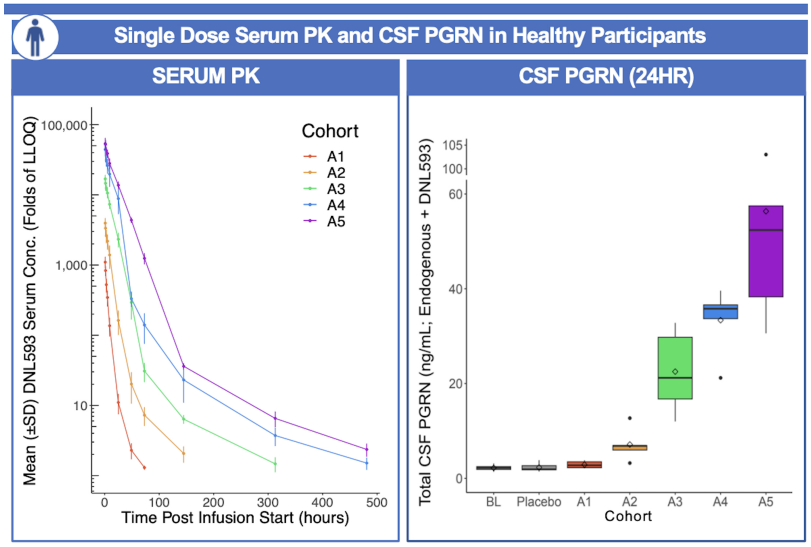

Figure 13: Dose-dependent increase in CSF PGRN in healthy volunteers with intravenous TAK-594/DNL593.

In January 2024, Denali announced that enrollment and dosing were voluntarily paused in Part B of the Phase 1/2 study to implement protocol modifications. The pause was based on infusion-related reactions reported in two study participants, one Grade 2 and one Grade 3 in severity and both deemed serious adverse events. Both study participants' infusion-related reactions resolved within the same day with infusion discontinuation and standard treatment measures. TAK-594/DNL593 was otherwise well-tolerated in the study, with all other adverse events reported as mild in severity. In August 2024, we announced that the protocol amendment for the Phase 1/2 study was finalized, allowing for premedication and other measures aimed at reducing the risk of infusion-related reactions, and prescreening of participants for Cohort B2 had begun. In January 2025, we announced that dosing was ongoing in the study. In February 2026, we announced that enrollment in the study is complete with a total of 40 participants with FTD-*GRN* enrolled.

2026 expected progress and milestones:

- Interim data from Phase 1/2 Part B study in participants with FTD-*GRN.*

DNL952 (ETV:GAA) for Pompe disease

Acid alpha-glucosidase ("GAA") is an enzyme that breaks down glycogen into glucose in the body's lysosomes. Pompe disease occurs due to lack of GAA enzyme activity, which leads to lysosomal glycogen accumulation and autophagic buildup resulting in cellular disruption. There are two types of Pompe disease: Infantile Onset Pompe Disease ("IOPD") and Late Onset Pompe Disease ("LOPD"). IOPD affects the heart and causes ventilatory failure leading to early death, typically before one year age if left untreated. LOPD can occur from early childhood through later decades in life and is characterized by slow progression, limb-girdle weakness leading to inability to walk, respiratory weakness leading to ventilator dependence, and central nervous system involvement. The estimated prevalence of Pompe disease is 5,000 to 10,000 people worldwide excluding India and China. The current standard of care is enzyme replacement therapy. Progressive motor weakness and respiratory failure remain unmet needs.

DNL952 (ETV:GAA) is composed of GAA fused to TV and is engineered to replace GAA in all tissues, including TfR-enabled biodistribution to muscle and brain, for the treatment of Pompe disease. In preclinical studies, compared to standard of care enzyme replacement therapies, ETV:GAA has demonstrated superior correction of glycogen load in the brain and in muscle tissue with normalization of lysosomal volume and correction of autophagy (**Figure 14**).

In November 2025, we announced submission of an Investigational New Drug ("IND") application to the FDA to begin clinical studies of DNL952. In December 2025, we announced that the IND application for the Phase 1 study of DNL952 has been placed on clinical hold. The FDA requested a protocol amendment to include a lower starting dose, revised inclusion criteria, certain safety monitoring commitments, and stopping rules. These requests were related to preclinical hypersensitivity reactions observed in GAA mouse models, which are commonly observed across all GAA enzyme replacement therapies in mice. The FDA did not request additional nonclinical studies. We submitted a response to the FDA in December 2025 and announced in January 2026 that the FDA lifted the clinical hold. We are proceeding with the planned Phase 1 study. As part of our global development strategy for DNL952, we submitted a Clinical Trial Application ("CTA") in the UK and Europe in the first quarter of 2026.

The clinical development plan for DNL952 includes an initial Phase 1 study in participants with LOPD, with planned cohorts evaluating different dose regimens of DNL952 in participants previously treated with second-generation enzyme replacement therapies, as well as optional additional cohorts, including treatment-naïve participants. The study is intended to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of DNL952.

2026 expected progress and milestones:

- Initiate dosing in Phase 1 clinical study of DNL952 in participants with LOPD.

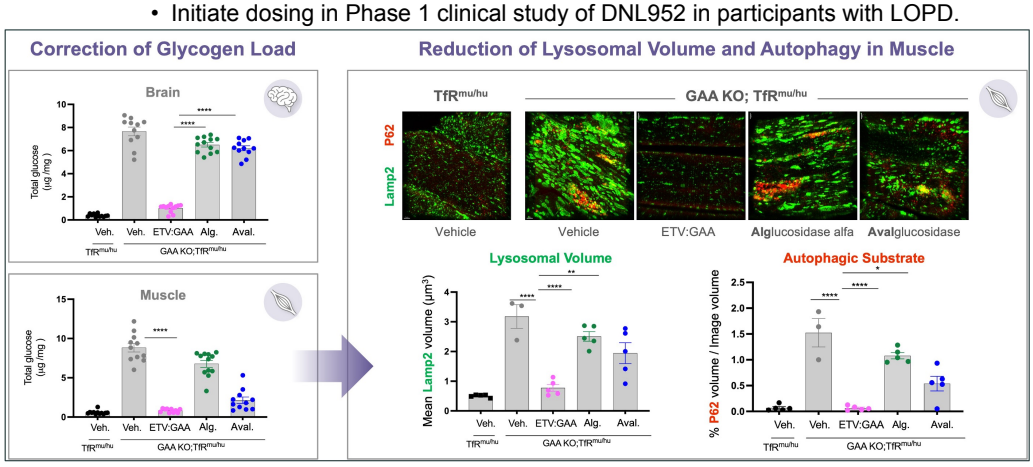

Figure 14: In a rodent model of Pompe, ETV:GAA is superior to standard of care, alglucosidase alfa (Alg.) and avalglucosidase alfa-ngpt (Aval.), in correction of glycogen load in brain and in muscle (left) and superior reduction of lysosomal volume and autophagy in muscle (right).

DNL111 (ETV:Gcase) for Parkinson's disease and Gaucher disease

Glucocerebrosidase ("GCase") is an enzyme that breaks down lipids in the lysosome. Aberrant GCase substrate storage drives lysosomal dysfunction and is associated with Gaucher disease and Parkinson's disease. Homozygous loss-of-function mutations in the GBA1 gene, which encodes the GCase enzyme, leads to Gcase enzyme deficiency resulting in Gaucher disease. Gaucher disease can be associated with debilitating symptoms including a swollen belly from spleen and liver enlargement; bone pain and easily fractured and weak bones; anemia resulting in fatigue. Some people with Gaucher disease have central nervous system involvement: abnormal eye movements, muscle rigidity, swallowing difficulties, and seizures. There are an estimated 10,000 to 15,000 people with Gaucher disease worldwide (excluding China and India). Approximately 10% of all Parkinson's disease patients are heterozygous carriers of a loss-of-function GBA1 mutation, leading to lysosomal dysfunction which is strongly associated with neuroinflammation/degeneration. There are an estimated 300,000 GBA-PD patients worldwide (excluding China and India). Peripheral enzyme replacement therapy is the current standard of care for Gaucher disease, and no GBA-PD specific treatments currently approved.

DNL111 is composed of an engineered GCase variant with improved potency, fused to TV to enable replacement of GCase in peripheral tissues and the brain via blood–brain barrier transport. In preclinical studies, ETV:GCase demonstrated enhanced substrate reduction in brain, liver, and serum compared to GCase enzyme alone. This engineered ETV:GCase approach may enable a stable, potent, brain-penetrant enzyme replacement therapy for Parkinson's disease and Gaucher disease. DNL111 is currently in the IND-enabling stage of preclinical development.

DNL622 (ETV:IDUA) for MPS I (Hurler syndrome)

Alpha-L-iduronidase ("IDUA") is as enzyme responsible for degrading heparan and dermatan sulfate in the lysosome. Genetic defects in the gene encoding IDUA result in deficient enzyme activity, leading to MPS I (Hurler syndrome). MPS I is characterized by alterations in the skeleton, heart, respiratory system, and brain and affects approximately 1,500 individuals worldwide.

DNL622 (ETV:IDUA) is composed of IDUA fused to TV, which is engineered to cross the blood-brain barrier via receptor-mediated transcytosis into the brain and to enable broad delivery of IDUA into cells and tissues throughout the body with the goal of treating MPS I. DNL622 is currently in the IND-enabling stage of preclinical development.

Alzheimer's Disease Portfolio

Alzheimer's disease represents a large and growing unmet medical need, and recent advances in biomarkers and disease-modifying therapies have increased confidence in the ability to intervene earlier and more effectively in the disease course. Despite these advances, existing antibody and nucleic acid therapeutic approaches are limited by suboptimal delivery to the brain, dose-related safety concerns, and, specific to antibodies or nucleic acid therapies respectively, difficultly engaging intracellular targets or the need for frequent or invasive administration. We believe that improved delivery of biotherapeutics across the blood-brain barrier is critical to achieving greater efficacy, improved safety, and more convenient dosing in Alzheimer's disease, particularly as treatment paradigms shift toward earlier-stage and presymptomatic patient populations

Our approach to Alzheimer's disease leverages the TV platform to enhance brain delivery of antibodies and oligonucleotide-based therapeutics targeting key disease-driving pathologies, including amyloid beta and tau. Our Alzheimer's disease portfolio includes TV-enabled antibody programs designed to improve plaque clearance while potentially reducing vascular-related safety risks, as well as oligonucleotide programs intended to achieve broad and uniform distribution throughout the brain. We expect to use validated fluid and imaging biomarkers to inform patient selection, assess target engagement, and enable efficient clinical development. Through this strategy, we aim to apply the TV platform to address limitations of existing therapies and advance next-generation treatments with the potential to modify disease progression across multiple stages of Alzheimer's disease.

DNL628 Oligonucleotide TransportVehicle™ Microtubule-Associated Protein Tau (OTV:MAPT) for Alzheimer's disease

Oligonucleotide-based therapeutics, such as ASOs and siRNAs, are designed to modify gene expression and hold promise as therapeutics for neurological disorders. A major challenge in their development, however, is that oligonucleotides are unable to cross the blood-brain barrier on their own. Currently, oligonucleotides must be delivered directly to the central nervous system through invasive routes such as intrathecal delivery and still may not distribute uniformly throughout the brain where treatment is needed. We are using our OTV platform to enable brain delivery of oligonucleotides by crossing the blood-brain barrier following systemic administration.

In August 2024, our preclinical research related to OTV was published in *Science Translational Medicine*. Denali scientists describe using OTV, which is an engineered TV conjugated to an ASO, for delivery of therapeutic molecules to the mouse and nonhuman primate brain. Our research demonstrated that OTV can successfully cross the blood-brain barrier following intravenous administration and provide cumulative and sustained knockdown of the ASO target gene expression across multiple central nervous system regions and all major cell types, including endothelial cells, neurons, astrocytes, microglia, and oligodendrocytes. In comparison to other clinically relevant ASO delivery platforms, including intrathecal delivery of a non-TV-enabled ASO, systemic OTV enabled a much more uniform ASO biodistribution profile (**Figure 15**) and knockdown of the target.

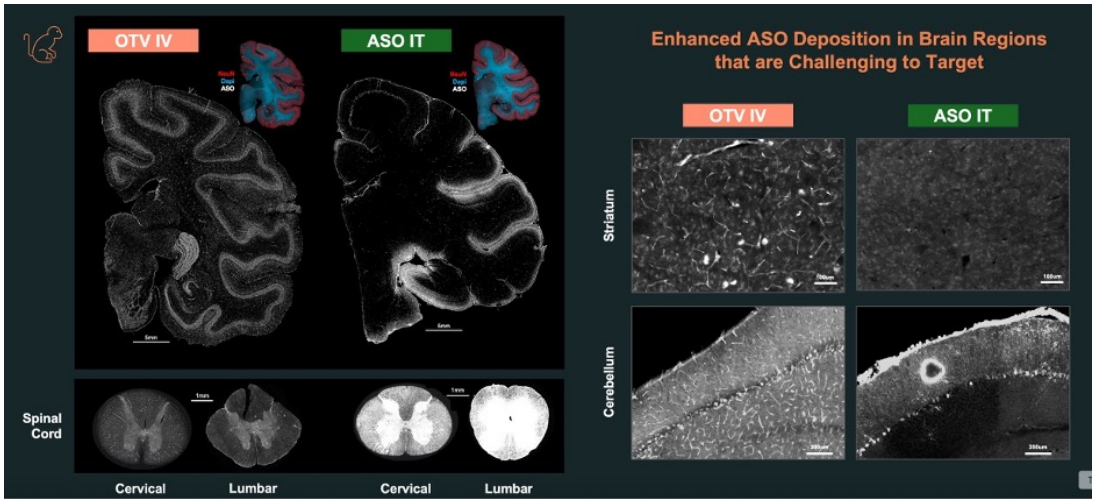

Figure 15: OTV demonstrated uniform ASO deposition in the nonhuman primate brain with intravenous (IV) delivery in contrast to intrathecally administered oligonucleotides, which showed limited penetration into deeper brain regions and high localized exposure in the spinal cord (left panel). OTV delivered IV showed enhanced ASO deposition in brain regions that are challenging to target including the striatum and cerebellum (right panel).

DNL628 is our TV-enabled ASO program targeting microtubule-associated protein tau (*MAPT*) for the treatment of Alzheimer's disease and other tauopathies. Using the TV platform, DNL628 is engineered to facilitate efficient delivery across the blood-brain barrier, with the goal of achieving sustained reduction of tau expression in relevant neuronal populations. DNL628 is designed to address key limitations of existing tau-targeted approaches by enabling systemic administration with broad and uniform distribution throughout the brain and reducing intracellular tau that is inaccessible to antibody-based approaches.

Preclinical studies in disease-relevant animal models expressing human tau demonstrated DNL628 achieved potent and durable reductions in MAPT RNA and tau protein levels following systemic dosing, with sustained knockdown observed well beyond the dosing period (**Figure 16**). These data support the potential for less frequent dosing and more uniform target engagement compared to existing approaches, which we believe may be important for achieving meaningful and durable therapeutic effects in tau-driven neurodegenerative diseases.

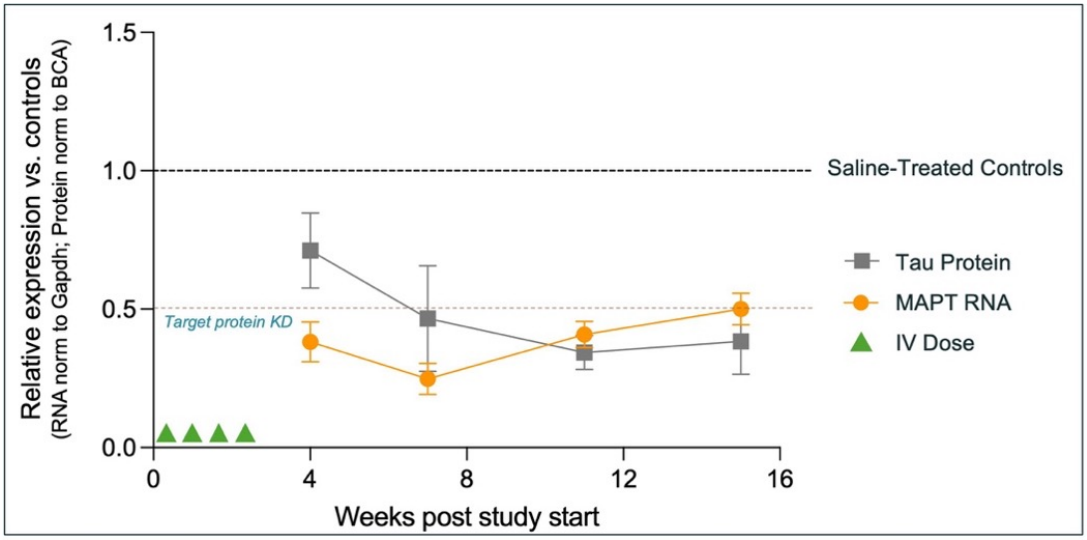

Figure 16: Brain MAPT RNA and tau protein knockdown (KD) persisted for >12 weeks after dosing with DNL628 in mice.

Based on these preclinical findings, we believe DNL628 has the potential to be a best-in-class tau-targeted therapy by combining potent tau reduction with improved brain distribution and a differentiated safety and convenience profile. By reducing total tau expression rather than targeting specific post-translational tau species, DNL628 is designed to broadly address tau pathology across disease stages and brain regions. The clinical development plan for DNL628 includes a Phase 1b multiple ascending dose study, which will evaluate safety, pharmacokinetics, and pharmacodynamic biomarkers of tau reduction. We expect to leverage cerebrospinal fluid and imaging biomarkers to assess target engagement and inform dose selection, with the goal of generating initial clinical biomarker data in the first half of 2027 to guide subsequent development decisions.

2026 expected progress and milestones:

- Initiate dosing in Phase 1b clinical study of DNL628 in participants with Alzheimer's disease

DNL921 Antibody TransportVehicle™ Amyloid beta (ATV:Abeta) program for Alzheimer's disease

The accumulation of Abeta plaque in the brain is a defining feature of Alzheimer's disease. Recently approved Abeta-directed antibody therapeutics were shown in clinical studies to reduce Abeta plaque and have modest efficacy in slowing disease progression; however, these therapies are limited by suboptimal brain distribution, dose- and exposure-related safety concerns, including amyloid-related imaging abnormalities ("ARIA"), and administration and safety monitoring requirements that may constrain broader or earlier use. As treatment paradigms increasingly shift toward earlier and potentially preclinical stages of Alzheimer's disease, there remains a significant unmet need for therapies that can achieve more efficient and uniform brain target engagement with improved safety and dosing flexibility. Thus, there is a significant opportunity for improving the efficacy and safety of Abeta-directed antibodies, and we are using our ATV platform to develop the next generation of these therapies.

Our ATV:Abeta program utilizes the ATV platform to enable increased brain exposure and target engagement of Abeta plaques while avoiding ARIA. In preclinical studies in mice, ATV:Abeta was shown to be superior in reducing amyloid plaque load and oligomeric Abeta load (**Figure 17**) compared to a conventional Abeta antibody. ATV-enabled antibodies also essentially eliminate ARIA (**Figure 18**). These preclinical studies provide the first mechanistic understanding of how ARIA can be prevented by virtue of ATV-enabled brain delivery of Abeta antibodies through microvessels and largely bypassing arteries, which contain the majority of the vascular amyloid that is responsible for inducing ARIA. Furthermore, as published in Pizzo *et al.*, *Science,* 2025, our unique Fc engineering allows for conditional effector function through a cisLALA mutation, which preserves the ability for ATV:Abeta to engage microglia for plaque phagocytosis while mitigating TfR-related hematology liabilities such as depletion of reticulocytes (**Figure 18).**

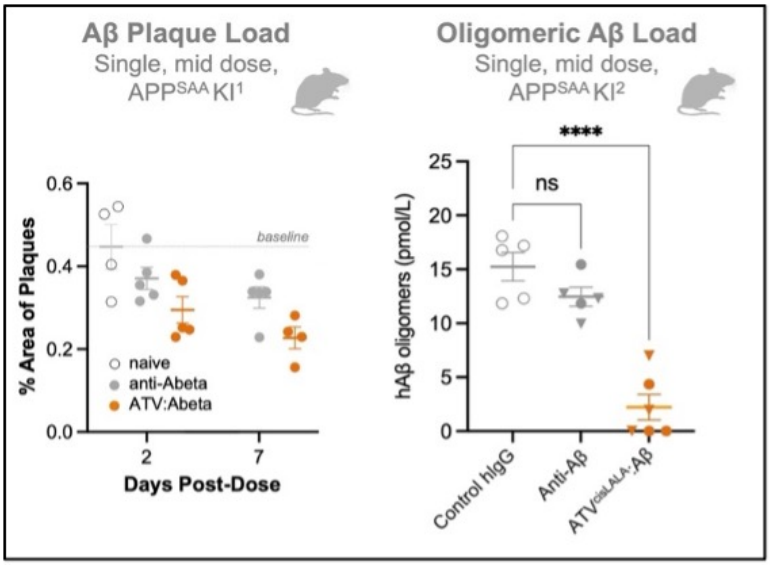

Figure 17: Preclinical mouse data showing superior amyloid plaque reduction (left), superior oligomeric plaque reduction (right) with DNL921 compared to a non-TV enabled anti-Abeta

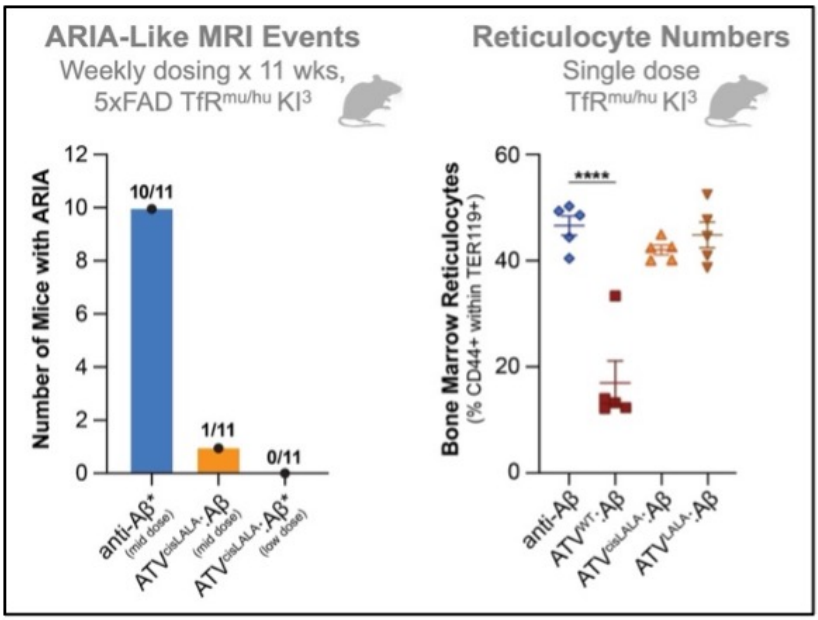

Figure 18: Preclinical studies in a mouse model demonstrated that an ATV-enabled Abeta displays fewer to no ARIA events (left) and preservation of reticulocytes (right).

DNL921 (ATV:Abeta) is our TV-enabled antibody targeting amyloid beta and is designed to enhance brain delivery while maintaining antibody effector function in a differentiated molecular architecture. By incorporating the TV directly into the antibody structure, DNL921 is engineered to engage the transferrin receptor to facilitate receptor-mediated transport across the blood-brain barrier, enabling deeper and more uniform penetration into brain parenchyma compared to conventional antibodies. This integrated design is intended to improve plaque engagement throughout the brain while reducing perivascular localization, which we believe may contribute to vascular-related safety liabilities observed with existing therapies.

In preclinical studies, DNL921 demonstrated substantially greater amyloid plaque engagement and deeper brain penetration compared to first-generation anti-amyloid antibodies, with labeling observed across cortical and subcortical regions rather than being restricted to superficial or perivascular areas (**Figure 19**). In head-to-head comparisons with other transferrin receptor-enabled competitor molecules, DNL921 showed increased plaque binding efficiency at lower doses and reduced vascular engagement with higher engagement of plaque-associated microglia, which are involved in amyloid clearance (**Figure 20**). In preclinical studies comparing DNL921 with other TfR-based brain shuttle approaches in a humanized mouse model that allows for cross-platform comparisons (**Figure 21**), DNL921 demonstrated approximately two-fold higher brain concentrations. This increased brain uptake was associated with greater *in vivo* molecular stability, with a higher proportion of intact DNL921 maintained over time relative to Fab-based shuttle formats. In addition, DNL921 preserved effector function without inducing measurable reductions in reticulocytes, in contrast to certain TfR-binding molecules associated with hematologic effects.

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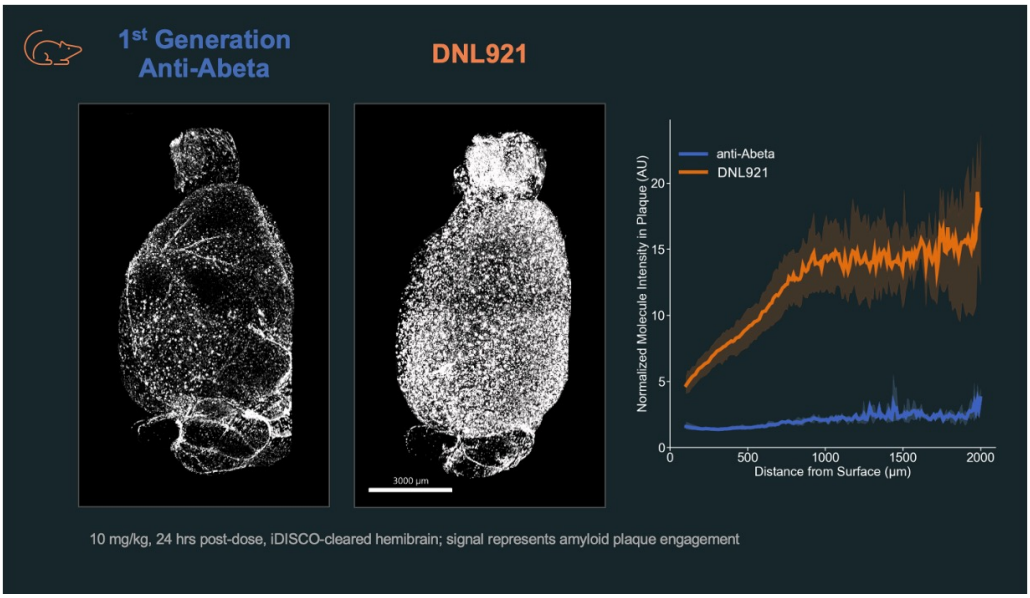


Figure 19: Whole mount imaging of brains from a mouse model of Alzheimer's disease reveals substantially improved engagement of antibody with plaque following dosing with DNL921 compared to a non-TV enabled anti-Abeta antibody.

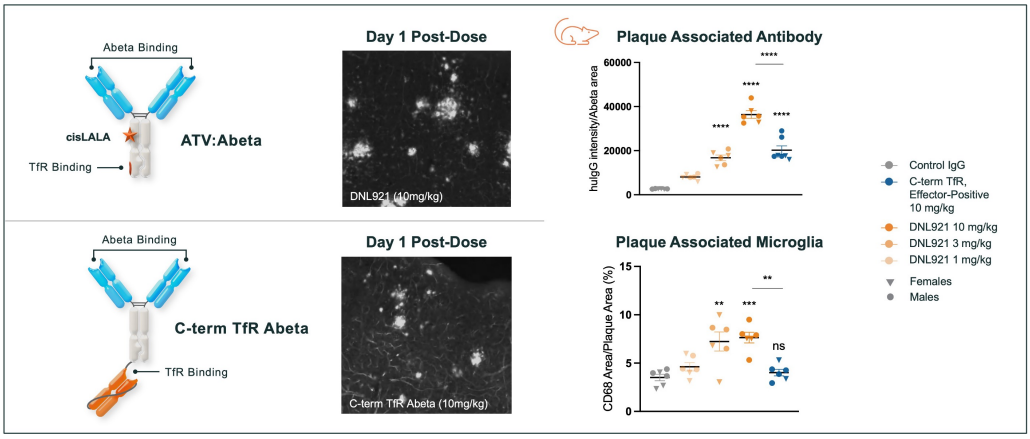


Figure 20: Images show increased antibody associated with amyloid plaque and less vascular staining with DNL921 compared to a non-TV enabled Abeta antibody. The increased antibody engagement leads to increased engagement with plaque-associated microglia.

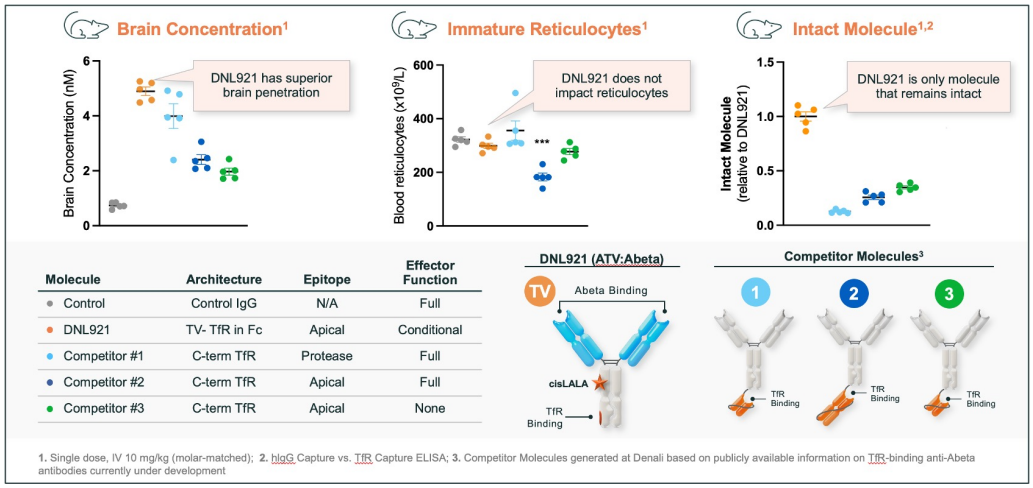


Figure 21: Studies comparing TV-enabled DN921 to molecules representing competitor TfR-based blood-brain barrier programs in a mouse model that expressed the full TfR extracellular domain reveals higher brain uptake and more intact molecule with DNL921 compared to competitor platforms.

Based on these data, we believe DNL921 has the potential to be a best-in-class amyloid beta therapy by combining efficient brain delivery, robust plaque engagement, and a differentiated safety profile that may enable lower doses, longer dosing intervals, or alternative routes of administration. The clinical development plan for DNL921 includes an initial Phase 1/1b study designed to evaluate safety, tolerability, pharmacokinetics, and biomarker-based measures of target engagement, including amyloid imaging and fluid biomarkers. The study is structured to enable rapid assessment of proof of mechanism and dose selection, with the potential to advance efficiently into later-stage clinical development. We expect to leverage validated biomarkers to inform patient selection and clinical decision making, with the goal of generating early clinical data to guide subsequent development in Alzheimer's disease.

2026 expected progress and milestones:

- Initiate dosing in Phase 1/1b clinical study of DNL921 in healthy volunteers and participants with Alzheimer's disease.

Our Small Molecule Programs

BIIB122/DNL151 LRRK2 Inhibitor Program for Parkinson's disease

Parkinson's disease is one of the most common brain diseases, affecting approximately 10 million people worldwide. It is considered to be a movement disorder because patients can experience tremors, slowness of movement, stiffness and difficulty with walking and balance. In addition, Parkinson's patients can have other non-motor type problems such as constipation, depression and memory loss. The Parkinson symptoms are a result of the loss of dopamine-producing cells in the brain, which is currently thought to be caused by a combination of genetic and environmental risk factors.

Mutations in the LRRK2 gene are one of the most common genetic risk factors for Parkinson's disease. LRRK2 is involved in maintaining a healthy cellular environment by regulating lysosomal function through modification of Rab proteins. Increased levels of LRRK2 kinase activity lead to lysosomal dysfunction, which is believed to contribute to neurodegeneration. Inhibition of LRRK2 activity has the potential to slow the progression of Parkinson's disease in patients, with and without known genetic risks based on restoration of lysosomal function.

As described in more detail in “Business - Licenses and Collaborations” below, we are collaborating with Biogen to co-develop and co-commercialize our small molecule inhibitors of LRRK2 for Parkinson's disease. BIIB122/DNL151 is the most clinically advanced small molecule inhibitor of LRRK2 currently in clinical testing for Parkinson's disease. Biogen is conducting the global Phase 2b LUMA study, which commenced in May 2022 and is evaluating the efficacy and safety of BIIB122/DNL151 as compared to placebo. Enrollment of 650 participants with early-stage Parkinson's disease was completed in March 2025.

Results from Phase 1 and Phase 1b trials of BIIB122/DNL151 in healthy volunteers and patients with Parkinson's disease, respectively, showed robust target and pathway engagement as measured by pS935 LRRK2 and pT73 Rab10 (“pRab10”), respectively. Furthermore, reduction in total LRRK2 in the CSF demonstrated central target engagement, and a dose-dependent reduction in urine of the lysosomal lipid 22:6-bis(monoacylglycerol)phosphate (“BMP”), a biomarker of lysosomal function, suggested improvement of lysosomal function. BIIB122/DNL151 was generally well tolerated across a broad range of doses for up to 28 days, the longest treatment duration in both studies.

In February 2024, we announced the execution of a Collaboration and Development Funding Agreement in January 2024 with a third party related to a global Phase 2a study of BIIB122/DNL151, which Denali is operationalizing to evaluate safety and biomarkers associated with dosing BIIB122 in participants with Parkinson’s disease and confirmed pathogenic variants of LRRK2. This agreement includes committed funding of $75.0 million, of which $50.0 million has been received through 2025, and the remainder will be triggered based on operational milestones in the study. Biogen will continue to conduct the ongoing global Phase 2b LUMA study in early-stage Parkinson’s disease. Denali and Biogen will co-commercialize BIIB122/DNL151 assuming regulatory approval. The third party will be eligible to receive low single-digit royalties from Denali on annual worldwide net sales of LRRK2 inhibitors for the treatment of Parkinson’s disease, with royalty amounts varying based on the scope of the label.

In December 2024, we announced that dosing had commenced in the Phase 2a study, called BEACON, which is expected to enroll approximately 50 participants into a double-blind treatment period of three months followed by an open label extension.

2026 expected progress and milestones:

- Data from the Phase 2b LUMA study in early-stage PD in mid-2026.

Other LRRK2 Compounds

Genetic and functional studies have linked LRRK2 and other proteins that modulate lysosomal function to Crohn's disease. Excessive LRRK2 activity leads to a reduction in lysosomal function, which contributes to the inflammation and intestinal dyshomeostasis that are characteristic of this disorder. We have discovered potent and selective small molecule inhibitors of LRRK2 and have selected a lead clinical candidate (DNL975) for treatment of Crohn's disease. As described in more detail in “Business - Licenses and Collaborations” below, we are collaborating with Biogen on the Peripheral LRRK2 program.

Eclitasertib (SAR443122/DNL758) RIPK1 Inhibitor Program for Peripheral Inflammatory Diseases: UC

As part of our parallel development strategy, we have also developed peripherally-restricted RIPK1 inhibitor molecules, which are included as part of the collaboration agreement with Sanofi, described in more detail in “Business - Licenses and Collaborations” below. Sanofi is solely responsible for the development and commercialization of peripherally restricted RIPK1 inhibitors.

Sanofi is conducting a Phase 2 study of eclitasertib in patients with ulcerative colitis; data readout expected in the first half of 2026, as planned.

2026 expected progress and milestones:

- Data from the Phase 2 UC study in the first half of 2026.

Discovery Programs

In addition to our development portfolio for neurodegenerative and lysosomal storage diseases, we have a robust discovery effort to further expand and capture the full potential of our TV platform to enhance delivery of biotherapeutics to all tissues in the body. For example, using ATV, we have engineered mono- and bispecific formats of HER2 antibodies. Human epidermal growth factor receptor 2 ("HER2") is a growth factor receptor that is over-expressed in multiple cancers, including breast, colorectal, and gastric cancer. Up to half of patients diagnosed with metastatic HER2-positive breast cancer develop brain metastases for which limited treatment options exist. In preclinical mouse studies, we have demonstrated improved anti-tumor activity of ATV-enabled HER2 antibodies in a HER2-positive peripheral tumor model. Our bispecific ATV:HER2 antibody demonstrated improved peripheral anti-tumor activity as compared to non-ATV HER2 antibodies as well as enhanced brain uptake as compared to a non-ATV HER2 antibody. The data support the potential for ATV:HER2 to treat HER2-positive peripheral tumors and brain metastases and to further validate the potential for TV applications in oncology.

Licenses and Collaborations

Biogen License and Collaboration Agreement and Right of First Negotiation, Option and License Agreement

Overview

In October 2020, we entered into a Definitive LRRK2 Collaboration and License Agreement (“LRRK2 Agreement”) pursuant to which we granted Biogen a license to co-develop and co-commercialize our small molecule LRRK2 inhibitor program (the "LRRK2 Program"), and a Right of First Negotiation, Option and License Agreement (the "ROFN and Option Agreement"), pursuant to which we granted an option and right of first negotiation to certain of our programs utilizing our TV technology platform, including our amyloid beta program (collectively the "Biogen Collaboration Agreement"), with Biogen Inc.’s subsidiaries, Biogen MA Inc. (“BIMA”) and Biogen International GmbH (“BIG”) (BIMA and BIG, collectively, “Biogen”). In August 2023, we executed an Amendment to the Definitive LRRK2 Collaboration and License Agreement and Waiver of and Amendment to Right of First Negotiation, Option, and License Agreement (the "Biogen Amendment").

LRRK2 Agreement

The LRRK2 Agreement includes our small molecule LRRK2 inhibitors (“LRRK2 Products”) that penetrate the BBB, including DNL201 and BIIB122/DNL151, as well as those that do not penetrate the BBB, with BIIB122/DNL151 currently proceeding in clinical development.

Payments

Under the terms of the LRRK2 Agreement, Biogen paid us a $400.0 million upfront payment in October 2020. With respect to the LRRK2 Program, Biogen is required to make milestone payments up to approximately $1.125 billion upon achievement of certain development and sales milestone events. Such milestone payments include $375.0 million in development, $375.0 million upon first commercial sale, and $375.0 million in net sales-based milestones. The Biogen Amendment changed certain milestone criteria while the total amount of development, regulatory, and commercial milestones across all indications remained the same. We will share profits and losses equally with Biogen for LRRK2 Products in the United States and will share profits and losses in China with Biogen sharing 60% of such profits and losses and us sharing 40% of such profits and losses. We will be entitled to receive royalties in the high teens to low twenties percentages on net sales for LRRK2 Products outside of the United States and China. Information on cost sharing reimbursements between us and Biogen is included in this Annual Report on Form 10-K in our financial statements and the related notes and the section titled “Management’s Discussion and Analysis of Financial Condition and Results of Operations.”

License Grant to LRRK2 Program

Under the LRRK2 Agreement, we granted Biogen a co-exclusive, worldwide license under intellectual property that we control related to our LRRK2 inhibitors, including certain intellectual property licensed to us by a third party.

Development and Commercialization of LRRK2 Program

We and Biogen are jointly developing LRRK2 Products pursuant to a clinical development plan set forth within the LRRK2 Agreement. We and Biogen share responsibility and costs for global development of LRRK2 Products pursuant to a mutually agreed development plan and budget, with Biogen funding 60% of such costs and us funding 40% of such costs. We have the ability to opt out of the development cost sharing arrangement, as further described below.

Biogen will lead commercialization activities globally for LRRK2 Products. We will co-commercialize the LRRK2 Products with Biogen in the United States and China, provided that the profit-sharing arrangement for the LRRK2 Products is still in effect, as further described below.

We may opt out of development cost sharing worldwide and upon such election, from any further profit-sharing from the LRRK2 Program. We also have the right to opt out of the profit-sharing arrangement for the LRRK2 Program or for only those LRRK2 Products that do not penetrate the BBB ("Peripheral LRRK2 Products"), in each of the United States and China. After such an opt out, we will no longer be obligated to share in the development and commercialization costs for, or be entitled to share in the applicable revenues from, such LRRK2 Program (or from the Peripheral LRRK2 Products) for such country, as applicable. If we choose to exercise our opt out rights, we will be entitled to receive tiered royalties on net sales of the applicable LRRK2 Program in the relevant country (or countries). The royalty rates for the applicable LRRK2 Program will be a percentage in the high teens to low twenties, but may increase to the low twenties to mid-twenties if we have met certain co-funding thresholds or there has been a first commercial sale at the time of our election.

LRRK2 Program Manufacturing

Biogen will be responsible for delivering all supplies for clinical trials and commercial production for LRRK2 Products, except that we will deliver such supplies until the point of transition which will be mutually agreed by us and Biogen, but in no event later than commencement of activities to support commercial launch, and in any event we retain manufacturing rights for certain independent clinical activities.

LRRK2 Program Royalty Term

For any LRRK2 Product for which Biogen is required to pay royalties, Biogen will pay us royalties on a country-by-country basis and product-by-product basis until the latest of (i) the expiration of certain patents covering the relevant product, (ii) the expiration of all regulatory exclusivity for that product in the applicable country, and (iii) an agreed period of time after the first commercial sale of that product in the applicable country. If, in a particular country, a LRRK2 Product for which Biogen is required to pay royalties is not covered by specified patent rights in that country or where generic competition exists, Biogen's royalty obligations in the applicable country would be reduced.

Exclusivity of LRRK2 Program

During the term of the LRRK2 Agreement, neither we nor Biogen may conduct preclinical, clinical or commercial activities involving any small molecule that targets LRRK2 as its primary mechanism of action anywhere in the world, unless such molecule is included under the collaboration and only to the extent such activity is permitted under the LRRK2 Agreement or, with respect to Biogen, the molecule is an ASO product that is the subject of a collaboration between Biogen and a particular third party.

ROFN and Option Agreement

Option & ROFN Programs

In addition to the LRRK2 Program, Biogen also received an exclusive option to license two preclinical programs enabled by our TV technology platform, including our ATV:Abeta program ("Option Programs"). In April 2023, Biogen exercised its option to develop and commercialize our ATV:Abeta program. As Biogen exercised its option with respect to the ATV:Abeta Program, we granted Biogen an exclusive, worldwide license under certain intellectual property to develop, manufacture, and commercialize products that are the subject of the ATV:Abeta Program. In August 2023, Biogen agreed to waive the remaining option upon execution of the Biogen Amendment.

In August 2023, upon execution of the Biogen Amendment, Biogen also agreed to waive its right of first negotiation on two additional TV-enabled therapeutics, which we initially granted to Biogen under the ROFN and Option Agreement.

On July 26, 2024, a Side Letter to the ROFN and Option Agreement was executed, pursuant to which, effective as of the date of the Side Letter, Biogen terminated its license to the ATV:Abeta program enabled by our TfR-targeting technology against amyloid beta for the potential treatment of Alzheimer's disease, and granted us rights to data generated during the collaboration. The side letter also effected the immediate termination of the ROFN and Option Agreement; as such, we expect to receive no future milestone or royalty payments from Biogen related to the ATV:Abeta program.

Common Stock Purchase Agreement

In August 2020, in connection with our collaboration with Biogen, we entered into a common stock purchase agreement with BIMA, pursuant to which we sold 13,310,243 shares of our common stock to BIMA for an aggregate purchase price of $465.0 million in September 2020. In connection with the sale of shares, we entered into a standstill and stock restriction agreement (the "Biogen Standstill Agreement") with Biogen, pursuant to which Biogen agreed to certain transfer and standstill restrictions, which have now expired, with the exception of certain volume limitations.

Sanofi Collaboration and License Agreement

Overview

In October 2018, we entered into the Collaboration Agreement with Genzyme Corporation, a wholly owned subsidiary of Sanofi S.A. ("Sanofi") pursuant to which certain small molecule compounds that bind to and inhibit RIPK1 (“RIPK1 Inhibitors”) contributed by Sanofi and by us will be developed and commercialized. The Sanofi Collaboration Agreement became effective in November 2018 when the requirements of the Hart-Scott-Rodino Antitrust Improvements Act of 1976 were satisfied, and included our and Sanofi’s RIPK1 Inhibitors that measurably penetrate the BBB ("CNS Products"), and our and Sanofi’s RIPK1 Inhibitors that do not measurably penetrate the BBB ("Peripheral Products").

We and Sanofi were jointly developing products containing RIPK1 Inhibitors for neurological indications, such as Alzheimer’s disease and MS, until the 2024 discontinuations of the HIMALAYA and K2 phase 2 studies evaluating SAR443820/DNL788 in participants with ALS and multiple sclerosis, respectively. On February 24, 2025, Denali and Sanofi executed a side letter terminating Sanofi's license to the CNS Products program including SAR443820/DNL788. Sanofi continues to develop eclitasertib (SAR443122/DNL758), a Peripheral Product discovered by us, and licensed to Sanofi who is leading a Phase 2 clinical trial in patients with UC.

License Grant

Under the Sanofi Collaboration Agreement, we granted Sanofi an exclusive, worldwide license under intellectual property that we control related to our RIPK1 Inhibitors, including certain intellectual property licensed to us by an academic institution.

Payments

When the Sanofi Collaboration Agreement became effective in November 2018, Sanofi paid us $125.0 million upfront. Sanofi is required to make milestone payments totaling up to approximately $495.0 million upon achievement of certain clinical, regulatory and sales milestone events for the Peripheral Products. Such milestone payments include $120.0 million in clinical milestone payments, $175.0 million in regulatory milestone payments and $200.0 million in commercial milestone payments for Peripheral Products, as defined, that are developed and approved in the United States, Europe and in Japan for three indications. Sanofi has made payments of $35.0 million for Peripheral Product clinical milestones through December 31, 2025, and a further $65.0 million for CNS Product clinical milestones through the same date. Subsequent to the side letter executed on February 24, 2025, we expect to receive no future milestone or royalty payments from Sanofi related to the CNS Products program. We will receive variable royalties on net sales for Peripheral Products sold worldwide, each as further described below.

RIPK1 Inhibitors contributed by Sanofi and developed and commercialized under the Sanofi Collaboration Agreement will be subject to lower milestone and royalty payments to us compared to RIPK1 Inhibitors contributed by us. We will also retain responsibility for certain payment obligations under our agreement with an academic institution which licensed certain intellectual property to us that we are sublicensing to Sanofi under the Sanofi Collaboration Agreement.

Program for Development and Commercialization of Peripheral Products

Sanofi will be responsible, at its cost, for conducting activities relating to the development and commercialization of all Peripheral Products. Sanofi will lead commercialization activities globally for Peripheral Products. We will be entitled to receive tiered royalties in the low- to mid- teen percentages on net sales of Peripheral Products.

Manufacturing

Sanofi will be responsible for delivering all supplies for current and future clinical trials and commercial production for Peripheral Products. However, we retain manufacturing rights for certain independent clinical activities.

Royalty Term

For each Peripheral Product, Sanofi will pay royalties to us on a country-by-country basis until the latest of (i) the expiration of certain patents covering the relevant product, (ii) the expiration of all regulatory exclusivity for that product in the applicable country, and (iii) an agreed period of time after the first commercial sale of that product in the applicable country. If, in a particular country, a Peripheral Product is not covered by specified patent rights in that country or net sales in that country decrease below specified thresholds as a result of generic competition, Sanofi's royalty obligations in the applicable country would be reduced or would terminate as specified in the Sanofi Collaboration Agreement.

Exclusivity

During the term of the Sanofi Collaboration Agreement, neither we nor Sanofi may conduct IND-enabling, clinical or commercial activities involving any Peripheral Product, anywhere in the world, unless the Peripheral Product is included by us or Sanofi, as the case may be, under the collaboration and only to the extent such activity is permitted under the Sanofi Collaboration Agreement.

Termination

Each party may terminate the Sanofi Collaboration Agreement in its entirety, or with respect to a particular program, as applicable, if the other party remains in material breach of the Sanofi Collaboration Agreement following a cure period to remedy the material breach. After giving a specified amount of prior notice to us, Sanofi may terminate the Sanofi Collaboration Agreement for convenience in its entirety, with respect to any particular program, or with respect to one or more specified regions of the world. Sanofi may also terminate the Sanofi Collaboration Agreement with respect to any program or a particular RIPK1 Inhibitor if a material safety event has occurred and cessation of all development and commercialization of all RIPK1 Inhibitors in the affected program or the affected RIPK1 Inhibitor is recommended. We and Sanofi may each terminate the Sanofi Collaboration Agreement in its entirety if the other party is declared insolvent or in similar financial distress or if, subject to a specified cure period, the other party challenges any patents licensed to it under the Sanofi Collaboration Agreement.

Following any termination of the Sanofi Collaboration Agreement with respect to a particular program or a particular region (or regions) of the world or termination of the Sanofi Collaboration Agreement in its entirety, our rights to each of our RIPK1 Inhibitors that were licensed to Sanofi will revert to us. Sanofi will conduct certain development, manufacturing and commercialization activities on a transitional basis following termination of the Sanofi Collaboration Agreement, as outlined in the Sanofi Collaboration Agreement or agreed by Sanofi, depending upon the basis for the applicable termination.

If the Sanofi Collaboration Agreement is terminated for any reason other than by Sanofi for our material uncured breach, our insolvency or our challenge to any of the patents licensed to us by Sanofi, Sanofi will grant us an exclusive license to certain intellectual property controlled by Sanofi with respect to such RIPK1 Inhibitors (which could be subject to low single digit royalties payable to Sanofi).

Takeda Option and Collaboration Agreement

Overview

In January 2018, we entered into a Collaboration Agreement ("Takeda Collaboration Agreement") with Takeda Pharmaceutical Company Limited ("Takeda"), pursuant to which we granted Takeda an option with respect to our ATV:BACE1/Tau, ATV:TREM2 and PTV:PGRN programs. Takeda paid us a $40.0 million upfront payment related to the collaboration, and an additional $110.0 million under a share purchase agreement in February 2018. The Takeda Collaboration Agreement became effective in February 2018, following satisfaction of certain requirements of the Hart-Scott-Rodino Antitrust Improvements Act of 1976. In February 2019, we amended the agreement to replace the ATV:BACE1/Tau program with the ATV:Tau program and in March 2022, the parties mutually agreed to terminate activity on the ATV:Tau program over which Takeda had its option to develop and commercialize jointly with the Company. Takeda exercised its option for the PTV:PGRN program in November 2021. Takeda exercised its option for the ATV:TREM2 program in December 2021. In February 2025, after mutual agreement to discontinue preclinical activities on ATV:TREM2, Takeda delivered notice of its election to terminate the ATV:TREM2 program on February 26, 2025, as per the terms of the Takeda Collaboration Agreement. The ATV:TREM2 program termination became effective 60 days following the notice date.

Research Phase and Takeda's Option

Under the Takeda Collaboration Agreement we were responsible, at our cost, for conducting activities relating to pre-IND development of biologic products directed to the identified targets and enabled by our TV technology targeting TfR during the applicable option period. The option period continued for each target until the first biologic product candidate directed to the relevant target was IND-ready or about five years after selection of the target, whichever was earlier.

Takeda was obligated to pay us up to an aggregate of $25.0 million with respect to each of the programs under the Takeda Collaboration Agreement directed to a target and based upon the achievement of certain preclinical milestone events, up to $55.0 million in total after the ATV:Tau program termination, all of which was earned and received as of September 30, 2022.

Collaboration Activities Following Takeda's Option Exercise

Subsequent to Takeda exercising its option with respect to a particular target and collaboration program (i.e., the biologic products directed to the target for which Takeda has exercised its option), Takeda has the right to develop and commercialize, jointly with us, a specified number of biologic products enabled by our TV technology that were developed during the option period and which are directed to the relevant target, and we are obligated to grant to Takeda a co-exclusive license under the intellectual property we control related to those biologic products.

Takeda was obligated to pay us a $5.0 million option fee for each target for which Takeda exercised its option, and we received fees totaling $10.0 million from Takeda in 2021 for option exercise payments for the PTV:PGRN and ATV:TREM2 programs.

Subsequent to the ATV:TREM2 termination, Takeda may be obligated to pay us milestones related to the PTV:PGRN program, including up to $140.0 million upon achievement of certain clinical milestone events and up to $100.0 million in regulatory milestone events relating to receipt of regulatory approval in the United States, certain European countries and Japan. Further, Takeda may also be obligated to pay us up to $75.0 million upon achievement of a certain sales-based milestone.

Further, we and Takeda share equally the development and commercialization costs, and, if applicable, the profits, for the PTV:PGRN program. However, we may elect not to continue sharing development and commercialization costs, or Takeda may elect to terminate our cost-profit sharing rights and obligations if, following notice from Takeda and a cure period, we fail to satisfy our cost sharing obligations. After such an election by us or termination by Takeda becomes effective, we will no longer be obligated to share in the development and commercialization costs for the PTV:PGRN program, and we will not share in any profits from that program. Instead, we will be entitled to receive tiered royalties. The royalty rates will be in the low- to mid-teen percentages on net sales, or low- to high-teen percentages on net sales if we have met a certain co-funding threshold at the time of our election to opt out of co-development or Takeda's termination of our cost-profit sharing rights and obligations, and, in each case, these royalty rates will be subject to certain reductions specified in the Takeda Collaboration Agreement. Takeda will pay these royalties to us, on a country-by-country basis, until the latest of (i) the expiration of certain patents covering the biologic product, (ii) the expiration of all regulatory exclusivity for that biologic product, and (iii) an agreed period of time after the first commercial sale of that biologic product in the applicable country, unless biosimilar competition in excess of a significant level specified in the Takeda Collaboration Agreement occurs earlier, in which case Takeda's royalty obligations in the applicable country would terminate.

For the PTV:PGRN program for which we are sharing costs and profits with Takeda, we will lead the conduct of clinical activities for each indication up to the first trial with a clinical outcomes-based efficacy endpoint, and Takeda will lead the conduct of all subsequent clinical activities for that indication. We and Takeda will jointly commercialize biologic product(s) included in the PTV:PGRN program in the United States and China. Takeda will lead commercialization activities in the United States and China and will solely conduct commercialization activities in all other countries.

We have the right to lead all manufacturing activities for the PTV:PGRN program.

Information on cost sharing reimbursements between us and Takeda is included in this Annual Report on Form 10-K in our financial statements and the related notes and the section titled “Management’s Discussion and Analysis of Financial Condition and Results of Operations.”

Exclusivity

Unless the Takeda Collaboration Agreement is terminated earlier, until expiration of an agreed period of time after the first regulatory approval in the United States or Europe of a biologic product within the PTV:PGRN program, neither party may conduct clinical or commercial activities involving antibodies or protein-based therapeutic products directed to the same target (or in the case of a bi-specific program, the same combination of targets) that have an intended therapeutic effect in diseases and conditions of the CNS (including lysosomal storage diseases), except to the extent permitted under the Takeda Collaboration Agreement.

Termination

Each party may terminate the Takeda Collaboration Agreement in its entirety, or with respect to a particular collaboration program, as applicable, if the other party remains in material breach of the Takeda Collaboration Agreement following a cure period to remedy the material breach. Takeda may terminate the Takeda Collaboration Agreement in its entirety or with respect to any particular collaboration program, for convenience and after giving a specified amount of prior notice to us. Takeda may also terminate the Takeda Collaboration Agreement with respect to any collaboration program if the joint steering committee established under the Takeda Collaboration Agreement unanimously agrees that a material safety event has occurred with respect to the applicable collaboration program. We may terminate the Takeda Collaboration Agreement with respect to a particular collaboration program if Takeda fails to conduct material development and commercial activities for a specified period of time with respect to a collaboration program, unless Takeda cures such failure within a certain period of time. We and Takeda may each terminate the Takeda Collaboration Agreement in its entirety if the other party is declared insolvent or in similar financial distress or if, subject to a specified cure period, the other party challenges any patents licensed to it under the Takeda Collaboration Agreement.

Following any termination of the Takeda Collaboration Agreement with respect to a particular collaboration program or the Takeda Collaboration Agreement in its entirety, our rights to each terminated collaboration program will revert to us, Takeda will grant us a license to intellectual property owned by Takeda with respect to such collaboration program (which could be subject to certain royalty payments that would be negotiated at the time of such a termination) and, unless the termination was by Takeda on the basis of a material safety event, Takeda will conduct certain development, manufacturing and commercialization wind-down activities.

Common Stock Purchase Agreement

Pursuant to the terms of the Takeda Collaboration Agreement, we entered into a common stock purchase agreement with Takeda in January 2018, pursuant to which we sold 4,214,559 shares of our common stock (the “Shares”) to Takeda for an aggregate purchase price of $110.0 million. We closed the sale to Takeda in February 2018.

At closing, we also entered into a standstill and stock restriction agreement (the “Takeda Standstill Agreement”) with Takeda. Pursuant to the terms of the Takeda Standstill Agreement, Takeda agreed to certain transfer and standstill restrictions for a specified period of time following the closing of the sale, which have now expired. Takeda remains entitled to certain demand registration rights with respect to the Shares following termination of the transfer restrictions if the Shares cannot be resold without restriction pursuant to Rule 144 promulgated under the Securities Act of 1933, as amended (the "Securities Act").

F-star License and Collaboration Agreement

Overview

In August 2016, we entered into a License and Collaboration Agreement (“F-star Collaboration Agreement”) with F-star Gamma Limited (“F-star Gamma”), F-star Biotechnologische Forschungs-und Entwicklungsges m.b.H ("F-star GmbH") and F-star Biotechnology Limited ("F-star Ltd") (collectively "F-star"). The goal of the collaboration was 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 was designed to leverage F-star’s modular antibody technology and our expertise in the development of therapies for neurodegenerative diseases. The agreement included the purchase of an option for $0.5 million to acquire all outstanding shares pursuant to a pre-negotiated buy-out option agreement. We exercised this buy-out option in May 2018 and entered into a Share Purchase Agreement with the shareholders of F-star Gamma and Shareholder Representative Services LLC (the "Acquisition").

As a result of the Acquisition, F-star Gamma became a wholly-owned subsidiary of the Company and we changed the entity’s name to Denali BBB Holding Limited. In addition, we became a direct licensee of certain intellectual property of F-star Ltd (by way of the Company’s assumption of F-star Gamma’s license agreement with F-star Ltd, dated August 24, 2016, (the “F-star Gamma License”)). We made initial exercise payments under the Purchase Agreement and the F-star Gamma License of $18.0 million in the aggregate, less the net liabilities of F-star Gamma, which were approximately $0.2 million. In addition, we are required to make contingent payments, to F-star Ltd and the former shareholders of F-star Gamma, up to a maximum amount following completion of the research phase of the F-star collaboration of $243.0 million in the aggregate upon the achievement of certain defined preclinical, clinical, regulatory and commercial milestones. These include up to $3.0 million in preclinical contingent payments, $30.0 million in clinical contingent payments, $60.0 million in regulatory contingent payments, including $36.0 million due upon regulatory approval of tividenofusp alfa in the United States, and $150.0 million in commercial contingent payments. We have made payments of $49.8 million through December 31, 2025 in the aggregate consisting of up-front, preclinical and clinical contingent consideration.

Under the terms of the original F-star Collaboration Agreement, we could nominate up to three Fcab targets (“Accepted Fcab Targets”) within the first three years of the date of the F-star Collaboration Agreement. Upon entering into the F-star Collaboration Agreement, we had selected TfR as the first Accepted Fcab Target and paid F-star Gamma an upfront fee of $5.5 million, which included selection of the first Accepted Fcab Target. In May 2018, we exercised our right to nominate two additional Fcab Targets and identified CD98 as the second Accepted Fcab Target. We made a one-time payment for the two additional Accepted Fcab Targets of, in the aggregate, $6.0 million and extended the time period for our selection of the third Accepted Fcab Target until approximately the fourth anniversary of the date of the original F-star Collaboration Agreement. We did not identify a third Fcab Target. We were also responsible for certain research costs incurred by F-star Ltd in conducting activities under an agreed development plan for each Fcab, for up to 24 months after the target Fcab is accepted. In July 2021, we executed a side letter to our agreements with F-star which confirmed the completion of the research services performed by F-star Ltd that were funded by us.

Genentech Exclusive License Agreement

In June 2016, we entered into an exclusive license agreement with Genentech, Inc. (“Genentech”). The agreement gives us access to Genentech’s LRRK2 inhibitor small molecule program for Parkinson’s disease. Under the agreement, Genentech granted us (i) an exclusive, worldwide, sublicensable 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, sublicensable 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 upon entering 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, which are subject to equal cost sharing with Biogen since execution of the Biogen Collaboration Agreement. These milestones include up to $37.5 million in clinical milestone payments, $102.5 million in regulatory milestone payments and $175.0 million in commercial milestone payments. We have made milestone payments to Genentech of $15.0 million through December 31, 2025.

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. Under the terms of our LRRK2 Agreement with Biogen, Biogen is responsible for 50% of any payment obligation to Genentech under this agreement accruing after October 2020.

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.

Royalty Pharma Funding Agreement

In December 2025, we entered into a synthetic royalty funding agreement (the "Royalty Agreement") with Royalty Pharma plc ("Royalty Pharma"). Pursuant to the Royalty Agreement, Royalty Pharma has agreed to provide us with up to $275.0 million in funding in exchange for a 9.25% royalty on future net sales of tividenofusp alfa. The transaction is subject to various closing conditions, including our achieving U.S. Food and Drug and Administration (FDA) accelerated approval of tividenofusp alfa on or before June 30, 2026. At the closing, Royalty Pharma will make an initial payment of $200.0 million. We will receive an additional payment of $75.0 million upon approval of tividenofusp alfa by the European Medicines Agency (EMA) on or before December 31, 2029. The royalty payments to Royalty Pharma will cease upon reaching a multiple of 3.0x, or 2.5x if achieved by the first quarter of 2039. We will retain all worldwide development and commercialization rights to tividenofusp alfa.

Manufacturing

We believe it is important to our business success to have a reliable, high-quality drug supply chain to support our preclinical and clinical development activities and, if approved, the commercialization of our product candidates. We currently rely on third-party contract development and manufacturing organizations ("CDMOs") to manufacture and supply preclinical and clinical materials used in the development of our product candidates, and we have established relationships with several CDMOs, including Lonza Sales AG ("Lonza"), which provides development and manufacturing services with respect to certain of our biologic products on a fee-for-service basis. As we mature as a company and advance product candidates toward commercialization, securing and maintaining reliable, high-quality drug supply chains for each product candidate will be critical. We have established a third-party supply chain for tividenofusp alfa and, if approved for the treatment of Hunter syndrome, we plan to continue to rely on third-party contract manufacturers for its commercial supply.

Over time, we intend to complement our use of third-party manufacturers by selectively developing internal manufacturing capabilities, including for commercial supply, to support the advancement and commercialization of our product candidates.

In early 2025, we commenced operations at our clinical manufacturing site in Salt Lake City, Utah, expanding our clinical manufacturing capabilities for biologic therapeutics, including the manufacture of materials for toxicology studies and drug substance for human clinical studies. This facility represents an initial step in building internal manufacturing capabilities, with the goal of increasing flexibility and speed in advancing new investigational therapies into clinical trials.

Commercialization Plan

We do not currently have any approved drugs. The PDUFA date for our lead asset, tividenofusp alfa, is currently April 5, 2026. With this timeline in mind, over the course of 2025 we invested in building right-sized marketing, product distribution, and sales capabilities for the U.S. market. As of the date of this filing, we have established our U.S. commercial infrastructure to support a potential commercial launch following the PDUFA date. We expect to continue to refine these capabilities through and following launch, including distribution planning and logistics, to support the U.S. launch of tividenofusp alfa. In parallel, we are engaging in discussions with potential regional commercial partners regarding possible paths for selective expansion into certain markets outside the United States, subject to applicable regulatory requirements.

Our vision is to become a fully integrated, independent global leader in delivering the power of biotherapeutics to the whole body, including the brain, transforming the lives of people living with serious diseases. We apply our capabilities in discovery, development, manufacturing, and commercial in order to optimize speed, quality, and patient access to our medicines. We look to grow strategically both in terms of therapeutic areas of high unmet need, starting with lysosomal storage diseases and expanding into large neurodegenerative disorders and other serious diseases, as well as from a geographic perspective, with an initial focus on building a commercial presence in the United States and the European Union ("EU"), and establishing a network of specialized regional partners to access other major markets.

For programs covered by collaboration agreements (including those with Takeda, Sanofi, and Biogen), we expect to commercialize only in certain geographies, as defined by the terms of the agreements with the counterpart, and rely on our partners to provide commercialization infrastructure for the rest of the world.

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 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:* Treatments currently approved in some geographies for Alzheimer's Disease include the amyloid beta-directed antibody therapies ADUHELM (Biogen), LEQEMBI (Eisai/Biogen), and KISLUNA (Eli Lilly). Additionally, potentially disease modifying therapeutics are being developed by several large and specialty pharmaceutical and biotechnology companies, including Biogen/Ionis, Arrowhead, Eli Lilly (including Prevail Therapeutics, its wholly owned subsidiary), Roche (including Genentech, its wholly owned subsidiary), AbbVie, Bristol Myers Squibb, Prothena, Regeneron, Alnylam, Eisai, and BioArctic in various stages of development.

- *Parkinson's Disease:* Potentially disease modifying therapeutics are being developed by several large and specialty pharmaceutical and biotechnology companies, including Roche/Prothena (including Genentech, its wholly owned subsidiary), Ionis, Eli Lilly (including Prevail Therapeutics, its wholly owned subsidiary), AstraZeneca, Takeda, Oncodesign/Servier, Neuron23 and AbbVie in various stages of development.

- *FTD-GRN:* Potentially disease modifying therapeutics are being developed by several large and specialty pharmaceutical and biotechnology companies, including GSK/Alector, Eli Lilly (including Prevail Therapeutics, its wholly owned subsidiary), Passage Bio, AviadoBio, Vesperbio, Arkuda Therapeutics, and Orchard Therapeutics in various stages of development.

- *Lysosomal storage diseases:* The currently approved treatments for lysosomal storage diseases are conventional enzyme-based therapies. Various BBB-penetrant and direct to CNS delivered ERTs and gene therapies are being developed by several large and specialty pharmaceutical and biotechnology companies, including JCR Pharmaceuticals, RegenxBio, Kyowa Kirin/Orchard Therapeutics, and Ultragenyx, and are in various stages of development.

In addition, companies are developing technologies that would compete directly with our TV technology. These include several large and specialty pharmaceutical and biotechnology companies developing BBB delivery technologies that utilize RMT, including JCR Pharmaceuticals, Roche (including Genentech, its wholly owned subsidiary), Eli Lilly (including Prevail Therapeutics, its wholly owned subsidiary), Abbvie, Regeneron, BioArctic, Alector, Bicycle Therapeutics, Ossianix, Vect-Horus, Sanofi, and ABL Bio, 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 TV platform, 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 invention and licensing opportunities to develop and maintain our proprietary position.

As of December 31, 2025, our owned and licensed patent portfolio includes over 1,600 patents and patent applications, including over 30 licensed U.S. issued patents and 40 owned U.S. issued patents, covering certain aspects of our proprietary technology, our product candidates, and related inventions and improvements. The patent portfolio also includes over 500 licensed patents issued in jurisdictions outside of the United States, and over 950 owned patents and patent applications pending in jurisdictions outside of the United States that, in many cases, are counterparts to the foregoing U.S. patents and patent applications. For our product candidates and our TV platform, we generally pursue or in-license patent protection covering compositions of matter, methods of use, and manufacture.

TV Platform

We own 10 patent families related to our TV platform. These include a family directed to the composition and sequences of our TfR-binding TVs, the earliest of which are expected to expire in 2038, not including any patent term adjustments and any patent term extensions. We also have 7 issued U.S. patents, which are also expected to expire in 2038, not including any patent term adjustments and any patent term extensions, as well as pending patent applications, to other TV platform. Other families related to TV platform, if issued, are expected to expire in 2038 or later, all not including any patent term adjustments and any patent term extensions. In addition, we license multiple patent families from F-star, the earliest issued patents of which are expected to expire in 2026, not including any patent term adjustments and any patent term extensions.

ETV Platform and Programs

We own 12 patent families directed to our ETV platform and related products, including ETV:IDS, ETV:SGSH, ETV:GAA, ETV:Gcase, and ETV:IDUA. This includes 1 issued U.S. patent, which is expected to expire in 2038, not including any patent term adjustments and any patent term extensions, directed to the composition of matter of our ETV:IDS molecules, including DNL310. We also own 5 additional patent families directed to various aspects of our DNL310 program, which if issued, are expected to expire in 2039 or later, all not including any patent term adjustments and any patent term extensions. Of the 12 patent families, 3 families relate to the composition of matter of our ETV:SGSH structures, including DNL126. This includes 1 issued U.S. patent, which is expected to expire in 2041, not including any patent term adjustments and any patent term extensions. Any patents issuing from these families are expected to expire between 2039 and 2046, respectively, not including any patent term adjustments and any patent term extensions. Of the 12 patent families, 2 families relate to the composition of matter of our ETV:GAA structures, including DNL952. This includes 1 issued U.S. patent, which is expected to expire in 2044, not including any patent term adjustments and any patent term extensions.

PTV:PGRN Program

We own 4 patent families directed to our PTV:PGRN program. This includes 1 issued U.S. patent, which is expected to expire in 2040, not including any patent term adjustments and any patent term extensions, directed to the composition of matter of our PTV:PGRN molecules, including TAK-594/DNL593. We also own an additional patent family directed to the composition of matter of our PTV:PGRN structures, including TAK-594/DNL593, the earliest of which are expected to expire in 2039, not including any patent term adjustments and any patent term extensions. We also own additional patent families directed to various aspects of our TAK-594/DNL593 program, which, if issued, are expected to expire in 2039 or later, all not including any patent term adjustments and any patent term extensions. Our PTV:PGRN program is subject to our Takeda collaboration.

Oligonucleotide Transport Vehicle Platform and Programs

We own 7 patent families directed to our OTV platform, including OTV:MAPT and OTV:SNCA. These families are directed to compositions and methods of use of our OTVs, including DNL628 (OTV:MAPT) and DNL422(OTV:SNCA), and if issued, are expected to expire between 2042 and 2045, not including any patent term adjustments and any patent term extensions.

LRRK2 Inhibitor Program

Our LRRK2 program is subject to our collaboration agreement with Biogen. For this program, we license multiple patent families from Genentech directed to, among other things, DNL201, BIIB122/DNL151 and other related compounds, which are expected to expire in 2031, not including any patent term adjustments and any patent term extensions. Furthermore, we own additional patent families that have projected expiration dates in 2038 or later, not accounting for any patent term adjustments and any patent term extensions, related to the LRRK2 program. We also own a patent family that includes 3 issued U.S. patents, which are expected to expire in 2037, not including any patent term adjustments and any patent term extensions, directed to the composition of matter of BIIB122/DNL151 and methods of treatment using BIIB122/DNL151, respectively, as well as pending patent applications and granted patents in jurisdictions outside the U.S.

RIPK1 Inhibitor Program

Our RIPK1 program is subject to our collaboration agreement with Sanofi. We own 6 patent families directed to our RIPK1 inhibitor program. These include 13 issued U.S. patents, including one directed to the composition of matter of eclitasertib (SAR443122/DNL758), which is expected to expire in 2037, not including any patent term adjustments and any patent term extensions.

ATV:Abeta Program

We own 4 patent families directed to our ATV:Abeta program. This includes a family directed to our composition of matter of DNL921, which is expected to expire in 2046, not accounting for 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. 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 invention 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. Geopolitical actions in the United States and in foreign countries could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications or those of any current or future licensors and the maintenance, enforcement or defense of our issued patents or those of any current or future licensors. 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 United States Patent and Trademark Office (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 ("FDCA"), and its implementing regulations, and biologics under the FDCA, the Public Health Service Act ("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 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 ("NDA"), or a biologics license application ("BLA"), process before they may be legally marketed in the United States. The process generally involves the following:

- Completion of extensive nonclinical studies in accordance with applicable regulations, including studies conducted in accordance with good laboratory practice ("GLP"), requirements;
- Submission of an IND to the FDA, which must become effective before human interventional clinical trials may begin;
- Approval by an independent institutional review board ("IRB") 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 ("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 ("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 inspection 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 ("REMS"), and the potential requirement to conduct post-approval studies.

Preclinical Studies and IND

The preclinical developmental stage generally involves laboratory evaluations of drug chemistry, formulation and stability, as well as studies to evaluate pharmacology, pharmacokinetics and toxicity in animals, which support subsequent clinical testing. The sponsor must submit the results of the preclinical studies, together with chemistry, manufacturing, and control information, analytical data, including pharmacology and toxicology information, any available clinical data or literature, investigator's brochure, and a proposed clinical protocol, among other information, 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 pharmacology, pharmacokinetics, and 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, chronic toxicity 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 that precludes study initiation 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. Interventional 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 trial not conducted under an IND if the trial 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, which may overlap or be combined:

- 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, and initial side effect tolerability and safety of the drug.

- Phase II clinical trials involve studies in a limited number of disease-affected patients to evaluate the preliminary efficacy, optimal dosages, and dosing schedule and to identify possible adverse side effects and safety risks.

- 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.

When these phases overlap or are combined, the trials may be referred to as Phase 1/2 or Phase 2/3. 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. Expedited written IND safety reports must be submitted to the FDA, IRBs, 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 or severity 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.

We may be required to develop and implement additional clinical trial policies and procedures designed to help protect subjects from public health concerns, such as a global pandemic. For example, the FDA has issued various guidance documents on conducting clinical trials during the COVID-19 pandemic, including certain reporting requirements and additional guidance on good manufacturing practice considerations for responding to global pandemic infection.

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 the proposed labeling, and information relating to the product's chemistry, manufacturing, and controls, among other information, to ensure consistent product quality, safety, and efficacy. In short, the NDA or BLA is a request for approval to market the drug or biologic for the specified indication(s) and must contain sufficient evidence of efficacy, acceptable safety profile, and appropriate quality attributes. 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 and/or from a number of alternative sources, including but not limited to studies initiated by investigators or cooperative clinical groups. 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 ("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 FY 2026 user fee schedule, effective through September 30, 2026, the user fee for an application requiring clinical data, such as an NDA or BLA, is $4,682,003. PDUFA also imposes an annual program fee for each marketed human drug or biologic of $442,213. Fee waivers or reductions are available in certain limited circumstances. Additionally, no user fees are assessed on NDAs or BLAs for products designated as orphan drugs for an orphan indication submission.

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, such as the issuance of a Refuse to File ("RTF") letter. 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 may be extended by FDA requests for additional information or clarification.

Before approving an NDA or BLA, the FDA may 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. Further, FDA's "real time" release of newly issued Complete Response Letters associated with withdrawn or abandoned applications, if applicable to any of our product candidates, can materially impact our business and competitive advantage.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the BLA with a Risk Evaluation and Mitigation Strategy, or REMS, to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a product and to enable patients to have continued access to such medicines by managing their safe use, and 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. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies.

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 EU has similar, but not identical, requirements and benefits.

In view of the court decision in *Catalyst Pharms., Inc. v. Becerra*, 14 F.4th 1299 (11th Cir. 2021), in January 2023, the FDA published a notice in the Federal Register to clarify that while the agency complies with the court's order in Catalyst, the FDA intends to continue to apply its longstanding interpretation of the regulations to matters outside of the scope of the Catalyst order – that is, the agency will continue tying the scope of orphan-drug exclusivity to the uses or indications for which a drug is approved, which permits other sponsors to obtain approval of a drug for new uses or indications within the same orphan designated disease or condition that have not yet been approved. The Consolidated Appropriations Act of 2026, signed into law in February 2026, codified this longstanding FDA interpretation of the Orphan Drug Act.

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 the combination of 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.

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 facilitate an efficient drug development program.

Any product submitted to the FDA for marketing, including under a fast track or breakthrough therapy designation 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. Priority review reduces the review time for an initial or supplemental marketing application by four months.

A product may be eligible for accelerated approval, if it treats a serious or life-threatening condition and generally provides a meaningful advantage over available therapies based on 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 ("IMM"), that is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of accelerated approval, the FDA requires that a sponsor of a drug or biologic receiving accelerated approval subsequently provide additional data confirming the anticipated clinical benefit, for example by performing adequate and well-controlled post-marketing clinical trials. If clinical benefit is not confirmed, accelerated approval may be revoked. 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. Further, the Food and Drug Omnibus Reform Act made several changes to the FDA's authorities and its regulatory framework, including, among other changes, requiring the FDA to specify conditions for post-approval study requirements and setting forth procedures for the FDA to withdraw a product on an expedited basis for non-compliance with post-approval requirements.

Fast track designation, breakthrough therapy designation, priority review, and accelerated approval 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 ("PPACA"), Affordable Care Act ("ACA"), signed into law in 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 ("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; and
- animal studies (including the assessment of toxicity).

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 complying 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 in the United States 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, an applicant would be required to submit and obtain FDA approval of a new NDA/BLA or a supplement before any material modifications can be implemented for a drug or biologic, including changes in labeling or manufacturing processes or facilities, which may require the development of additional data or nonclinical studies and clinical trials.

The FDA may also place other conditions on approvals including the requirement for a 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.

For example, in June 2024, the U.S. Supreme Court overruled the *Chevron* doctrine, which gives deference to regulatory agencies' statutory interpretations in litigation against federal government agencies, such as the FDA, where the law is ambiguous. This landmark Supreme Court decision may invite various stakeholders to bring lawsuits against the FDA to challenge longstanding decisions and policies, which could lead to uncertainties in the industry. Further, changes in the leadership of the FDA and other federal agencies under the current administration, as well as new legislative, executive, and other administration actions implemented by the government may impact our clinical development and timelines.

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 USPTO, 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 ("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 EU are subject to significant regulatory controls. In the EU, a clinical trial application, or CTA, must be submitted to the Clinical Trials Information System under the Clinical Trial Regulation EU No 536/2014 and an independent ethics committee, respectively. Once the CTA is approved in accordance with a EMA requirements, clinical study development may proceed. The clinical studies must be conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. The Clinical Trials Regulation EU No 536/2014, which replaced the Clinical Trials Directive, entered into application on January 31, 2022. The Clinical Trials Regulation harmonizes the processes for assessment and supervision of clinical trials throughout the EU. Under the Regulation, sponsors submit one online application via a single online platform known as the Clinical Trials Information System ("CTIS") for approval to run a clinical trial in several European countries, making it more efficient to carry out such multinational trials. A transition period applies to clinical trial submissions under the Regulation. For example, from 31 January 2023 onwards, clinical trial sponsors need to apply via the Clinical Trials Information System to start a clinical trial. From 31 January 2025, any trials approved under the Clinical Trials Directive that continue running will need to comply with the Clinical Trials Regulation and their sponsors must enter information on the trials in the CTIS.

European Union Drug Review and Approval

In the European Economic Area ("EEA"), which is comprised of the 27 Member States of the EU, plus Norway, Iceland and Liechtenstein, medicinal products can only be commercialized after obtaining a Marketing Authorization ("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 ("CHMP"), of the 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 may also apply 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 ("RMS"). The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics ("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 procedures described above, before granting the MA, the EMA or the competent authorities of the Member States of the EEA assess the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy. Starting in January 2021, the MHRA assumed additional regulatory responsibilities for medical products marketed in the UK, as pan-EU regulatory procedures before the EMA no longer apply in the UK. MHRA and the National Institute for Biological Standards and Control ("NIBSC") recently issued new guidance documents to the industry regarding regulation under the UK system. Proposals set forth in the new MHRA guidance will take effect through legislative changes that are subject to parliamentary approval, which may increase the amount of resources and time needed for obtaining regulatory approval in the UK and delay our clinical development and commercialization. On January 1, 2024, MHRA launched a new streamlined international recognition framework replacing the current European Commission Decision Reliance Procedure ("ECDRP") and allow the MHRA to rely on or give regard to a European decision or decision of other regulators to grant a new marketing authorization for a product.

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 ("AMP"), to 23.1% of AMP and adding a new rebate calculation for "line extensions" (e.g., 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 ("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 ("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.

There have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs.

In August 2022, Congress passed the Inflation Reduction Act of 2022 ("IRA"), which includes prescription drug provisions that have significant implications for the pharmaceutical industry and Medicare beneficiaries. These include allowing the federal government to negotiate a maximum price paid by Medicare for certain single source drugs responsible for significant Medicare spending, imposing penalties and excise tax for manufacturers that fail to comply with the drug price negotiation requirements, requiring inflation rebates for all Medicare Part B and Part D drugs, with limited exceptions, if their drug prices increase faster than inflation, and redesigning Medicare Part D to reduce out-of-pocket prescription drug costs for beneficiaries, among other changes. Various industry stakeholders have initiated lawsuits against the federal government asserting that the price negotiation provisions of the IRA are unconstitutional. Further, the current administration has issued executive orders focused on decreasing prescription drug prices, including directing the Secretary of HHS to establish a mechanism through which American patients can buy drugs directly from manufacturers who sell at a most-favored-nation price and directing the U.S. Trade Representative and Secretary of Commerce to take action to ensure foreign countries are not engaged in practices that purposefully and unfairly undercut market prices and drive price hikes in the United States. In November 2025, CMS announced a voluntary initiative called the GENEROUS Model (GENErating cost Reductions for U.S. Medicaid Model) to introduce the option of most-favored-nation pricing to the Medicaid program, whereby a drug manufacturer may voluntarily offer supplemental rebates to participating state Medicaid programs for a manufacturer's covered outpatient drugs. Government agreements with pharmaceutical companies and other government measures that use most-favored-nation pricing targets for prescription drugs, including the use of international pricing reference to set drug prices in the United States, or that increase generic and biosimilar drug entry sooner than expected can have a material adverse effect on our industry, ability to set adequate pricing for new drugs to recover research and development costs, ability to attract potential investors and potential buyers in the future. The impact of these legislative, executive, and administrative actions, and any future healthcare measures and agency rules implemented by the new administration on us and the pharmaceutical industry as a whole is unclear. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates if approved.

At the state level, legislatures have also increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. For example, a number of states are considering or have recently enacted state drug price transparency and reporting laws that could substantially increase our compliance burdens and expose us to greater liability under such state laws once we begin commercialization after obtaining regulatory approval for any of our products. We are unable to predict the future course of federal or state healthcare legislation in the United States directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. These and any further changes in the law or regulatory framework that reduce our revenue or increase our costs could also have a material and adverse effect on our business, financial condition and results of operations.

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 indicates continued 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 EU 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 EU do not follow price structures of the United States and generally prices tend to be significantly lower.

U.S. Physician Payment Transparency ("Sunshine Act") and Open Payments

The Physician Payments Sunshine Act, enacted as part of the Affordable Care Act, and its implementing regulations require certain pharmaceutical and biological product manufacturers to collect and report annually to the Centers for Medicare & Medicaid Services ("CMS") information regarding payments and other transfers of value provided to U.S. physicians, certain other healthcare providers, and teaching hospitals, as well as ownership and investment interests held by such individuals. CMS makes this information publicly available through the Open Payments program.

Although we are not currently subject to the Sunshine Act's reporting requirements with respect to commercial activities, we expect that, upon obtaining FDA approval of our lead asset, tividenofusp alfa, and commencing commercialization in the United States, we will become subject to these requirements. As we prepare for potential commercialization, we are continuing to develop and implement policies, procedures, systems, and internal controls designed to identify, track, review, and report applicable payments and other transfers of value accurately and in a timely manner.

Compliance with the Sunshine Act and Open Payments program will require ongoing investment in compliance infrastructure and may result in increased operational complexity and administrative burden. Information disclosed through Open Payments is publicly available and may be subject to review, dispute, and scrutiny by healthcare providers, regulators, payors, the media, and the public. Such disclosure may result in reputational risk, misinterpretation of reported data, or increased scrutiny of our interactions with healthcare providers.

The regulatory requirements governing Open Payments are complex and continue to evolve, including through changes in interpretation, expansion of covered recipients, and modifications to reporting thresholds and categories. Failure to comply with applicable Sunshine Act reporting and recordkeeping requirements, whether due to errors in data collection, interpretation, or reporting, or the actions of third parties acting on our behalf, could subject us to civil monetary penalties, enforcement actions, and reputational harm, which could adversely affect our business, financial condition and results of operations.

Financial Information about Segments

We manage our operations as a single reportable segment for the purposes of assessing performance and making operating decisions. See "Note 14 - Segment information" in the notes to the consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Employees and Human Capital Resources

As of December 31, 2025, we had approximately 503 full-time employees. A large majority of our employees work out of our headquarters location in South San Francisco, CA, with the remainder working remotely or out of our locations in Salt Lake City, Utah and Zurich, Switzerland.

Our human capital strategy is to inspire talented individuals to contribute to our mission through a combination of financial incentives, opportunities for professional growth, and a supportive, values-driven culture. We offer competitive compensation packages comprised of cash-based salaries and bonus opportunities as well as long-term equity incentive grants. We support our employees and their dependents with a comprehensive benefits package, which includes a 401(k) match and the opportunity to participate in an Employee Stock Purchase Plan. We foster professional growth through formal and informal learning opportunities, and encourage frequent feedback through our continuous engagement management approach. Our culture is rooted in our core Denali values of trust, growth, grit, and unity, and we collaboratively strive towards our company goal of delivering effective medicines to transform the lives of people living with neurodegenerative, lysosomal, and other serious diseases.

Key areas of focus for Denali include:

Health and Safety. Our health and safety programs are designed around global standards with specifications addressing regulations, specific hazards, and the unique working environment of our operations. We mandate employee health and safety training and ergonomic assessments, and require specialized training for all lab-based employees. We conduct regular internal safety audits to ensure that proper safety policies and program procedures are in place. In addition, we engage both internal and third-party compliance assessments and audit selected operations for adherence to health and safety standards. Denali's safety programs have been highly effective: since we commenced operations in 2015, we have had zero reportable regulatory safety incidents.

Unity and Collaboration. Denali embraces differences and acknowledges the value that multiple perspectives brings to problem-solving. Employee-led teams spearhead action-oriented programs, such as social responsibility through volunteerism and investment in STEM-focused outreach. To foster an inclusive workplace, we enable multiple avenues for employees to raise concerns, including an anonymous hotline and direct access to our human resources department.

Training and Development. We believe training and development are an important part of creating a safe, productive, fair, and equal environment. We encourage continuous feedback, improvement, and growth for our employees. We provide technical, leadership and compliance training to all employees in several formats, including through live seminars, online trainings and professional organizations. Managers are given training to hone their supervisory skills and better support their employees' development; they are, in turn, accountable for continuously engaging with employees and providing ongoing feedback and support.

Flexible Work Options. Denali values workplace flexibility and hybrid ways of working, and has a policy which we believe balances more workplace flexibility with time together to collaborate and connect in person. We use tools and technology designed to help us optimize productivity and collaboration.

Corporate Information

We were incorporated in Delaware in 2013. Our principal executive offices are located at 161 Oyster Point Blvd., South San Francisco, California 94080. Our telephone number is (650) 866-8547. Our website address is www.denalitherapeutics.com. We also use our website as a channel of distribution of important company information, including news or announcements regarding our financial performance, investor events and press releases. We intend to use our website as a means of disclosing material non-public information and for complying with our disclosure obligations under Regulation FD.

We file electronically with the Securities and Exchange Commission ("SEC") our annual reports on Form 10-K, quarterly reports on Form 10-Q, and current reports on Form 8-K pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended ("Exchange Act"). We make available on our website at www.denalitherapeutics.com, free of charge, copies of these reports, including amendments to such reports, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. The SEC maintains a website that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of that website is www.sec.gov. The information in or accessible through the SEC and our website or social media sites does not constitute part of this Annual Report on Form 10-K or any other report or document we file with the SEC, and any references to our website and social media sites are intended to be inactive textual references only.

We use Denali®, the Denali Therapeutics logo, ATV, ETV, OTV, PTV, TV, TransportVehicle™, and other marks as trademarks in the United States and other countries. This Annual Report on Form 10-K 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 Annual Report on Form 10-K, 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.

ITEM 1A. 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 Annual Report on Form 10-K, including our financial statements and the related notes and the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations." 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 and the market price of our common stock.

Risk Factor Summary

This summary of risks provides an overview of the principal risks we are exposed to. These risks are more fully described below.

Risks Related to Our Business, Financial Condition and Capital Requirements

- We are in the clinical stages of drug development and have a 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 have incurred significant net losses since our inception and anticipate that we will continue to incur net losses for the foreseeable future.
- Drug development is a highly uncertain undertaking. We have never generated any revenue from product sales, and may never do so.
- 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.

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

- We are heavily dependent on the successful development of our TV technology and the programs currently in our pipeline, which are in the preclinical and clinical development stages.
- 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 a substantial portion of our efforts on the treatment of neurodegenerative and lysosomal storage diseases, fields that have 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 may encounter difficulties enrolling and/or retaining patients in our clinical trials, and our clinical development activities could thereby be delayed or otherwise adversely affected.
- Our clinical trials may reveal significant adverse events, toxicities, or other side effects and may fail to demonstrate substantial evidence of the safety and efficacy or potency of our product candidates, which would prevent, delay or limit the scope of regulatory approval and commercialization.
- We face significant competition and our operating results may suffer if we fail to compete effectively.
- If we are unable to establish sales and marketing capabilities or enter into agreements with third parties, we may not be successful in commercializing product candidates if and when they are approved.
- If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

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.
- We currently conduct clinical trials outside the United States, and the FDA, EMA and applicable foreign regulatory authorities may not accept data from such trials.
- To the extent we seek orphan drug designation for any of our product candidates, we may be unable to obtain such designations or to maintain the benefits associated with orphan drug status.
- Healthcare legislative measures aimed at reducing healthcare costs may have a material adverse effect on our business and results of operations.
- Our business is subject to complex and evolving U.S. and foreign laws and regulations, information security policies, and contractual obligations relating to privacy, data protection, and data security.

Risks Related to Our Reliance on Third Parties

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

- Our reliance on third parties for the manufacture of the significant majority of the materials for our research programs, preclinical studies and clinical trials. This reliance on third parties may increase the risk that we will not have sufficient quantities of such materials or product candidates.
- We depend on third-party suppliers for key raw materials used in our manufacturing, and the loss of these suppliers or their inability to supply us with adequate raw materials could harm our business.

Risks Related to Our Intellectual Property

- If we are unable to obtain and maintain patent protection for our product candidates or our TV technology, our competitors could develop and commercialize products or technology similar or identical to ours, and adversely affect our ability to commercialize any product candidates.
- 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.
- Our rights to develop and commercialize our TV technology and product candidates are subject, in part, to the terms of licenses granted to us by others or licenses granted by us to others.
- We may not be able to protect our intellectual property and proprietary rights throughout the world.
- Our patent protection could be reduced or eliminated if we are unable to comply with requirements imposed by government patent agencies.
- Changes in U.S. patent law could impair our ability to protect our products.
- Issued patents covering our TV technology, product candidates and other technologies could be found invalid or unenforceable if challenged.
- Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.
- We may be subject to claims challenging the inventorship of our intellectual property.
- If we are unable to protect the confidentiality of our trade secrets, our business would be harmed.
- We may not be successful in obtaining, through acquisitions, in-licenses, or otherwise, necessary rights to our TV platform, product candidates or other technologies.
- 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.
- Third-party intellectual property claims against us, our licensors or our collaborators may prevent or delay the development of our TV platform, product candidates and other technologies.

Risks Related to Our Operations

- If we are not successful in attracting, motivating and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.
- We have engaged in and may in the future engage in acquisitions or strategic partnerships, which may increase our capital requirements, dilute our stockholders, or cause us to incur debt or assume contingent liabilities.
- Our internal computer systems, or those used by our collaborators, CROs or other contractors, may fail or suffer security breaches or incidents that could compromise the confidentiality, integrity, and availability of such systems and data, expose us to liability, and affect our reputation.
- Our business is subject to risks associated with international operations.

Risks Related to Ownership of Our Common Stock

- The market price of our common stock has been and may continue to be volatile, which could result in substantial losses for investors.
- If securities analysts publish negative evaluations of our stock, or if they do not publish research or reports about our business; the price of our stock and trading volume could decline.
- 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.
- Delaware law and provisions in our charter documents might prevent a change in control of our company or changes in our management, depressing the trading price of our common stock.
- Our amended and restated certificate of incorporation provides exclusive forums for disputes between us and our stockholders, limiting their ability to obtain a favorable judicial forum.

Risks Related to Our Business, Financial Condition and Capital Requirements

We are in the clinical stages of drug development, have no approved products, and may never become profitable.

We are a clinical-stage biopharmaceutical company with a limited operating history, focused on developing therapeutics for neurodegenerative diseases, including Alzheimer's disease and Parkinson's disease, and lysosomal storage diseases, including Hunter syndrome and Sanfilippo syndrome. We commenced operations in May 2015, have no products approved for commercial sale and have not generated any revenue from product sales. Drug development is a highly uncertain undertaking and involves a substantial degree of risk. Our clinical-stage programs are in various phases ranging from Phase 1 through Phase 3. To date, we have not completed a pivotal clinical trial, obtained marketing approval for any product candidates, or manufactured a commercial scale product. Our limited operating history makes any assessment of our future success and viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by biopharmaceutical companies, 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.

To obtain revenue from the sales of our product candidates that are significant or large enough to achieve profitability, we must succeed, either alone or with third parties, in developing, obtaining regulatory approval for, manufacturing, and marketing therapies with significant commercial success.

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

- successfully prioritizing and 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 TV platform, 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;
- receiving milestone and other payments under our current and any future collaboration arrangements;

- maintaining, protecting, expanding, and enforcing our portfolio of intellectual property rights;
- attracting, hiring, and retaining qualified personnel;
- general economic conditions; and
- addressing any delays in our clinical trials or other impacts from a global emergency.

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 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 current 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.

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

We have incurred significant net losses since our inception. Our net losses were $512.5 million, $422.8 million, and $145.2 million for the years ended December 31, 2025, 2024, and 2023, respectively. As of December 31, 2025, we had an accumulated deficit of $2.05 billion.

We have invested significant financial resources in research and development activities, including for our preclinical and clinical product candidates and our TV platform. The amount of our future net losses will depend, in part, on the level of our future expenditures and 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. 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.

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. We currently fund our operations primarily with the proceeds from our follow-on offerings completed in October 2022 and December 2025, payments received from our collaboration agreements with Biogen, Sanofi, Takeda, and a strategic private offering transaction completed in February 2024. Developing our product candidates is expensive, and we expect to continue to spend substantial amounts as we fund our early-stage research projects and advance our programs through preclinical and clinical development.

As of December 31, 2025, we had $966.2 million in cash, cash equivalents and marketable securities. We believe that our existing cash, cash equivalents and marketable securities will be sufficient to fund our projected operations through at least the next twelve 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 proven inaccurate, and we could use our available capital resources sooner than we currently expect. Changing circumstances, some of which may be beyond our control, such as geopolitical uncertainty, rising inflation or interest rates, the imposition of tariffs, risks associated with transactions denominated in foreign currency, or a perceived or actual economic downturn, may cause us to increase our spending significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned. We may also need to raise additional funds sooner than we anticipate if we choose to expand more rapidly than we presently anticipate.

We have no committed source of additional capital, and we cannot be certain that additional funding will be available when we need it, on terms acceptable to us or at all. 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, which could materially affect our business, financial condition, results of operations, and growth prospects and cause the price of our common stock to decline.

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.

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, divest, 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.

One of our strategies is to identify and pursue clinical development of additional product candidates. We currently have several programs in the research, discovery, and preclinical stages of development. Identifying, developing, obtaining regulatory approval for, and commercializing additional product candidates for the treatment of neurodegenerative and lysosomal storage diseases will require substantial additional funding and is prone to the risks of failure inherent in drug development. We cannot provide you with 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 make incorrect determinations regarding the viability, indication size, or market potential of any of our programs or product candidates or misread trends in the biopharmaceutical industry, our business, financial condition, results of operations, and growth prospects could be materially adversely affected.

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

We are heavily dependent on the successful development of our TV platform and the programs currently in our pipeline. 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.

Investment in biopharmaceutical product development involves significant risk that any product candidate will fail to demonstrate adequate efficacy or potency, or an acceptable safety profile, gain regulatory approval, or become commercially viable. To date, we have invested substantially all of our efforts and financial resources to identify, acquire intellectual property for, and develop our TV platform and our programs, including conducting preclinical studies and clinical trials, 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 any of the reasons set forth in these Risk Factors. In that event, we may be forced to abandon our development efforts for a program or programs, which could have a material adverse effect on our business.

We have previously discontinued the development of certain molecules prior to completion of preclinical development because we did not believe they met our criteria for potential clinical success. Further, we cannot be certain that any of our product candidates will be successful in clinical trials. For instance, in January 2025, we announced that the Phase 2/3 HEALEY ALS Platform Trial evaluating DNL343 for ALS did not meet primary and key secondary endpoints. We may in the future advance product candidates into clinical trials and terminate such trials prior to their completion.

Our product candidates are based on novel technology in fields that have seen limited success in drug development, 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 and lysosomal storage diseases. Collectively, efforts by biopharmaceutical companies in the fields of neurodegenerative and lysosomal storage diseases have seen limited success in drug development. There are few effective therapeutic options available for patients with neurodegenerative diseases, such as Alzheimer's disease and Parkinson's disease, and lysosomal storage diseases, such as Hunter syndrome and Sanfilippo syndrome. Our future success is highly dependent on the successful development of our TV platform and our product candidates for treating neurodegenerative and lysosomal storage diseases. Developing and, if approved, commercializing our product candidates for treatment of neurodegenerative and lysosomal storage 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 and lysosomal storage diseases aims to identify and select targets with a genetic link to neurodegenerative and lysosomal storage 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 may not be able to discover, develop, and utilize biomarkers to demonstrate target engagement, pathway engagement, and the impact on disease progression of our molecules. 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 difficulties enrolling patients, 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 IND, or a clinical trial application ("CTA"), will result in the FDA 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 trial design;
- delays involving our clinical trial sites, including delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites, delays in identifying, recruiting and training suitable clinical investigators, and delays in obtaining required 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 trial sites; developments in trials conducted by competitors for related technology that raise 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;
- 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 ("cGCPs") requirements, 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;
- delays due to changes in the staffing, priorities, or leadership of the FDA or other regulatory authorities, or changes to regulatory approval policies or regulations;
- 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 us or our collaborators 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 CDMO or by us, and delays or failure by our CDMOs or us to make any necessary changes to such manufacturing process;

- 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; and

- delays associated with a pandemic or other public health emergency.

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 or our collaborators may be required to or 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 or our collaborators, by the data safety monitoring board for such trial, or by any 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, developments in trials conducted by us or our competitors for related technology that raise regulatory concerns about risk to patients of the technology broadly, or lack of adequate funding to continue the clinical trial.

Our product candidates have been subject to clinical holds in the past and we cannot assure you that others will not be subject to new, partial, or full clinical holds in the future. For example, in August 2023, following imposition of a clinical hold by the FDA, we announced that we and Takeda would discontinue clinical development of TAK-920/DNL919 in Alzheimer's disease. Additionally, in December 2025, we announced that DNL952 was placed on clinical hold. Although protocol amendments were implemented for DNL952 and the program resumed, there could be safety findings or concerns that result in additional pauses, protocol modifications, or permanent discontinuation of development. Any clinical holds by the FDA, if not timely lifted, could impact our development plans.

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 and/or retaining 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 and retention in our clinical trials for a variety of reasons, including:

- the size and nature of the patient population, the proximity of patients to trial sites, and the size of the study population required for analysis of the trial's primary endpoints;
- 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 design of the trial;
- 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 inability to enroll and retain a sufficient number of patients for our clinical trials may increase development costs for our product candidates, delay our ability to obtain clinical data and/or obtain marketing approval, or may require us to abandon one or more clinical trials altogether.

Our clinical trials may reveal significant adverse events, toxicities, or other side effects and may fail to demonstrate substantial evidence of the safety and efficacy or potency 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. It is impossible to predict when or if our product candidates will prove effective or safe in humans, or if our product candidates will receive marketing authorization. Clinical testing is expensive and can take many years to complete, and the outcome is inherently uncertain. Open-label extension studies may also extend the timing and increase the cost of clinical development substantially. Failure can occur at any time during the clinical trial process.

In addition, 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. In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product or product candidate due to numerous factors, including changes in clinical trial procedures set forth in protocols, differences in the size and type of the patient populations, adherence to the dosing regimen and other clinical trial protocols and the rate of discontinuation among clinical trial participants. If we fail to produce positive results in our planned clinical trials of any of our product candidates, the development timeline and marketing authorization and commercialization prospects for our product candidates, and, correspondingly, our business and financial prospects, would be materially and adversely affected.

We cannot be certain that our current clinical trials or any 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.

Even if such clinical trials are successfully completed, we cannot guarantee that the FDA will approve the product candidates for the proposed indications, and more information or trials could be required before we submit our product candidates for approval. For instance, although the FDA has accepted our biologics license application ("BLA") for accelerated approval of DNL310, our PDUFA target date was extended to enable the submission of updated clinical pharmacology information in response to an information request from the FDA. To the extent that the FDA or foreign regulatory authorities are not satisfied with the support we have provided, we may be required to expend significant resources 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, such as requiring us to narrow our indications to a smaller subset, may also limit its commercial potential.

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, our collaborators, 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. It is possible that as we test our product candidates in larger, longer and more extensive clinical trials, including with different dosing regimens, or as the use of our product candidates becomes more widespread following any marketing authorization, illnesses, injuries, discomforts and other adverse events that were observed or went undetected in earlier trials will be reported. If such events become known later in development or upon approval, if any, or if such events are incorrectly believed to have been caused by our products, then our business, financial condition, results of operations and prospects may be harmed. For any products approved in the future, these events could hinder or prevent market acceptance of any approved products or reduce the duration of time that physicians expect to use our product in particular patients.

Our most advanced product candidates, DNL310, DNL126, BIIB122/DNL151, eclitasertib (SAR443122/DNL758), TAK-594/DNL593, DNL628, and DNL952, are currently our only clinical stage product candidates. Adverse events and other side effects may result from higher dosing, repeated dosing, and/or longer-term exposure to our product candidates and could lead to delays and/or termination of the development of these product candidates. For example, in December 2025, we announced the imposition of a clinical hold on the DNL952 (ETV:GAA) IND application related to hypersensitivity reactions in preclinical studies. This hold was lifted in January 2026 following amendments to the study protocol's starting dosage, inclusion criteria, safety monitoring commitments, and stopping rules.

Drug-related side effects could affect patient recruitment, the ability of enrolled patients to complete the trial, and/or result in potential product liability claims. Additionally, if one or more of our product candidates receives marketing approval, and we or others, including our collaborators, later identify undesirable side effects or adverse events caused by such products, regulatory authorities could withdraw approval, and/or require a product recall, additional label warnings, changes to the way our product is administered, or additional clinical trials or post-approval studies. We could also be sued and held liable for harm caused to patients. Any of these events could harm our reputation, business, financial condition, and growth prospects.

Interim, topline, and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available, and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary, interim, or topline data from our nonclinical studies and clinical trials, which are based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations, and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, preliminary, interim, or topline data should be viewed with caution until the final data are available. In addition, we may report interim analyses of only certain endpoints rather than all endpoints. Adverse changes between interim data and final data could significantly harm our business and prospects. Further, additional disclosure of interim data by us or by our competitors in the future could result in volatility in the price of our common stock.

Further, others, including our collaborators or regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions, or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approval or commercialization of the particular product candidate and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is typically selected from a more extensive amount of available information. You or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the preliminary or topline data that we report differ from late, final, or actual results, or if others, including our collaborators or regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize our product candidates may be harmed.

We face significant competition in an environment of rapid technological and scientific change, and our operating results may suffer if we fail to compete effectively.

The development and commercialization of new drug products is highly competitive. Moreover, the neurodegenerative and lysosomal storage fields are characterized by strong and increasing competition. Our potential competitors include pharmaceutical companies, biotechnology companies, academic institutions, government agencies, and other public and private research organizations that conduct research. Our competitors, either alone or with collaborative partners, may succeed in developing, acquiring, or licensing on an exclusive basis drug or biologic products that are more effective, safer, more easily commercialized, or less costly than our product candidates or may develop proprietary technologies or secure patent protection that we may need for the development of our technologies and products.

A number of large pharmaceutical and biotechnology companies are developing products for the treatment of the neurodegenerative and lysosomal storage disease indications for which we have research programs, including Alzheimer’s disease, Parkinson’s disease, Hunter syndrome, Sanfilippo syndrome, Pompe disease, and FTD-GRN. Companies that we are aware are developing therapeutics in the neurodegenerative and lysosomal storage disease areas include companies with significant financial resources, established presence in the market, and expertise in research, development, manufacturing, and commercialization. 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.

Mergers and acquisitions 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. Our 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 or lysosomal storage disease indications, which could give such products significant regulatory and market timing advantages over any of our product candidates. Our competitors also may obtain regulatory approval for their products more rapidly than we do, and may obtain orphan product exclusivity 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.

We may fail to successfully manufacture our product candidates, operate our own manufacturing facility, or obtain regulatory approval to utilize or commercialize from our manufacturing facility, which could adversely affect our clinical trials and the commercial viability of our product candidates.

The processes involved in manufacturing our drug and biological product candidates, particularly those that utilize our TV platform, 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 and capabilities. Under a lease for approximately 60,000 rentable square feet of laboratory, office, and warehouse premises, we have completed the build-out of our Utah site and have begun to manufacture materials for toxicology studies and drug substance for human clinical studies. There can be no assurance that our current and future efforts to scale our internal manufacturing capabilities will succeed.

In addition, the manufacturing process, including any material modifications in the manufacturing process for any products that we may develop, is subject to regulatory authority approval processes and continuous oversight, and we will need to contract with manufacturers who can meet all applicable regulatory authority requirements, including complying with current good manufacturing practices ("cGMPs"), on an ongoing basis. If we or our third-party manufacturers are unable to reliably produce products to specifications acceptable to 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 CDMOs will be able to manufacture the approved product to specifications acceptable to the 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 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 have initiated the build-out of our sales and marketing infrastructure and have begun to enter into arrangements with third parties for the commercialization of DNL310. 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.

Furthermore, if we receive commercial approval in the United States and intend to seek approval in other countries, we may rely on third-party distributors and other commercial partners outside the United States, such as local agents, wholesalers, importers and logistics providers, to market, distribute and support any potential commercial products, and our ability to enter and compete in non-U.S. markets may depend on the performance of these third parties. These partners are subject to complex and evolving foreign laws and regulatory regimes and may be required to obtain, maintain and renew various licenses, approvals and registrations and to comply with local requirements relating to importation, storage and handling, serialization and traceability, pharmacovigilance, recordkeeping and reporting, and promotional and marketing activities. If any such third party fails to obtain or maintain required authorizations, violates applicable laws or industry codes, engages in misconduct or misrepresentations, or otherwise performs poorly (including through inadequate forecasting, inventory management, product storage or handling, documentation, complaint management or recall support), we could experience delayed market entry, interruption of supply, product seizures, import holds or other enforcement actions, and we may incur significant costs to investigate, remediate or transition to alternative partners. In addition, we may have limited ability to monitor and control our foreign distributors' activities, and we could be subject to regulatory scrutiny, civil or criminal penalties, reputational harm, reduced sales, or termination of our commercial agreements as a result of their acts or omissions.

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 or potency 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, 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 ("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 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 small molecule product candidates 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.

If any of our small molecule product candidates obtain regulatory approval, competitors may file abbreviated new drug applications under the Drug Price Competition and Patent Term Restoration Act of 1984 (the "Hatch-Waxman Act") seeking approval of generic versions, or submit 505(b)(2) new drug applications referencing our approved products. Although the Hatch-Waxman Act provides certain periods of regulatory exclusivity and we may obtain patent protection eligible for listing in the FDA's Orange Book, we cannot predict which patents, if any, will be eligible for listing, whether generic applicants will challenge those patents through Paragraph IV certifications, or the outcome of any resulting litigation. If any of our Orange Book-listed patents are successfully challenged, the affected product could immediately face generic competition and its sales would likely decline rapidly and materially, which could require us to write off a portion or all of the intangible assets associated with the affected product and could materially and adversely affect our results of operations and cash flows. 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, including DNL310, are regulated by the FDA as biologic products. We are seeking approval for DNL310 pursuant to a BLA pathway and may do so for other large molecule product candidates in our pipeline. The Biologics Price Competition and Innovation Act of 2009 (the "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, if competitors are able to obtain marketing approval for biosimilars referencing our large molecule product candidates, 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 any of our small molecule product candidates 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 (the "Hatch-Waxman Act"), a pharmaceutical manufacturer may file an abbreviated new drug application ("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 ("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.

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. See "Risks Related to Our Intellectual Property."

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 costs to defend litigation and a diversion of management's time and resources. Regardless of the merits or eventual outcome, liability claims may result in a decreased or interrupted demand for our products, injury to our reputation, withdrawal of clinical trial participants and inability to continue clinical trials, and initiation of investigation by regulators. Any successful liability claims could result in 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. In June 2024, the U.S. Supreme Court overruled the *Chevron* doctrine, which gives deference to regulatory agencies' statutory interpretations in litigation against federal government agencies, such as the FDA, where the law is ambiguous. This landmark Supreme Court decision may invite more companies and other stakeholders to bring lawsuits against the FDA to challenge longstanding decisions and policies of the FDA, including the FDA's statutory interpretations of market exclusivities and the "substantial evidence" requirements for drug approvals, which could undermine the FDA's authority, lead to uncertainties in the industry, and disrupt the FDA's normal operations, any of which could delay the FDA's review of our regulatory submissions.

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, regulatory authorities may fail to approve companion diagnostics that we contemplate using with our therapeutic product candidates. We have not 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. Even if we do receive approval from the FDA for our pending BLA or for a future application, we may not receive, or be deemed ineligible to receive, a Rare Pediatric Disease Priority Review Voucher. Changes to the leadership and staffing at federal agencies may also impact our clinical development and timelines.

Applications for our product candidates could fail to receive regulatory approval in an initial or subsequent indication for many reasons, including but not limited to the following:

- regulatory authorities may disagree with the design, implementation, or results of our clinical trials;
- 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 or potency and safety in the full population for which we seek approval;
- 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 regulatory authorities that a product candidate's risk-benefit ratio for its proposed indication is acceptable;
- regulatory authorities may fail to approve our manufacturing processes, test procedures and specifications, or facilities or those of our third-party manufacturers; and
- the approval policies or regulations of the 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.

We currently and 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 currently conduct clinical trials outside the United States and may continue to do so in the future. The acceptance of 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, and 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, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities.

While healthcare professionals are free to use and prescribe drug products for off-label uses, the FDA strictly regulates manufacturers' promotional claims of drug products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the FDA-approved labeling. A company that is found to have improperly promoted off-label uses may be subject to large civil and criminal fines, penalties, and enforcement actions. If we cannot successfully manage the promotion of our approved product candidates, we could become subject to significant liability, which could materially adversely affect our business and financial condition.

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. 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. 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 non-biologic products or safety, purity, and potency for our biologic products, in general or in specific patient subsets.

We are seeking accelerated approval of DNL310. If successful, the FDA may require us to conduct a confirmatory study to verify the predicted clinical benefit and safety profile. The Food and Drug Omnibus Reform Act reformed the accelerated approval pathway, such as requiring the FDA to specify conditions for post-approval study requirements and setting forth procedures for the FDA to withdraw a product on an expedited basis for non-compliance with post-approval requirements. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of our 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, impose penalties, suspend regulatory approvals, or require a product recall. Any of these actions by a regulatory agency could require us to expend significant time and resources, generate negative publicity, and adversely affect the value of our company.

To the extent we seek orphan drug designation for any of our product candidates, 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 where 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. Once granted, orphan drug designation entitles a party to financial incentives and certain exclusivity protections. In February 2019, the FDA granted orphan drug designation for our DNL310 program in Hunter syndrome. However, the FDA can still approve other drugs that have a different active ingredient for use in treating the same indication or disease, and can waive orphan exclusivity if we are unable to manufacture sufficient supply of our product. We plan to seek orphan drug designations for some other product candidates, but we may be unable to obtain such designations.

Further, in response to *Catalyst Pharms., Inc. v. Becerra*, 14 F.4th 1299 (11th Cir. 2021), the FDA clarified in a January 2023 notice that the FDA intends to continue to apply its longstanding interpretation of the regulations to matters outside of the scope of the Catalyst order – that is, the agency will continue tying the scope of orphan-drug exclusivity to the uses or indications for which a drug is approved, which permits other sponsors to obtain approval of a drug for new uses or indications within the same orphan designated disease or condition that have not yet been approved. The Consolidated Appropriations Act of 2026, signed into law in February 2026, codified this longstanding FDA interpretation of the Orphan Drug Act, allowing the FDA to approve multiple versions of the same orphan drug for different subindications and subpopulations.

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

We may face difficulties from changes to current regulations and future legislation. Current and future legislation may increase the difficulty and cost for us to commercialize our drugs, if approved, and affect the prices we may obtain, including changes in coverage and reimbursement policies in certain market segments for our product candidates, which could make it difficult for us to sell our product candidates, if approved, profitably. 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. These include the enactment of the Affordable Care Act of 2010 (“ACA”), the American Rescue Plan Act of 2021, which will eliminate a statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs, and the July 2021 executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at increasing competition for prescription drugs. In August 2022, Congress passed the Inflation Reduction Act of 2022 ("IRA"), which includes prescription drug provisions that have significant implications for the pharmaceutical industry and Medicare beneficiaries, including allowing the federal government to negotiate a maximum fair price for certain high-priced single source Medicare drugs, imposing penalties and excise tax for manufacturers that fail to comply with the drug price negotiation requirements, requiring inflation rebates for all Medicare Part B and Part D drugs, with limited exceptions, if their drug prices increase faster than inflation, and redesigning Medicare Part D to reduce out-of-pocket prescription drug costs for beneficiaries, among other changes. Various industry stakeholders have initiated lawsuits against the federal government asserting that the price negotiation provisions of the IRA are unconstitutional. Further, the current administration has issued executive orders focused on decreasing prescription drug prices, including directing the Secretary of HHS to establish a mechanism through which American patients can buy drugs directly from manufacturers who sell at a most-favored-nation price and directing the U.S. Trade Representative and Secretary of Commerce to take action to ensure foreign countries are not engaged in practices that purposefully and unfairly undercut market prices and drive price hikes in the United States. In November 2025, CMS announced a voluntary initiative called the GENEROUS Model (GENErating cost Reductions fOr U.S. Medicaid Model) to introduce the option of most-favored-nation pricing to the Medicaid program, whereby a drug manufacturer may voluntarily offer supplemental rebates to participating state Medicaid programs for a manufacturer’s covered outpatient drugs. Government agreements with pharmaceutical companies and other government measures that use most-favored-nation pricing targets for prescription drugs, including the use of international pricing reference to set drug prices in the United States, or that increase generic and biosimilar drug entry sooner than expected can have a material adverse effect on our industry, ability to set adequate pricing for new drugs to recover research and development costs, ability to attract potential investors and potential buyers in the future. The impact of these legislative, executive, and administrative actions and any future healthcare measures and agency rules implemented by the government on us and the pharmaceutical industry as a whole is unclear. At the state level, a number of states are considering or have recently enacted state drug price transparency and reporting laws that could substantially increase our compliance burdens and expose us to greater liability under such state laws once we begin commercialization after obtaining regulatory approval for any of our products.

Since its enactment, there have been executive, judicial and congressional challenges to certain aspects of the ACA and IRA. It is unclear how future litigation or healthcare measures will impact our business, financial condition, and results of operations. Complying with any new legislation or changes in healthcare regulation could be time-intensive and expensive, resulting in material adverse effect on our business. We expect that the ACA and IRA, 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. In addition, increased scrutiny by the U.S. Congress of the FDA’s approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

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 any product candidates that are approved, our ability to receive or set a price we believe is fair for our products, our ability to attract investment, our ability to generate revenue or achieve profitability, the level of taxes we are required to pay, and the availability of capital.

If we or our employees, independent contractors, consultants, commercial partners, and vendors fail to comply with healthcare laws or regulatory requirements, we could face substantial penalties and our business, operations, and financial conditions could be adversely affected.

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 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. The laws that may impact our operations include the federal Anti-Kickback Statute, the False Claims Act, the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH"), the federal Physician Payment Sunshine Act, federal consumer protection and unfair competition laws, and analogous state and foreign laws and regulations. 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, the promotion, sales, and marketing of healthcare items and services is subject to extensive laws and regulations 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, marketing and promotion, sales commission, customer incentive, and other business arrangements. 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. Further, 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. 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.

Our business is subject to complex and evolving U.S. and foreign laws and regulations, information security policies, and contractual obligations relating to privacy and data protection and security, including the use, processing, and cross-border transfer of personal information. These laws and regulations are subject to change and uncertain interpretation, and could result in claims, changes to our business practices, or monetary penalties, and otherwise may harm our business.

We receive, generate, store, and otherwise process significant and increasing volumes of sensitive information and business-critical information, including employee and personal data (including protected health information), research and development information, commercial information, and business and financial information. We heavily rely on external security and infrastructure vendors to manage our information technology systems and data centers. We face a number of risks relative to protecting this critical information, including the loss of access, inappropriate use or disclosure, inappropriate modification, and the risk of our being unable to adequately monitor, audit, and modify our controls over our critical information. This risk extends to third-party vendors and subcontractors we use to manage this sensitive data.

A wide variety of provincial, state, national, and international laws and regulations apply to the collection, use, retention, protection, disclosure, transfer, and other processing of data relating to individuals. These laws and regulations are evolving and may result in ever-increasing regulatory and public scrutiny and escalating levels of enforcement and sanctions. For example, the collection and use of personal data in the EU are governed by the EU General Data Protection Regulation ("GDPR"), which became fully effective on May 25, 2018. The GDPR imposes stringent data protection requirements, including, for example, more robust disclosures to individuals and a strengthened individual data rights regime, shortened timelines for data breach notifications, limitations on retention of information, increased requirements pertaining to special categories of data, such as health data, and additional obligations when we contract with third-party processors in connection with the processing of the personal data. The GDPR also imposes strict rules on the transfer of personal data out of the EU to the United States and other countries, and in the context of clinical trials we currently rely on patient informed consent as the legal basis for such transfers. In addition, the GDPR provides that EU member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data. The GDPR provides for penalties for noncompliance of up to the greater of €20 million or four percent of worldwide annual revenues. The GDPR applies extraterritorially, and we may be subject to the GDPR because of our data processing activities that involve the personal data of individuals located in the EU, such as in connection with any EU clinical trials. Additionally, the UK has implemented legislation that substantially implements the GDPR (the "UK GDPR"), with substantial penalties for noncompliance.

Further, various states, such as California, Massachusetts, and Washington have implemented privacy laws and regulations that impose restrictive requirements regulating the use and disclosure of health information and other personal information. Where state laws are more protective than HIPAA, we must comply with the stricter provisions. In addition to fines and penalties imposed upon violators, some of these state laws also afford private rights of action to individuals who believe their personal information has been misused. For example, California has enacted legislation, the California Consumer Privacy Act ("CCPA"), which, among other things, requires covered companies to provide new disclosures to California consumers, and affords such consumers new abilities to opt-out of certain sales of personal information. The CCPA, as amended and expanded by the California Privacy Rights Act ("CPRA"), requires covered companies to provide new disclosures to individuals and consumers in California, and afford such individuals and consumers new data protection rights, including the ability to opt-out of certain sales of personal information. Numerous other states in the United States have proposed or enacted similar legislation. Further, some states have enacted more specific legislation, such as Washington's enactment of the My Health, My Data Act, which includes a private right of action. The U.S. federal government is also contemplating federal privacy legislation. Additionally, the U.S. Department of Justice recently implemented a final rule that places limitations, and in some cases prohibitions, on certain transfers of sensitive personal data to business partners located in China or with other specified links to China (and other designated countries). The GDPR, UK GDPR, CCPA, CPRA, and many other federal, state, and foreign laws and regulations relating to privacy and data protection are still being tested in courts, and they are subject to new and differing interpretations by courts and regulatory officials. Additionally, the interplay of federal and state laws may be subject to varying interpretations by courts and government agencies, creating complex compliance issues for us and data we receive, use and share, potentially exposing us to additional expense, adverse publicity and liability.

It is possible that the GDPR, UK GDPR, CCPA, CPRA, or other laws and regulations relating to privacy and data protection may be interpreted and applied in a manner that is inconsistent from jurisdiction to jurisdiction or inconsistent with our current policies and practices. We cannot guarantee that we or our vendors are in compliance with all such applicable data protection laws and regulations and we cannot be sure how these regulations will be interpreted, enforced or applied to our operations. Furthermore, other jurisdictions outside the EU are similarly introducing or enhancing laws and regulations addressing privacy and data protection and security, which could increase our compliance costs and the risks associated with noncompliance. It is possible that these laws, regulations, or other actual or asserted obligations may be interpreted and applied in a manner that is inconsistent with our practices and our compliance efforts may be unsuccessful. Our ongoing efforts to comply with evolving laws and regulations may be costly and require ongoing modifications to our policies, procedures and systems. In addition, if we are unable to properly protect the privacy and security of protected health information, we could be alleged or found to have breached certain contractual obligations.

Our actual or perceived failure to adequately comply with applicable laws and regulations or other actual or asserted obligations relating to privacy and data protection and security, or to protect personal data and other data we process or maintain, could result in regulatory enforcement actions against us, including fines, imprisonment of company officials and public censure, claims for damages by affected individuals, other lawsuits or reputational damage, all of which could materially affect our business, financial condition, results of operations and growth prospects.

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 growth prospects.

Our business activities may be subject to the Foreign Corrupt Practices Act and similar anti-bribery and anti-corruption laws, as well as U.S. and certain foreign export controls, trade sanctions, and import laws and regulations.

Our business activities may be subject to the Foreign Corrupt Practices Act of 1977, as amended (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 certain 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.

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, business, operating results, financial condition, and international expansion efforts.

In addition, if we enter a commercialization phase, our products may be subject to U.S. and foreign export controls, trade sanctions, and import laws and regulations. Governmental regulation of the import or export of our products, or our failure to obtain any required import or export authorization for our products, when applicable, could harm our international sales and adversely affect our revenue.

Inadequate funding for the FDA, USPTO, SEC, and other government agencies could hinder or result in the suspension of their operations, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, shifting policy priorities, and statutory, regulatory, and policy changes. Average review times at the FDA have fluctuated in recent years as a result. In addition, government funding of the SEC, USPTO, and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other government agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years the U.S. government shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical government employees and stop critical activities. Regulatory agency staffing changes may disrupt normal operations of federal agencies, including the FDA. If a prolonged government shutdown or other disruption occurs, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, or to provide feedback on our clinical development plans, which could have a material adverse effect on our business. Further, future government shutdowns or other disruptions to normal operations could impact our ability to access the public markets and obtain the funding necessary to properly capitalize and continue our operations.

Risks Related to Our Reliance on Third Parties

We depend on collaborations with third parties for the research, development, and commercialization of certain product candidates. 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 collaborations with F-star, Takeda, Sanofi, Biogen, and others to further our development of product candidates and to enhance our research efforts directed to better understanding neurodegenerative and lysosomal storage 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;
- collaborators may control certain interactions with regulatory authorities, which may impact on our ability to obtain and maintain regulatory approval of our products candidates;
- 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 terminate or 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 may restrict us from researching, developing, or commercializing certain products or technologies without their involvement;
- 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 agreements with our collaborators, including if we undergo a change of control;
- collaborators may grant sublicenses to our technology or product candidates or undergo a change of control and the sublicensees or 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;
- if our collaborators do not satisfy their obligations under our agreements with them, or if they terminate our collaborations with them, we may not be able to develop or commercialize product candidates as planned; and

- collaborations may require us to share in development and commercialization costs pursuant to budgets that we do not fully control and our failure to share in such costs could have a detrimental impact on the collaboration or our ability to share in revenue generated under the collaboration.

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. The failure to develop and commercialize a product candidate pursuant to our agreements with our current or future collaborators could prevent us from receiving future payments under such agreements, which could negatively impact our revenues. 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 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 time frames. Failure to do so can result in fines, adverse publicity, and civil and criminal sanctions.

Our third-party service providers are not our employees, and we are therefore unable to directly monitor whether or not they devote sufficient time and resources to our clinical and nonclinical programs. These third-party service providers may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. 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, including with the shipment of any drug supplies, 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.

Our reliance on third parties for the manufacture of the majority of the materials for our research programs, preclinical studies, and clinical trials 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.

Although we have begun to manufacture biologic therapeutics, in our Utah site, we currently rely on third-party manufacturers for the manufacture of many of our materials for preclinical studies and clinical trials, and expect to continue to do so for the foreseeable future for a portion of our materials for preclinical studies, clinical trials, and commercial supply.

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, termination, or non-renewal of the agreement by the third party, which may be costly or inconvenient, and the inability of the third party to produce the required volume in a timely manner. We may also be exposed to the risks of relying on the third party for regulatory compliance, quality assurance, safety, and pharmacovigilance and related reporting.

Third-party manufacturers may not be able to comply with U.S. export control regulations, 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 a need to replace current third-party manufacturers including the possibility of supply delays, 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 growth 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. 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 third parties for the manufacture of our product candidates 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. Unexpected changes in tariffs, trade barriers, price and exchange controls, and other regulatory requirements, including recently imposed tariffs which may impact certain of our key raw materials that we import, could impact our cost of goods for our product candidates. As a small company, our negotiation leverage is limited and we are likely to get lower priority than our larger competitors. 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.

Further, we have in the past and may in the future experience delayed shipments of raw materials due to interruptions relating to the aforementioned events. We do not currently have arrangements in place for redundant supply for certain components of our product candidates. 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 TV platform, 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 TV platform 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 TV platform, programs and product candidates, as well as other technologies that are important to our business. Our portfolio includes technology and product candidates that are in the early stages of development, and the corresponding intellectual property is also at an early stage. In addition, we cannot be certain that any patents we own or in-license in the United States adequately cover the Fc domain portion of our TV platform that binds to transferrin receptor, or adequately cover the antibodies, enzymes or proteins being developed in our TV-enabled programs. We have filed or intend to file patent applications on these aspects of our technology and 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 twelve 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 TV platform, 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 TV platform, 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 TV platform, programs and product candidates could have a material adverse effect on our business, financial condition, results of operations and growth 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, including delays as a result of a global pandemic impacting our or our licensors' operations. 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 nondisclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, 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 TV platform, 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 TV platform, 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 growth 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 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 TV platform, 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 TV platform, 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. If we or our collaborators are unsuccessful in any such proceeding or other priority or inventorship dispute, we may be required to obtain and maintain licenses from third parties, including parties involved in any such interference proceedings or other priority or inventorship disputes. Such licenses may not be available on commercially reasonable terms or at all, or may be non-exclusive. If we are unable to obtain and maintain such licenses, we may need to cease the development, manufacture, and commercialization of one or more of the product candidates we may develop. The loss of exclusivity or the narrowing of our owned and licensed patent claims could limit our ability to stop others from using or commercializing similar or identical technology and products.

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 TV platform 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. 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 growth prospects.

Our rights to develop and commercialize our TV platform and product candidates are subject, in part, to the terms and conditions of licenses granted to us by others or licenses granted by us to 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 TV platform and product candidates. For example, in June 2016, we entered into a 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 BIIB122/DNL151 product candidate.

Our agreements with F-star and other license agreements may not provide exclusive rights to use certain 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 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. Also, under our agreements with Takeda, Sanofi and Biogen, they control prosecution, and in specified circumstances, enforcement of certain of the patents and patent applications licensed to them. We cannot be certain that our in-licensed or out-licensed patents and patent applications that are controlled by our licensors or licensees will be prepared, filed, prosecuted, maintained, enforced, and defended in a manner consistent with the best interests of our business. If our licensors or licensees 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 TV platform 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.

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 TV platform. 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 TV platform, which could harm our business, financial condition, results of operations, and growth prospects significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our current technology, including our TV platform, 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 current 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 TV platform. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and growth 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 growth 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 growth prospects.

In addition, the United States federal government retains certain rights in inventions produced with its financial assistance under the Patent and Trademark Law Amendments Act, or the Bayh-Dole Act. The federal government retains a “nonexclusive, nontransferable, irrevocable, paid-up license” for its own benefit. The Bayh-Dole Act also provides federal agencies with “march-in rights.” March-in rights allow the government, in specified circumstances, to require the contractor or successors in title to the patent to grant a “nonexclusive, partially exclusive, or exclusive license” to a “responsible applicant or applicants.” If the patent owner refuses to do so, the government may grant the license itself. If, in the future, we co-own or license in technology which is critical to our business that is developed in whole or in part with federal funds subject to the Bayh-Dole Act, our ability to enforce or otherwise exploit patents covering such technology may be adversely affected.

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

Filing, prosecuting, and defending patents on our TV platform, 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. Further, our ability to pursue patents throughout the world may be delayed or affected due to a public health crisis such as the global pandemic. 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. In Europe, as of June 1, 2023, the Unitary Patent Court ("UPC") has exclusive jurisdiction over Unitary Patents and offers a uniform and specialized framework for patent litigation at the European level. Furthermore, European applications have the option, upon grant of a patent, of becoming a Unitary Patent and therefore subject to UPC. This is a significant change in European patent practice. As the UPC is a new court system, there is limited precedent for the court, increasing the uncertainty. 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.

Geopolitical actions in the United States and in foreign countries could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications or those of any current or future licensors and the maintenance, enforcement or defense of our issued patents or those of any current or future licensors. For example, the United States and foreign government actions related to Russia's invasion of Ukraine may limit or prevent filing, prosecution, and maintenance of patent applications in Russia. Government actions may also prevent maintenance of issued patents in Russia. These actions could result in abandonment or lapse of our patents or patent applications, resulting in partial or complete loss of patent rights in Russia. If such an event were to occur, it could have a material adverse effect on our business. Accordingly, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

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 growth 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 growth prospects.

Geopolitical actions in the United States and in foreign countries could prevent us from continuing to make these periodic payments in certain locations. For example, the United States and foreign government actions related to Russia's invasion of Ukraine may limit our ability to make or prevent us from making these payments in Russia. These actions could result in abandonment or lapse of our patents or patent applications, resulting in partial or complete loss of patent rights in Russia, which could adversely affect our business.

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 (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 TV platform, product candidates or other technologies or (ii) invent any of the inventions claimed in our or our licensor’s patents or patent applications. Further, changes in the leadership or staffing of the PTO and other federal agencies may lead to new policies and changes in the regulations that may impact the timelines of our patents 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 growth 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. For example, the Supreme Court of the United States held in *Amgen v. Sanofi* (2023) that a functionally claimed genus was invalid for failing to comply with the enablement requirement of the Patent Act. In addition, the Federal circuit recently issued a decision involving the interaction of patent term adjustment ("PTA"), terminal disclaimers, and obvious-type double patenting. 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. For example, in *Assoc. for Molecular Pathology v. Myriad Genetics, Inc.* (2013), the U.S. Supreme Court held that certain claims to DNA molecules are not patentable. While we do not believe that any of the patents owned or licensed by us will be found invalid based on this decision, we cannot predict how future decisions by the courts, the U.S. Congress or the USPTO may impact the value of our patents. For example, the IRA passed by Congress authorizes the Secretary of the Department of Health and Human Services ("HHS") to negotiate prices directly with participating manufacturers for selected medicines covered by Medicare even if these medicines are protected by an existing patent. For small molecule medicines, the process begins seven years after initial approval by the FDA. While we do not believe that the IRA or its effects will impact our ability to obtain patents in the near future, we cannot be certain whether it will affect our patent strategy in the long run.

Issued patents covering our TV platform, 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 TV platform, product candidates or other technologies, the defendant could counterclaim that such patent is invalid or unenforceable or raise a defense to infringement. 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 subject matter eligibility for patenting, 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. Grounds for defenses to infringement include statutory exemptions to patent infringement for uses related to submitting information to regulatory authorities to seek certain regulatory approvals. 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 TV platform, product candidates or other technologies. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, a judge or jury could find that our patent claims laws of nature or are otherwise ineligible for patenting, and 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 TV platform, 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 growth prospects.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Patent rights are of limited duration. In the United States, if all maintenance fees are paid timely, the natural expiration of a patent is generally 20 years after its first effective filing date. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such product candidates are commercialized. Even if patents covering our product candidates are obtained, once the patent life has expired for a product, we may be open to competition from biosimilar or generic products. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing product candidates similar or identical to ours. Upon issuance in the United States, the term of a patent can be increased by patent term adjustment, which is based on certain delays caused by the USPTO, but this increase can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. The term of a United States patent may also be shortened if the patent is terminally disclaimed over an earlier-filed patent. A patent term extension ("PTE") based on regulatory delay may be available in the United States. However, only a single patent can be extended for each marketing approval, and any patent can be extended only once, for a single product. Moreover, the scope of protection during the period of the PTE does not extend to the full scope of the claim, but instead only to the scope of the product as approved. Laws governing analogous PTEs in foreign jurisdictions vary widely, as do laws governing the ability to obtain multiple patents from a single patent family. Additionally, we may not receive an extension if we fail to exercise due diligence during the testing phase or regulatory review process, apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. If we are unable to obtain PTE or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain approval of competing products following our patent expiration and may take advantage of our investment in development and clinical trials by referencing our clinical and nonclinical data to launch their product earlier than might otherwise be the case, and our revenue could be reduced, possibly materially.

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 TV platform, 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 TV platform, 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 growth 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 TV platform, 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 nondisclosure 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 TV platform, product candidates or other technologies.

We currently have rights to intellectual property, through licenses from third parties, to identify and develop our TV platform and product candidates. Many pharmaceutical companies, biotechnology companies, and academic institutions are competing with us in the fields of neurodegenerative and lysosomal storage diseases and BBB technology and may have patents and have filed and plan to file 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 TV platform. 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 growth 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 growth 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 TV platform, product candidates, and other technologies.

The fields of discovering treatments for neurodegenerative and lysosomal storage 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 these fields, the intellectual property landscape is in flux, and it may remain uncertain in the future. As such, there may be significant intellectual property litigation and proceedings relating to our owned, 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 TV platform, product candidates, and other technologies may give rise to claims of infringement of the patent rights of others. We cannot assure you that our TV platform, 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 TV platform, product candidates, and other technologies might assert are infringed by our current or future TV platform, product candidates or other technologies, including claims to compositions, formulations, methods of manufacture or methods of use or treatment that cover our TV platform, 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 TV platform, product candidates, or other technologies, could be found to be infringed by our TV platform, 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 TV platform, product candidates, or other technologies may infringe. Generative artificial intelligence ("AI") resources that are publicly available may also present a risk that a company may inadvertently obtain, incorporate, or use a third party's intellectual property.

Third parties may have patents or obtain patents in the future and claim that the manufacture, use, or sale of our TV platform, 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 TV platform, 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 TV platform, 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 TV platform, 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 TV platform, 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 or growth prospects.

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 in which we have an interest 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, 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 growth 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 harm our business.

The majority of our operations are conducted at our facility in South San Francisco, 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.

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. Our 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 any of our 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 December 31, 2025, we had approximately 503 employees, all of whom were full-time. As our development plans and strategies develop, we must add additional managerial, operational, financial, and other personnel. Future growth will impose significant added responsibilities on members of management, including recruiting, integrating, and retaining additional employees; managing our internal development efforts; and expanding our controls, reporting systems, and procedures. 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.

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, we may be unable to effectively manage our outsourced activities or the quality or accuracy of the services provided by consultants may be compromised for any reason. If we are not able to effectively manage our growth, 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.

We have engaged in and may in the future engage in acquisitions or strategic partnerships, which 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 strategic partnerships, 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 as part of our business strategy. For example, we have collaboration agreements with Takeda, Sanofi and Biogen, and issued stock in connection with entering into certain of those agreements in 2018 and 2020. Any such transaction 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;
- the loss of key employees, 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 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.

In December 2025, we entered into a royalty funding agreement with Royalty Pharma. This agreement makes available to us up to $275.0 million in milestone payments. However, these milestone payments are subject to satisfaction of certain conditions related to the regulatory approval of tividenofusp alfa by specific deadlines. Should we not satisfy such conditions by the applicable deadlines, or if we fail to meet our obligations or default under this agreement, we may not receive any milestone payments, or the payments to us could be substantially less than the maximum amounts available under the agreement.

Our internal computer systems, or those used by our third-party research institution collaborators, CROs, or other contractors or consultants, may fail or suffer other breakdowns, cyberattacks, or information security breaches or incidents that could compromise the confidentiality, integrity, and availability of such systems and data, expose us to liability, and affect our reputation.

We are increasingly dependent upon information technology systems, infrastructure, and data to operate our business. We also rely on third-party vendors and their information technology systems. Commercialization will require the implementation of computer systems that are increasingly complex to install, secure, and maintain. Despite the implementation of security measures, our internal computer systems and those of our collaborators, CROs, and other contractors and consultants may be vulnerable to damage, outages and interruptions resulting from computer viruses and other malicious code or unauthorized access, or breached, compromised, or otherwise subject to security incidents due to operator error, malfeasance, or other system disruptions. Geopolitical events, such as war and armed conflicts, may increase the risks of cyber-attacks, disruptions, and security breaches and incidents that we and these third parties face. Security threats can come from a variety of sources, ranging in sophistication from an individual hacker to a state-sponsored attack. Cyber threats may be broad-based or otherwise generic in nature, or they may be custom-crafted against our information systems or those of our collaborators, CROs, or other contractors or consultants.

As the cyber-threat landscape evolves, cyber-attacks have become more prevalent, intense, sophisticated, and much harder to detect and defend against. Such attacks could include the use of key loggers or other harmful and virulent malware, including ransomware or other denials of service, and can be deployed through malicious websites, the use of social engineering and/or other means. We and our collaborators, CROs, or other contractors and consultants may not be able to anticipate all types of security threats, and we may not be able to implement preventive measures effective against all such security threats. The techniques used by cyber criminals change frequently, may not be recognized until launched, and can originate from a wide variety of sources. Although to our knowledge we have not experienced any such material system failure or security breach or incident to date, if a breakdown, cyberattack or other information security breach or incident were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to loss or misappropriation of trade secrets or loss of, or unauthorized modification, unavailability, disclosure, or other unauthorized processing of other proprietary information or other similar disruption and we could incur liability and reputational damage. For example, any corruption, loss, or other unavailability 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.

Cyber-attacks, breaches, interruptions, or other data security incidents could result in legal claims or proceedings by private parties or governmental authorities, liability under federal or state laws that protect the privacy of personal information, regulatory penalties, significant remediation costs, disrupt key business operations, and divert attention of management and key information technology resources. In the United States, notice of breaches must be made to affected individuals, the U.S. Secretary of the Department of Health and Human Services ("HHS"), and for extensive breaches, notice may need to be made to the media or U.S. state attorneys general. Such a notice could harm our reputation and our ability to compete. In addition, U.S. state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that threaten the privacy of state residents. There can be no assurance that we, our collaborators, CROs, contractors, consultants, and any other business counterparties will be successful in efforts to detect, prevent, protect against, or fully recover systems or data from all break-downs, service interruptions, attacks, or security breaches or incidents. Although we maintain standalone cybersecurity insurance, the costs related to significant security breaches, incidents, or disruptions could be material and exceed the limits of any insurance coverage we have, and may result in increases in our insurance costs. Relevant insurance may in the future become unavailable to us on commercially reasonable terms or at all. Any disruption or security breach or incident that results in or is perceived to have resulted in a loss of, or damage to, our data or systems, or inappropriate disclosure, use, acquisition, transfer, modification, unavailability, or other processing of confidential or proprietary information, including data related to our personnel, could result in the loss, unauthorized modification, use, unavailability, disclosure or other unauthorized processing of critical or sensitive data, and could cause us to incur liability. Further, in any such event, the development and commercialization of our product candidates could be delayed and our business and operations could be adversely affected. Any of the foregoing could result in financial, legal, business, or reputational harm to us.

We are increasing our use of artificial intelligence (AI) systems to enhance productivity and efficiency; however, the use of AI presents operational, legal, regulatory, cybersecurity, and reputational risks. Many AI systems generate probabilistic outputs based on patterns in training data rather than deterministic rules, and they may produce results that are inaccurate, incomplete, misleading, biased, or not explainable, including “hallucinations,” and their performance may vary based on inputs, updates, or changes in underlying data. As a result, our use of AI could lead to inaccurate analyses, degraded data quality, improper actions or decisions, operational disruptions, or data loss. Our use of AI may also raise ethical and legal challenges, including outcomes that reflect or amplify bias or discrimination, lack of transparency or traceability, and evolving compliance obligations under data protection, intellectual property, and laws and regulations specifically governing the development, deployment, and use of AI. In addition, AI tools may increase the risk that confidential, proprietary, or personal data is exposed, misused, or inappropriately processed (including through training, retention, or sharing by third-party providers), and could increase cybersecurity threats such as unauthorized access, prompt-injection, data exfiltration, or other security incidents. We may also face claims or investigations related to the use of AI, including alleged infringement or misappropriation of third-party intellectual property, or allegations that AI-generated outputs were relied upon inappropriately. These risks could require additional expenditures, reduce the effectiveness of our operations, result in regulatory scrutiny, litigation, fines, contractual liability, or reputational harm, and could materially adversely affect our business, operating results, financial condition, and stock price. If we do not adopt AI or other machine-learning technologies effectively or at an appropriate pace, we may also be less competitive relative to peers who do.

Business disruptions, including as a result of geopolitical events and global pandemics, 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, CDMOs, suppliers, clinical trial sites, and other third-party partners, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, public health crises, 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 bank failures or instability in the financial services sector, 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. Government responses to such events, such as to public health crises, may also result in disruption and delay of our business.

The majority of our operations are located in South San Francisco, California and Salt Lake City, Utah. Damage or extended periods of interruption to our corporate, development, research, or manufacturing facilities due to fire, extreme weather conditions or 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. In addition to a subsidiary located in Zurich, Switzerland, we have suppliers and collaborative relationships located outside the United States. Accordingly, our future results could be harmed by a variety of factors, including:

- economic weakness, including inflation, rising interest rates or political instability in certain non-U.S. economies and markets;
- differing and changing regulatory requirements in non-U.S. countries;
- potentially reduced protection for intellectual property rights;
- 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 government actions by U.S. or non-U.S. governments;
- differing reimbursement regimes, including price controls;
- negative consequences from changes in tax laws or tariffs;
- 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, UK Bribery Act, or comparable foreign laws;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- business interruptions resulting from geopolitical actions, including war and armed conflict, terrorism, natural disasters including earthquakes, typhoons, floods, and fires, or health epidemics; and
- cyberattacks, which are growing in frequency, sophistication and intensity, and are becoming increasingly difficult to detect.

In particular, there is currently significant uncertainty about the future relationship between the United States and various other countries, most significantly China, with respect to trade policies, treaties, tariffs, taxes, and other limitations on cross-border operations. The U.S. government has and continues to make significant additional changes in U.S. trade policy and may continue to take future actions that could negatively impact U.S. trade. For example, legislation has been introduced in Congress to limit certain U.S. biotechnology companies from using equipment or services produced or provided by select Chinese biotechnology companies, and others in Congress have advocated for the use of existing executive branch authorities to limit those Chinese service providers' ability to engage in business in the U.S. We cannot predict what actions may ultimately be taken with respect to trade relations between the United States and China or other countries, what products and services may be subject to such actions or what actions may be taken by the other countries in retaliation. If we are unable to obtain or use services from existing service providers or become unable to export or, if approved, sell our products, our business, liquidity, financial condition, and/or results of operations would be materially and adversely affected.

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, 2025, we had federal net operating loss carryforwards of approximately $964.9 million, federal research and development tax credit carryforwards of approximately $73.8 million, and orphan tax credit carryforwards of approximately $75.0 million, some of which will begin to expire in 2034. Under Sections 382 and 383 of the United States Internal Revenue Code of 1986, as amended, (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. We have experienced ownership changes in the past, and we may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership, including in connection with our October 2022 and December 2025 offerings, some of which are outside our control. Limitations may also apply under state law. For example, recently enacted California legislation limits the use of state net operating loss carryforwards for tax years beginning on or after January 1, 2024 and before January 1, 2027. As a result of this legislation or other unforeseen reasons, we may not be able to utilize some or all of our net operating loss carryforwards, even if we attain profitability.

Risks Related to Ownership of Our Common Stock

The market price of our common stock has been and may continue to be volatile, which could result in substantial losses for investors.

The trading price of our common stock has been and may continue to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this report, these factors include:

- 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;
- the timing and ability to obtain regulatory approval on our lead product candidates, including DNL310;
- failure to achieve development, regulatory, or commercialization milestones under our collaborations;
- failure or discontinuation of any of our product development and research programs;
- failure to commercialize our TV platform;
- results of preclinical studies, clinical trials, or regulatory approvals of product candidates of our competitors, or announcements about new research programs, product candidates, or technologies 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;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems or in accounting standards;

- ineffectiveness of our internal controls;
- significant lawsuits, including patent or stockholder litigation;
- market conditions in the pharmaceutical and biotechnology sectors; and
- other events or factors affecting general economic, industry, and market conditions, including bank failures or instability in the financial services sector, geopolitical events, such as war and armed conflict, natural disasters, and public health crises.

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. In the past, when the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our stockholders were to bring a lawsuit against us, the defense and disposition of any such lawsuits could be costly and divert the time and attention of our management and harm our operating results, regardless of the merits of such a claim.

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

The trading market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. If one or more of the analysts covering our business downgrade their evaluations of our stock, or if we fail to meet the expectations of analysts, 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 or trading volume to decline.

Sales of substantial amounts of our common stock in the public markets, or the perception that such sales might occur, 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, or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our common stock.

Furthermore, sales of our common stock by current stockholders may make it more difficult for us to sell equity or equity-related securities in the future at a time and price that we deem reasonable or appropriate, and make it more difficult for you to sell shares of our common stock. Certain holders of shares of our common stock 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. For example, on February 27, 2024, we entered into a Purchase Agreement with certain existing accredited investors in connection with a strategic private offering transaction. Pursuant to this transaction, we entered into an agreement granting an investor certain registration rights following such time that the investor may be deemed an affiliate of the Company. Any sales of securities by these stockholders, or the perception that sales will be made in the public market, could have a material adverse effect on the market price for our common stock.

We have registered on Form S-8 all shares of common stock that are issuable under our 2017 Equity Incentive Plan and 2017 Employee Stock Purchase Plan. As a consequence, these shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates.

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. For example, in December 2025, we sold 9,142,857 shares of common stock and pre-funded warrants to purchase 2,285,714 shares of our common stock in an underwritten public offering. In January 2026, in connection with the same offering, the underwriters exercised their option to purchase an additional 746,468 shares of common stock, on which date we received aggregate net proceeds of approximately $12.4 million. Our security holders may be further diluted by the exercise of the pre-funded warrants issued. We, and indirectly, our stockholders, will bear the cost of issuing and servicing all such securities. Additionally, 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. In December 2025, for example, we announced a royalty funding agreement that, upon certain conditions including regulatory approval within specified timelines and payment of milestones, would entitle Royalty Pharma plc to 9.25% royalty on future net sales of tividenofusp alfa.

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. In addition, any sales of our common stock or other securities under our shelf registration statement could put downward pressure on our stock price. 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.

Our principal stockholders and management own a significant percentage of our stock and will be able to exercise significant influence over matters subject to stockholder approval.

Our directors, executive officers, holders of more than 5% of our outstanding stock, and their respective affiliates beneficially own a significant percentage of our outstanding common stock. As a result, these stockholders, if they act together, may significantly influence all matters requiring stockholder approval, including approval of significant corporate transactions and the election of directors, as with the recent board nomination and election of a director designated by Baker Brothers Life Sciences L.P. and 667, L.P. ("Baker Brothers") pursuant to a nominating agreement.

Any concentration of ownership may result in such holders exerting influence over us and may have the effect of delaying or preventing a change in control of our company that our other stockholders may believe is in their best interests. This in turn could have a material adverse effect on our stock price and may prevent attempts by our stockholders to replace or remove the board of directors or management.

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

As a public company, we are subject to reporting and other obligations under the Securities Exchange Act of 1934, as amended, ("Exchange Act"), including the requirements of Section 404 of the Sarbanes-Oxley Act, which require annual management assessments of the effectiveness of our internal control over financial reporting.

The rules governing the standards that must be met for management and our auditors 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 or auditors may identify material weaknesses or deficiencies which may not be remedied in time to meet the deadline imposed by the Sarbanes-Oxley Act. 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 ("U.S. GAAP"). Any failure to maintain effective internal controls could have an adverse effect on our business, financial position, results of operations, and growth prospects.

We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake or system failures. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

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

We have never paid cash dividends on our common stock and do not anticipate that we will pay any dividends in the foreseeable future. We currently intend to retain our future earnings, if any, to maintain and expand our existing operations. If we do not pay dividends, our common stock may be less valuable because a return on your investment will only occur if our stock price appreciates, which may never occur.

Delaware law and provisions in our charter documents 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 amended and restated bylaws 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:

- 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, (the "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, 15.0% 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 common 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 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 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 or we do not enforce such provision, we may incur additional costs associated with resolving the dispute in other jurisdictions, which could seriously harm our business.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 1C. CYBERSECURITY

Denali's approach to cybersecurity seeks to defend the confidentiality, integrity and availability of our systems and information for our people and our patients.

Risk Management and Strategy

We have established policies and processes for assessing, identifying, and managing material risk from cybersecurity threats, and have integrated these processes into our overall risk management systems and processes. We routinely assess material risks from cybersecurity threats, including any potential unauthorized occurrence on or conducted through our information systems that may result in adverse effects on the confidentiality, integrity, or availability of our information systems or any information residing therein.

We conduct periodic risk assessments to identify cybersecurity threats, as well as assessments in the event of a material change in our business practices that may affect information systems that are vulnerable to such cybersecurity threats. These risk assessments include identification of reasonably foreseeable internal and external risks, the likelihood and potential damage that could result from such risks, and the sufficiency of existing policies, procedures, systems, and safeguards in place to manage such risks.

Following these risk assessments, we re-design, implement, and maintain reasonable safeguards to minimize identified risks; reasonably address any identified gaps in existing safeguards; and regularly monitor the effectiveness of our safeguards. We devote significant resources and designate high-level personnel, including our Vice President of Information Technology and Cybersecurity ("VP of IT"), to manage the risk assessment and mitigation process.

As part of our overall risk management system, we conduct annual security awareness training for personnel at all levels and functions, issue periodic simulated social engineering tests, and have established protocols to escalate cybersecurity incidents from identification through remediation. These activities are undertaken in collaboration with human resources, IT, and management.

We also engage consultants to assist us in monitoring and testing our safeguards. Performance of our cybersecurity controls for certain systems is periodically reviewed by our internal quality functions. We further require third-party service providers who will be handling our company's sensitive information to certify that they implement appropriate security measures, consistent with all applicable laws, to maintain reasonable security measures in connection with their work with us, and to promptly report any suspected breach of its security measures that may affect our company.

Additional information regarding whether any risks from cybersecurity threats, including as a result of any previous cybersecurity incidents, have materially affected or are reasonably likely to materially affect our company, including our business strategy, results of operations, or financial condition, are included in this Annual Report on Form 10-K in Item 1A, "Risk Factors".

Governance

One of the key functions of our board of directors is informed oversight of our risk management process, including risks from cybersecurity threats. Our board of directors is responsible for monitoring and assessing strategic risk exposure, and our executive officers are responsible for the day-to-day management of the material risks we face. Our board of directors administers its cybersecurity risk oversight function directly as a whole, as well as through the audit committee.

Our VP of IT is primarily responsible for assessing and managing our material risks from cybersecurity threats. He has prior work experience in cybersecurity, holds relevant degrees, and has current industry-recognized cybersecurity certifications. He oversees our cybersecurity policies and processes, including those described in "Risk Management and Strategy" above. The processes by which the VP of IT is informed about and monitors the prevention, detection, mitigation, and remediation of cybersecurity incidents include the following: the identification and assessment of assets and assessing potential associated risks, implementation of protective measures, continuous monitoring and detection of unusual or suspicious activities, incident response and recovery management, regular security awareness and training, and review and alignment of cybersecurity practices with industry recognized cybersecurity practices, compliance, and regulation concerns.

The Audit Committee of our Board of Directors provides direct oversight over cybersecurity risk. The Audit Committee receives quarterly updates from the VP of IT regarding our company's cybersecurity risks and activities, including any recent cybersecurity incidents and related responses, cybersecurity systems testing, activities of third parties, and cyberinsurance coverage; the Audit Committee in turn provides regular updates to the Board of Directors.

ITEM 2. PROPERTIES

Below is a summary of our key leased properties as of December 31, 2025:

California

Our corporate headquarters are located in South San Francisco, California, comprising 148,020 square feet of office, research and development, engineering, and laboratory space pursuant to a lease agreement which commenced on April 12, 2019 and expires on April 30, 2029, with an option to extend for a period of ten years. This facility houses the majority of our personnel.

Utah

Our manufacturing facility is located in Salt Lake City, Utah, comprising approximately 60,000 rentable square feet of office, lab, and clinical manufacturing space pursuant to a lease agreement which commenced on April 1, 2024, and is expected to terminate in 2039. We have two five-year renewal period options to extend the lease for a further ten years at the end of the lease term.

Switzerland

Our European headquarters are located in Zurich, Switzerland, comprising approximately 163 square meters (approximately 1,755 square feet) of office space pursuant to a lease agreement that commenced on November 1, 2025 and expires on October 31, 2030, with an option to extend the lease for an additional five-year period. This facility is used for office and administrative purposes.

We believe that our existing premises are adequate for our current needs.

ITEM 3. 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.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Our common stock has been listed on The Nasdaq Global Select Market under the symbol "DNLI" since December 8, 2017. Prior to that date, there was no public trading market for our common stock.

Holders of Common Stock

As of February 20, 2026, there were approximately 143 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust or by other entities.

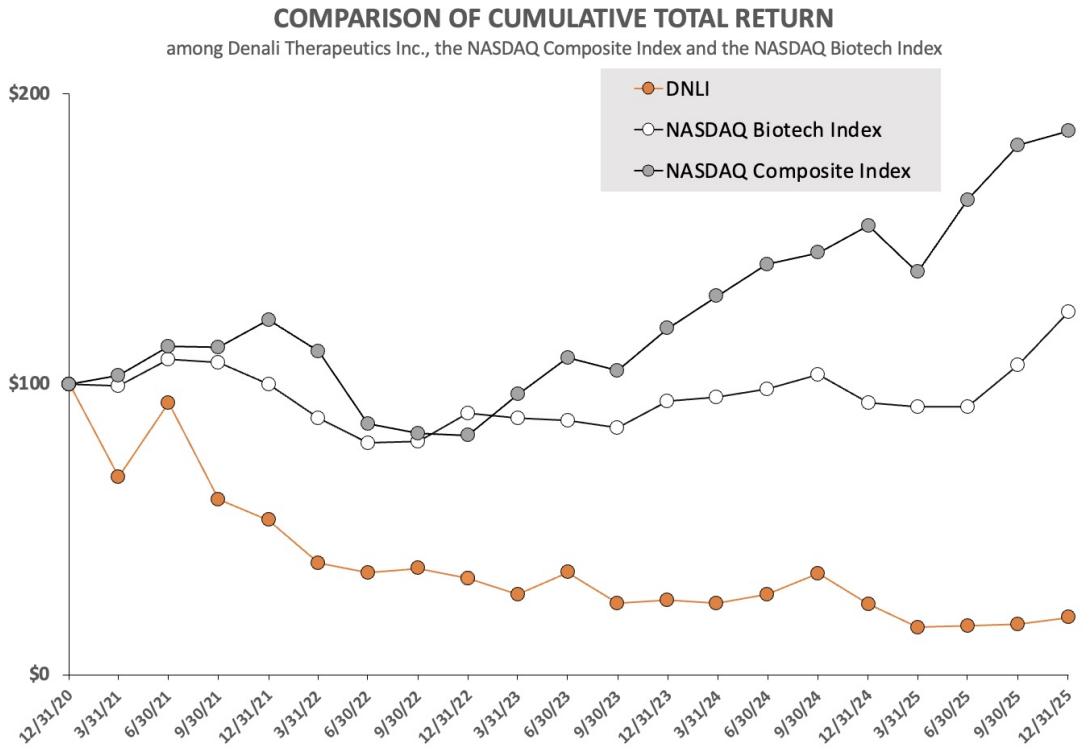
Dividend Policy

We have never declared or paid any cash dividends on our common stock or any other securities. We anticipate that we will retain all available funds and any future earnings, if any, for use in the operation of our business and do not anticipate paying cash dividends in the foreseeable future. In addition, future debt instruments may materially restrict our ability to pay dividends on our common stock. Payment of future cash dividends, if any, will be at the discretion of the board of directors after taking into account various factors, including our financial condition, operating results, current and anticipated cash needs, the requirements of current or then-existing debt instruments and other factors the board of directors deems relevant.

Performance Graph

This graph is not "soliciting material" or deemed "filed" with the SEC for purposes of Section 18 of the Exchange Act, or otherwise subject to liabilities under that Section, and shall not be deemed incorporated by reference into any filing of Denali Therapeutics Inc. under the Securities Act of 1933, as amended (the "Securities Act"), whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.

The following graph compares the cumulative total stockholder return on our common stock relative to the cumulative total returns of the Nasdaq Composite Index and the Nasdaq Biotechnology Index. An investment of $100 is assumed to have been made in our common stock and each index on December 31, 2020 and its relative performance is tracked through December 31, 2025. Pursuant to applicable Securities and Exchange Commission rules, all values assume reinvestment of the full amount of all dividends, however no dividends have been declared on our common stock to date. The stockholder returns shown on the graph below are based on historical results and are not necessarily indicative of future performance, and we do not make or endorse any predictions as to future stockholder returns.



Recent Sales of Unregistered Securities

On February 27, 2024, we entered into a securities purchase agreement (the "Purchase Agreement") with certain existing accredited investors for the private placement of (i) 3,244,689 shares of our common stock at a price of $17.07 per share and (ii) pre-funded warrants to purchase an aggregate of 26,046,065 shares of our common stock (the "Pre-Funded Warrants") at a purchase price of $17.06 per Pre-Funded Warrant. The private placement closed on February 29, 2024, at which time we received gross proceeds of $499.7 million. The Pre-Funded Warrants are exercisable at an exercise price of $0.01 and will be exercisable until exercised in full. The holders of Pre-Funded Warrants may not exercise a Pre-Funded Warrant if the holder, together with its affiliates, would beneficially own more than 4.99% of the number of shares of common stock outstanding immediately after giving effect to such exercise. The holders of Pre-Funded Warrants may increase or decrease such percentage not in excess of 19.99%, in the case of an increase, by providing at least 61 days' prior notice to the Company. We have also granted a certain investor certain director nomination and additional registration rights, subject to certain exceptions, conditions, and limitations. We intend to use the net proceeds from the private placement to support our ongoing research and development activities, the acceleration and expansion of our proprietary BBB-crossing TV technology, as well as general corporate purposes and working capital. We have invested the funds received in short-term and long-term, interest-bearing investment-grade securities and government securities. We filed a registration statement to register the shares of common stock sold in the private placement (including the shares of common stock underlying the Pre-Funded Warrants) on March 22, 2024.

We are relying on the exemptions from registration available under Section 4(a)(2) and/or Rule 506(b) of Regulation D promulgated under the Securities Act with respect to transactions by an issuer not involving any public offering, and we expect to file a Form D with respect to the private placement.

Use of Proceeds from Registered Securities

In October 2022, we sold 11,933,962 shares of common stock (inclusive of shares sold pursuant to an overallotment option granted to the underwriters in connection with the offering) through an underwritten public offering at a price of $26.50 per share for aggregate net proceeds of approximately $296.2 million.

In December 2025, we sold 9,142,857 shares of common stock, par value $0.01 per share (the “Common Stock”), at a price to the public of $17.50 per share (the “Firm Shares”) and 2,285,714 shares of pre-funded warrants at a price to the public of $$17.49 per underlying share, which represents the per share public offering price of each share of common stock less the $0.01 per share exercise price for each pre-funded warrant, through an underwritten public offering for aggregate net proceeds of approximately $189.2 million, after deducting issuance costs of approximately $0.7 million. In January 2026, the underwriters exercised their option to purchase an additional 746,468 shares of the Company’s Common Stock, on which date the Company received aggregate net proceeds of approximately $12.4 million.

There have been no material changes in the planned use of the net proceeds from the follow-on public offering as described in the Registration Statement. We have invested the funds received in short-term and long-term, interest-bearing investment-grade securities and government securities.

Issuer Purchases of Equity Securities

Not applicable.

ITEM 6. [RESERVED]

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis of our financial condition and results of operations should be read together with our consolidated financial statements and the related notes to those statements included elsewhere in this report. This discussion and analysis and other parts of this report 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 report.

Overview

Key elements of our strategy include:

1) **Discover:** Invent a new class of barrier-crossing therapeutics by leveraging our TV platforms and deep expertise in blood-brain barrier biology to enhance the delivery of biotherapeutics to the brain and throughout the body.

2) **Develop:** Accelerate and expand a broad portfolio of TV-based product candidates to fully unlock the potential of barrier-crossing therapeutics, applying patient-informed development and driving biomarker-guided regulatory approvals.

3) **Deliver:** Launch initial products targeting rare lysosomal storage diseases as a strategic foundation for expansion into common neurodegenerative conditions and other serious diseases, while building integrated capabilities for long-term growth and profitability.

Our clinical programs are as follows:

- Tividenofusp alfa (DNL310, ETV:IDS), composed of IDS fused to TV, is designed to deliver IDS into cells and tissues throughout the body, including the brain by crossing the BBB, with the goal of addressing the behavioral, cognitive, and physical manifestations of MPS II (Hunter syndrome);

- DNL126 (ETV:SGSH), composed of SGSH fused to TV, is designed to deliver SGSH into cells and tissues throughout the body, including the brain by crossing the BBB, with the goal of treating MPS IIIA (Sanfilippo syndrome type A);

- TAK-594/DNL593 (PTV:PGRN), composed of PGRN fused to TV, is designed to restore PGRN levels in the brain with the goal of treating FTD-*GRN* and is being developed in collaboration with Takeda;

- DNL952 (ETV:GAA), composed of acid alpha-glucosidase ("GAA") fused to TV and engineered to replace GAA in all tissues, with the goal of treating Pompe disease;

- DNL628 (OTV:MAPT), composed of an antisense oligonucleotide ("ASO") against MAPT fused to TV, designed to suppress gene expression of MAPT encoding the tau protein with the goal of treating Alzheimer's disease;

- BIIB122/DNL151, a small molecule LRRK2 inhibitor, is being developed in collaboration with Biogen for the potential treatment of Parkinson's disease; and

- Eclitasertib (SAR443122/DNL758), a peripheral and non-CNS penetrant small molecule RIPK1 inhibitor, is being developed by Sanofi, to address peripheral inflammatory diseases such as ulcerative colitis ("UC").

The following table summarizes key information about our clinical stage programs:

Program	Product Candidate	Clinical Study(ies)	Indication	Operational Control
ETV:IDS	tividenofusp alfa, or DNL310	Ph 1/2 Ph 2/3	Hunter syndrome (MPS II)	Denali
ETV:SGSH	DNL126	Ph 1/2	Sanfilippo syndrome Type A (MPS IIIA)	Denali
PTV:PGRN	TAK-594/DNL593	Ph 1/2	FTD-GRN	Joint with Takeda
ETV:GAA	DNL952*	Ph 1 (planned)	Pompe disease	Denali
OTV:MAPT	DNL628*	Ph 1b (planned)	Alzheimer's disease	Denali
LRRK2	BIIB122/DNL151	Ph 2a Ph 2b	Parkinson's disease	Denali Joint with Biogen
RIPK1 (Peripheral)	eclitasertib, or SAR443122/DNL758	Ph 2	UC	Sanofi

* Regulatory application to begin clinical testing has been approved by Health Authorities.

Since we commenced operations, we have devoted substantially all of our resources to discovering, acquiring and developing product candidates, building our TV platform, assembling our core capabilities in understanding key neurodegenerative and lysosomal storage disease pathways, operationalizing clinical trials, building manufacturing capabilities and establishing commercial capabilities.

Key operational and financing milestones for the year ended December 31, 2025 and in 2026 to date include:

- **Tividenofusp alfa DNL310 (ETV:IDS)**
  - In January 2025, we announced that the U.S. Food and Drug Administration ("FDA") granted Breakthrough Therapy Designation for tividenofusp alfa (DNL310) for the treatment of individuals with MPS II.
  - In February 2025, at the WORLD Symposium conference, we presented the primary analysis of the Phase 1/2 study in 47 participants with Hunter syndrome in the 24-week treatment period and additional long-term follow-up.
  - In May 2025, we completed a rolling submission of a Biologics License Application ("BLA") for tividenofusp alfa under the accelerated approval pathway;
  - In July 2025, we announced that the FDA accepted our BLA for tividenofusp alfa for priority review, assigning a Prescription Drug User Fee Act (PDUFA) target action date of January 5, 2026; In October 2025, we announced that the FDA extended its review timeline of the BLA seeking accelerated approval of tividenofusp alfa from January 5, 2026, to April 5, 2026;

- In December 2025, we entered into a synthetic royalty funding agreement with Royalty Pharma plc (“Royalty Pharma”), pursuant to which Royalty Pharma has agreed to provide us with up to $275.0 million in funding in exchange for a 9.25% royalty on future worldwide net sales of tividenofusp alfa, which will cease upon reaching a multiple of 3.0x, or 2.5x if achieved by the first quarter of 2039. The agreement is subject to various closing conditions, including Denali achieving U.S. FDA accelerated approval of tividenofusp alfa on or before June 30, 2026. At the closing, Royalty Pharma will make an initial payment of $200.0 million. Denali will be receive an additional payment of $75.0 million upon approval of tividenofusp alfa by the EMA on or before December 31, 2029. Denali will retain all worldwide development and commercialization rights to tividenofusp alfa;

- In December 2025, we announced that we are in ongoing dialogue with the FDA related to the eligibility of tividenofusp alfa to receive a Rare Pediatric Disease Priority Review Voucher (“PRV”) upon approval. Because we submitted a filing of our intent to request a PRV after the initial BLA submission, based on discussions with the FDA, we may not be eligible to receive the PRV. Therefore, we are not including any potential future proceeds from the sale of a PRV in our financial planning. We continue to work with the FDA and the FDA will determine whether to award a PRV upon approval of tividenofusp alfa. We also announced that a Late Cycle Meeting with the FDA was completed and labeling discussions were underway;

- In December 2025, we announced that *The New England Journal of Medicine* published the Phase 1/2 study results; and

- In January 2026, we announced that we are is preparing for commercial launch in anticipation of a regulatory decision on the BLA for tividenofusp alfa under the FDA accelerated approval pathway with a PDUFA target action date of April 5, 2026, and that enrollment in Cohort A (neuronopathic participants) was completed in the ongoing global Phase 2/3 COMPASS study in December 2025.

- **DNL126 (ETV:SGSH)**

  - In April 2025, we announced productive collaboration and discussions with the FDA under the START program (“Support for clinical Trials Advancing Rare Disease Therapeutics”) around the potential for an accelerated development and approval path for DNL126 in the treatment of Sanfilippo syndrome;

  - In August 2025, we announced we reached alignment with the FDA that cerebrospinal fluid heparan sulfate (CSF HS) may be considered a reasonably likely surrogate endpoint to predict clinical benefit and may therefore be used to support accelerated approval of DNL126 for MPS IIIA. We also announced that additional 49-week data from the ongoing open-label Phase 1/2 study were consistent with previously announced 25-week data, demonstrating a significant reduction in CSF HS from baseline, including normalization, and a safety profile that supports continued development; and

  - In September 2025, we completed enrollment in the ongoing Phase 1/2 study, and in December 2025 we announced that the Phase 1/2 study remains on track for completion in 2026, supporting a potential accelerated approval pathway and commercial launch by the second half of 2027, with planning for a global Phase 3 confirmatory study underway; and

  - In February 2026, we presented preliminary open-label Phase 1/2 data at the 2026 WORLD Symposium demonstrating substantial reductions in CSF HS, including normalization from baseline, and in urine HS with a safety profile consistent with other enzyme replacement therapies.

- **DNL 952 (ETV:GAA)**
  - In October 2025, we submitted an Investigational New Drug ("IND") application for DNL952 (ETV:GAA) to initiate a Phase 1 study, and in December 2025 we announced that the IND had been placed on clinical hold. In January 2026 we announced that the FDA has lifted the clinical hold on the IND application for DNL952, and we are proceeding with the Phase 1 study.
- **DNL 628 (OTV:MAPT)**
  - In January 2026, we announced that the Clinical Trial Application ("CTA") for DNL628 (OTV:MAPT) to initiate a Phase 1b study in Alzheimer's disease was approved and study start-up activities are underway.
- **BIIB122/DNL151 (LRRK2)**
  - In May 2025, Biogen announced completion of enrollment in the Phase 2b LUMA study for early-stage Parkinson's disease with a readout expected in 2026.
- **Other**
  - In January 2025, we announced topline results that the primary endpoint was not met in Regimen G of the Phase 2/3 HEALEY ALS Platform Trial evaluating DNL343 in the treatment of ALS. In March 2025, we provided an update that additional analyses did not demonstrate a treatment effect on neurofilament light ("NfL"), a biomarker of neuronal damage, over the 24-week, double-blind period and in a subset of participants that completed an additional 28 weeks in the open-label active treatment extension. Based on these outcomes, the active treatment extension in Regimen G was discontinued. Overall, DNL343 was found to be generally well tolerated;
  - In February 2025, we and Sanofi executed a side letter terminating Sanofi's license to the CNS Products program including SAR443820/DNL788;
  - In February 2025, after mutual agreement to discontinue preclinical activities on ATV:TREM2, Takeda delivered notice of its election to terminate the ATV:TREM2 program on February 26, 2025, as per the terms of the Takeda Collaboration Agreement. The ATV:TREM2 program termination became effective in April 2025; and
  - In December 2025, we sold 9,142,857 shares of common stock through an underwritten public offering at a price of $17.50 per share, and issued pre-funded warrants to purchase 2,285,714 shares of common stock at a price of $17.49, for aggregate net proceeds of $189.2 million. The pre-funded warrants have an exercise price of $0.01 per share of common stock, and are immediately exercisable and will remain exercisable until exercised in full. In January 2026, the underwriters partially exercised their option to purchase additional shares, and we issued 746,468 shares of common shares for net proceeds of $12.4 million.

We do not have any products approved for sale and have not generated any product revenue since our inception. We have funded our operations primarily from the issuance and sale of convertible preferred stock, the sale of common stock and pre-funded warrants to purchase shares of our common stock in public offerings and private placements, and payments received from our collaboration and funding agreements with Takeda, Sanofi, Biogen and other third parties.

We have incurred significant operating losses to date and expect to continue to incur operating losses for the foreseeable future. We had net losses of $512.5 million, $422.8 million, and $145.2 million for the years ended December 31, 2025, 2024, and 2023, respectively. As of December 31, 2025, we had an accumulated deficit of $2.05 billion. Our ability to generate product revenue will depend on the successful development and eventual commercialization of one or more of our product candidates. We expect to continue to incur significant expenses and operating losses as we advance our current clinical stage programs through healthy volunteer and patient trials; broaden and improve our TV platform; acquire, discover, validate and develop additional product candidates; obtain, maintain, protect and enforce our intellectual property portfolio; and hire additional personnel.

Through 2024, we relied entirely on third-party contract manufacturers to manufacture and supply our preclinical and clinical materials to be used during the development of our product candidates through 2024. In early 2025, we opened our clinical biomanufacturing facility in Salt Lake City, Utah, expanding U.S. manufacturing capabilities and strengthening supply chain control and operational efficiency. Going forward, we plan to use both our SLC facility and third-party contract manufacturers to supply our preclinical and clinical materials. If tividenofusp alfa is approved for the treatment of Hunter syndrome, we expect to use third-party contract manufacturers to supply commercial product.

License and Collaboration Agreements

Collaborations and partnering are central components of our strategy to build, develop and commercialize our portfolio of product candidates. We have numerous arrangements with biopharmaceutical companies, technology companies, academic institutions, foundations, and patient-focused data companies.

Biogen

In October 2020, we entered into the LRRK2 Agreement with Biogen pursuant to which we granted Biogen a license to co-develop and co-commercialize our small molecule LRRK2 Program, in addition to the ROFN and Option Agreement pursuant to which we granted an option and a right of first negotiation to certain of our programs utilizing our TV technology platform; collectively the "Biogen Collaboration Agreement." In connection with our collaboration with Biogen, we also entered into a common stock purchase agreement pursuant to which we sold 13,310,243 shares of our common stock to BIMA for an aggregate purchase price of $465.0 million. Under the terms of the Biogen Collaboration Agreement, we received $560.0 million in upfront payments in October 2020.

In April 2023, Biogen exercised its option to license our ATV:Abeta program and we received additional consideration of $5.0 million for an option exercise fee. In August 2023, we executed an Amendment (the “Biogen Amendment”) to the LRRK2 Agreement and ROFN and Option Agreement with Biogen. Pursuant to the Biogen Amendment, the schedule of potential LRRK2 Agreement milestones was amended, while maintaining the same total value of milestones that Denali is eligible to receive. In addition, Biogen waived its option right to the second option program and waived its rights of first negotiation for two other TV-enabled programs under the ROFN and Option Agreement. In July 2024, Denali and Biogen executed a Side Letter to the ROFN and Option Agreement, pursuant to which, effective as of the date of the Side Letter, Biogen terminated its license to the ATV:Abeta program enabled by Denali’s TfR-targeting technology against amyloid beta for the potential treatment of Alzheimer's disease, and granted Denali rights to data generated during the collaboration. The side letter also effected the immediate termination of the ROFN and Option Agreement; as such, the Company expects to receive no future milestone or royalty payments from Biogen related to the ATV:Abeta program. There were no changes to the terms of the LRRK2 Agreement in the year ended December 31, 2025. Further details regarding the terms of the agreements between us and Biogen are included in this Annual Report on Form 10-K in the section titled "Business - Licenses and Collaborations."

We did not recognize any collaboration revenue under the Biogen Collaboration Agreement in the years ended December 31, 2025 and 2024, and we recognized related party collaboration revenue of $295.5 million in the year ended December 31, 2023. Further, we recognized research and development expense of $15.8 million, $16.7 million and $17.7 million related to cost sharing payments we made to Biogen in the years ended December 31, 2025, 2024 and 2023, respectively. We have recorded cost sharing payables of $2.8 million and $2.5 million on the Consolidated Balance Sheets as of December 31, 2025 and 2024, respectively. Through December 31, 2025, we have earned $5.0 million in option fee payments but have not recorded any milestone revenue or product sales under the Biogen Collaboration Agreement.

Sanofi

In October 2018, we entered into the Sanofi Collaboration Agreement with Sanofi pursuant to which certain small molecule CNS and peripheral RIPK1 inhibitors contributed by Sanofi and by us are being, or will be developed and commercialized. On February 24, 2025, we and Sanofi executed a side letter terminating Sanofi's license to the CNS Products program including SAR443820/DNL788, though Sanofi continues to develop eclitasertib (SAR443122/DNL758). Further details regarding the terms of the agreement between us and Sanofi, and historic payments between the parties under the agreement, are included in this Annual Report on Form 10-K in the section titled "Business - Licenses and Collaborations."

We recognized no collaboration revenue associated with the Sanofi Collaboration Agreement in the years ended December 31, 2025 and 2024, and we recognized collaboration revenue of $25.0 million in the year ended December 31, 2023. No receivable from Sanofi was recorded on the Consolidated Balance Sheets as of December 31, 2025 and 2024. Through December 31, 2025, we had received milestone payments of $100.0 million and we have not recorded any product sales under the Sanofi Collaboration Agreement. Subsequent to the February 24, 2025 side letter, we expect to receive no future milestone or royalty payments from Sanofi related to the CNS Products program.

Takeda

In January 2018, we entered into the Takeda Collaboration Agreement pursuant to which we granted Takeda an option to develop and commercialize, jointly with us, our ATV:TREM2, PTV:PGRN and ATV:BACE1/Tau programs, the latter of which was later replaced with our ATV:Tau program. Pursuant to the terms of the Takeda Collaboration Agreement, we also entered into the Purchase Agreement with Takeda in January 2018, pursuant to which we sold 4,214,559 shares of our common stock to Takeda for an aggregate purchase price of $110.0 million.

In November 2021 and December 2021, Takeda exercised its options for the PTV:PGRN and ATV:TREM2 programs, respectively, subsequent to which we have shared equally in the development costs for the programs. In February 2025, after mutual agreement to discontinue preclinical activities on ATV:TREM2, Takeda delivered notice of its election to terminate the ATV:TREM2 program, and the ATV:TREM2 program termination became effective 60 days following the notice date. Further details regarding the terms of the agreement between us and Takeda, and historic payments between the parties under the agreements, are included in this Annual Report on Form 10-K in the section titled "Business - Licenses and Collaborations."

We did not recognize collaboration revenue under the Takeda Collaboration Agreement in the years ended December 31, 2025 and 2024, and we recognized collaboration revenue of $10.0 million in the year ended December 31, 2023. Further, we offset research and development expense due to cost sharing reimbursements received from Takeda of $6.6 million, $5.9 million and $12.2 million in the years ended December 31, 2025, 2024, and 2023, respectively. We recorded receivables of $1.6 million and $1.5 million from Takeda on the Consolidated Balance Sheets as of December 31, 2025 and 2024, respectively. Through December 31, 2025, we have received $65.0 million in milestone payments and $10.0 million of option exercise fees from Takeda, and we have not recorded any product sales under the Takeda Collaboration Agreement.

F-star

In August 2016, we entered into the F-star Collaboration Agreement with the F-star entities. The goal of the collaboration was the development of Fcabs to enhance delivery of therapeutics across the BBB into the brain. In connection with the entry into the F-star Collaboration Agreement, we also purchased an option to acquire all of the outstanding shares of F-star Gamma pursuant to a pre-negotiated buy-out option agreement. In May 2018, we exercised such buy-out option and entered into the F-star Purchase Agreement with the shareholders of F-star Gamma and Shareholder Representative Services LLC, pursuant to which we acquired all of the outstanding shares of F-star Gamma. As a result of the Acquisition, F-star Gamma became our wholly-owned subsidiary and the entity's name was changed to Denali BBB Holding Limited. In addition, we became a direct licensee of certain intellectual property of F-star Ltd by way of our assumption of F-star Gamma's license agreement with F-star Ltd, dated August 24, 2016. Further details regarding the terms of the arrangements between us and the F-star entities, and historic payments between the parties under the agreements, are included in this Annual Report on Form 10-K in the section titled "Business - Licenses and Collaborations."

Through December 31, 2025 we have recognized consideration paid under the F-star Purchase Agreement of $49.8 million as research and development expenses consisting of upfront, preclinical and clinical contingent consideration payments, including a $30.0 million contingent consideration payment triggered in March 2023 upon the achievement of a specified clinical milestone in the ETV:IDS program. We did not recognize contingent consideration in the years ended December 31, 2025 or 2024.

Genentech

In June 2016, we entered into an exclusive license agreement with Genentech. The agreement gives us access to Genentech's LRRK2 inhibitor program. Our collaboration partner in the LRRK2 program, Biogen, is responsible for 50% of any payment obligation to Genentech under the Biogen Collaboration Agreement.

We have made a total of $25.0 million in consideration payments under the Genentech agreement, and we have recognized $18.8 million of associated research and development expense, net of cost sharing reimbursements from Biogen. We did not recognize expenses under this agreement in the years ended December 31, 2025, 2024 and 2023.

Royalty Pharma Funding Agreement

In December 2025, we entered into a synthetic royalty funding agreement (the "Royalty Agreement") with Royalty Pharma plc ("Royalty Pharma"). Pursuant to the Royalty Agreement, Royalty Pharma has agreed to provide us with up to $275.0 million in funding in exchange for a 9.25% royalty on future net sales of tividenofusp alfa. The transaction is subject to various closing conditions, including our achieving U.S. Food and Drug and Administration (FDA) accelerated approval of tividenofusp alfa on or before June 30, 2026. At the closing, Royalty Pharma will make an initial payment of $200.0 million. We will receive an additional payment of $75.0 million upon approval of tividenofusp alfa by the European Medicines Agency (EMA) on or before December 31, 2029. The royalty payments to Royalty Pharma will cease upon reaching a multiple of 3.0x, or 2.5x if achieved by the first quarter of 2039. We will retain all worldwide development and commercialization rights to tividenofusp alfa.

Components of Operating Results

Collaboration Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from product sales for the foreseeable future. All revenue recognized to date has been collaboration and license revenue from our collaboration agreements with Takeda, Sanofi and Biogen.

Future revenue may be recognized from the Takeda Collaboration Agreement, Sanofi Collaboration Agreement, and Biogen Collaboration Agreement, and may be generated from product sales or milestone payments, royalties and profit sharing reimbursement from other collaboration agreements, strategic alliances and licensing arrangements. We expect that our revenue will fluctuate from quarter-to-quarter and year-to-year as a result of the timing and amount of license fees, option exercise fees, milestone payments, profit sharing reimbursement, other payments and product sales, to the extent any are successfully commercialized. If we fail to complete the development of our product candidates in a timely manner or obtain regulatory approval for them, our ability to generate future revenue, and our results of operations and financial position, would be materially adversely affected.

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 TV platform include:

- external research and development expenses, including:
  - expenses incurred under arrangements with third parties, such as contract research organizations ("CROs"), preclinical testing organizations, contract development and manufacturing organizations ("CDMOs"), 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 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 late-stage IND-enabling studies.

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 TV platform. These expenses include external expenses incurred by us relating to our Takeda Collaboration Agreement and Biogen Collaboration Agreement. All external costs associated with earlier stage programs, or that benefit the entire portfolio, are tracked as a group. We also incur personnel and other operating expenses for our research and development programs which are presented in aggregate. These expenses primarily relate to salaries and benefits, stock-based compensation, facility expenses including rent and depreciation, and lab consumables. Where we share costs with our collaboration partners, such as in our Biogen Collaboration Agreement and Takeda Collaboration Agreement, research and development expenses may include cost sharing reimbursements from, or payments to, our collaboration partners. Further, where we receive R&D funding from third parties, this may be recognized as a reduction to research and development expenses.

It is challenging to predict the nature, timing and estimated long-range costs of the efforts that will be necessary to complete the development of, and obtain regulatory approval for, any of our product candidates. This is made more challenging by events outside of our control, such as global pandemics and increased geopolitical uncertainty. 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 and commercial, sales and marketing 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 stock-based compensation expense, expenses for outside professional services, pre-commercialization activities, and allocated expenses. Outside professional services consist of legal, accounting and audit services and other consulting fees. Allocated expenses consist of rent, depreciation and other expenses related to our office and research and development facility not otherwise included in research and development expenses. We expect to increase our administrative headcount as we prepare for commercialization of Tividenofusp alfa (DNL310, ETV:IDS) and advance our other product candidates through clinical development, which will increase our general and administrative expenses.

Gain from divestiture of small molecule programs

The gain from the divestiture of small molecule programs consists entirely of the non-cash gain associated with the divestiture of assets associated with select preclinical small molecule programs, including specified intellectual property, tangible assets and equipment used to conduct early-stage small molecule drug discovery from the Company, in exchange for equity consideration.

Interest and Other Income, Net

Interest and other income, net, consists primarily of interest income, investment income earned on our cash, cash equivalents and marketable securities, and sublease income, as well as an offset for interest expense on our finance lease liability.

Results of Operations

Comparison of the years ended December 31, 2025 and 2024

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

	Year Ended December 31,		Change	
	2025	2024	$	%
Operating expenses:				
Research and development	418,778	396,440	22,338	6
General and administration	136,564	105,438	31,126	30
Total operating expenses	555,342	501,878	53,464	11
Gain from divestiture of small molecule programs	—	14,537	(14,537)	*
Loss from operations	(555,342)	(487,341)	(68,001)	14
Interest and other income, net	42,904	64,636	(21,732)	(34)
Loss before income taxes	(512,438)	(422,705)	(89,733)	21
Income tax expense	(102)	(68)	(34)	50
Net loss	$ (512,540)	$ (422,773)	(89,767)	21 %

* Percentage is not meaningful.

Research and development expenses. Research and development expenses were $418.8 million for the year ended December 31, 2025 compared to $396.4 million for the year ended December 31, 2024.

The following table provides a breakdown of our research and development expenses by category (in thousands):

	Year Ended December 31,		Change	
	2025	2024	$	%
External research and development expenses - TV programs, including cost sharing	$ 154,799	$ 138,196	16,603	12 %
External research and development expenses - small molecule programs, including cost sharing	8,800	42,623	(33,823)	(79)
Other research and development expenses	86,958	62,715	24,243	39
Personnel related expenses[(1)]	168,221	152,906	15,315	10
Total research and development expenses	$ 418,778	$ 396,440	22,338	6 %

(1) Personnel-related expenses include stock-based compensation expense of $59.5 million and $59.1 million for the years ended December 31, 2025 and 2024, respectively, reflecting an increase of $0.4 million.

The increase in research and development expenses of $22.3 million for the year ended December 31, 2025 compared to the year ended December 31, 2024 was primarily attributable to the following:

- an increase of $16.6 million in external research and development expenses for our TV programs driven by increased spend on multiple preclinical and clinical programs including DNL126, DNL628 and DNL952, partially offset by a decrease in expenses related to our DNL310 program;
- an increase of $24.2 million in other research and development expenses, including lab consumables, consultants and general facilities costs, primarily driven by the commencement of operations at our large molecule manufacturing facility in Salt Lake City, Utah; and
- an increase of $15.3 million in personnel-related expenses, including salaries and stock-based compensation, primarily driven by higher headcount related to the commencement of operations at our large molecule manufacturing facility in Salt Lake City, Utah.

These increases were partially offset by a $33.8 million decrease in external research and development expenses for our small molecule programs, primarily due to the wind-down of activities related to our DNL343 program in 2025.

General and administrative expenses. General and administrative expenses were $136.6 million for the year ended December 31, 2025 compared to $105.4 million for the year ended December 31, 2024. The increase of $31.2 million was primarily driven by headcount increases and other activities associated with preparing for the potential commercial launch for tividenofusp alfa.

Comparison of the years ended December 31, 2024 and 2023

Refer to “Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations—Results of Operations” in our 2024 Annual Report on Form 10-K for a discussion of the results of operations for the year ended December 31, 2024 compared to the year ended December 31, 2023.

Liquidity and Capital Resources

Sources of Liquidity

As of December 31, 2025, we had cash, cash equivalents and marketable securities in the amount of $966.2 million. We fund our operations primarily with the proceeds from the sale of common stock and payments received from our collaboration partners, including those received under agreements with Takeda, Sanofi, and Biogen. We have sold common stock and other securities in public offerings, a private placement, and stock purchase agreements with Takeda and Biogen.

Through December 31, 2025 we have obtained aggregate net proceeds of approximately $943.6 million from public offerings of our common stock, including $189.2 million obtained through the sale of 9.1 million shares of common stock and the issuance of pre-funded warrants to purchase 2.3 million shares of common stock in December 2025, and $296.2 million obtained through the sale of 11.9 million shares of common stock in October 2022. Under stock purchase agreements with collaboration partners we have received a further $575.0 million through December 31, 2025.

Further, in February 2024 we received net proceeds of approximately $499.3 million from our private placement through the sale of approximately 3.2 million shares of common stock and pre-funded warrants to purchase approximately 26.0 million shares of our common stock.

In February 2025, we established a registered “at-the-market” facility for the potential future sale of up to $400.0 million of shares of common stock from time to time by entering into an equity distribution agreement with Goldman Sachs & Co. LLC and Leerink Partners LLC as sales agents. The previous equity distribution agreement and related “at-the-market” facility entered into in February 2022 was terminated in February 2025. To date, no shares have been sold under either equity distribution agreement. All sales under the current equity distribution agreement are conditioned upon satisfaction of customary closing conditions.

Through December 31, 2025, we have received $115.0 million, $225.0 million, $565.0 million and $50.0 million, pursuant to our collaboration and research and development funding agreements with Takeda, Sanofi, Biogen and an unrelated third party, respectively. These payments include upfront, option and milestone payments. Additionally, we have received $55.0 million and $16.2 million in gross cost sharing reimbursements from Takeda and Biogen, respectively, and received $13.7 million in specified reimbursements from Sanofi.

Future Funding Requirements and Commitments

To date, we have not generated any product revenue. We do not expect to generate any product revenue unless and until we obtain regulatory approval of and commercialize any of our product candidates, 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 expand our research and development activities and continue the development of, and seek regulatory approvals for, our product candidates, and begin to commercialize any approved products. Further, we expect general and administrative expenses to increase as we continue to incur additional costs associated with supporting our growing operations. 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. 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 our existing collaboration agreements, or future agreements with other 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 $2.05 billion as of December 31, 2025. 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 twelve months following the filing date of this Annual Report on Form 10-K, including our existing commitments as outlined below. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. In the longer term, we anticipate that we will need substantial additional resources to fund our operations and meet future commitments.

Our existing commitments primarily relate to our obligations under existing lease agreements, certain pre-launch commercial product, clinical and manufacturing agreements. As of December 31, 2025, we had total undiscounted lease payment obligations of $54.2 million. We had total non-refundable purchase commitments of $45.8 million as of December 31, 2025. While the lease obligations span multiple years, the majority of the purchase commitments are due within the upcoming twelve months Further, we may be required to make contingent payments under existing arrangements upon the achievement of defined clinical, regulatory and commercial milestones in certain programs, including contingent consideration payments to former shareholders of F-star under the F-star Gamma license, and milestone and royalty payments to Genentech under the Genentech License Agreement. These commitments are more fully described in Note 4, "Acquisition, License Agreement and Research and Development Funding Collaboration Agreement" and Note 7, "Commitments and Contingencies" to the consolidated financial statements included in Item 8. of this Annual Report on Form 10-K.

Our future funding requirements, including any changes to existing commitments or the establishment of new commitments, will depend on many factors, including:

- our ability to obtain regulatory approval for our product candidates, establish sales and marketing capabilities, and successfully market such approved product candidates;
- 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 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,		
	2025	**2024**	**2023**
Net cash used in operating activities	$ (412,600)	$ (347,694)	$ (357,991)
Net cash provided by (used in) investing activities	255,281	(88,756)	249,308
Net cash provided by financing activities	189,216	484,304	17,820
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 31,897	$ 47,854	$ (90,863)

Net Cash Used In Operating Activities

During the year ended December 31, 2025, net cash used in operating activities was $412.6 million, which consisted of a net loss of $512.5 million, adjusted by non-cash items primarily related to stock-based compensation expense, depreciation and amortization, net accretion of discounts on marketable securities, and non-cash rent expenses. Cash used in operating activities was also driven by changes in our operating assets and liabilities.

Net Cash Provided By (Used In) Investing Activities

During the year ended December 31, 2025, net cash provided by investing activities was $255.3 million, which consisted of $706.0 million of proceeds from the maturities of marketable securities, partially offset by $441.3 million of purchases of marketable securities, and $9.4 million capital expenditures to purchase property and equipment.

Net Cash Provided By Financing Activities

During the year ended December 31, 2025, net cash provided by financing activities was $189.2 million, which consisted of $189.2 million of net proceeds from public offerings of our common stock and pre-funded warrants in December 2025, and $8.5 million of proceeds from the exercise of stock options and the Company's ESPP, partially offset by an aggregate of $8.2 million of payments related to our finance lease, and $0.3 million issuance costs related to the royalty financing.

Years ended December 31, 2024 and 2023

Refer to “Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations—Liquidity and Capital Resources” in our 2024 Annual Report on Form 10-K for a discussion of the cash flows for the years ended December 31, 2024 and 2023.

Critical Accounting 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 U.S. 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 revenues recognized and 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. Our significant accounting policies are described in detail in the notes to our consolidated financial statements included elsewhere in this report. We believe that the following accounting estimates involve a significant level of estimation uncertainty which could have a material impact on our financial condition or results of operations.

Revenue Recognition

We recognize revenue associated with our collaboration arrangements, which may require us to exercise considerable judgment in estimating revenue to be recognized, including judgments made on day one accounting and judgments associated with the amount of revenue to be recognized over time as performance obligations are satisfied.

Significant judgment is required to apply the authoritative accounting guidance at the outset of a collaboration arrangement, and over time, and the determinations including judgment are highly subjective and can differ between arrangement based on specific contractual terms. To date, there have been no material true ups to revenue as a result of changes in the key judgments detailed below.

The key areas of judgment identified are: (1) Identification of performance obligations at the outset of a collaboration arrangement (identifying the promised goods or services and determining whether these are distinct in the context of the contract); (2) Measurement of the transaction price at the outset of a collaboration arrangement and at each reporting period (estimating valuation of share premium payments, constraint of future variable consideration); (3) Allocation of the transaction price to the performance obligations at the outset of a collaboration arrangement (estimating the standalone selling price of identified performance obligations); and (4) Recognition of revenue when (or as) we satisfy each performance obligation, assessed at each reporting period (when the performance obligation has been satisfied for point-in time recognition, the extent of satisfaction of an obligation for recognition over time).

Research and Development Expenses

A significant portion of our research and development expenses in the Consolidated Statements of Operations and Comprehensive Loss are external costs. These research and development expenses include the conduct of preclinical studies and clinical trials, contract manufacturing activities and consulting services. The measurement of these research and development expenses can impact the measurement of research and development expenses in the Consolidated Statements of Operations and Comprehensive Loss, and of prepaid assets and accrued liabilities on the Consolidated Balance Sheets.

The level of judgment required to estimate research and development expenses varies based on the nature of the services being performed and the underlying support obtained. We estimate the amount of work completed based on information received from 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. 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, incomplete or inaccurate data from vendors could impact our understanding of the status and timing of services performed which could result in us reporting expenses that are too high or too low in any particular period.

In some cases, expense is recorded using an underlying assumption of the progress to completion of specific activities. For example, costs may be recognized based on the passage of time for activities that span reporting periods. If the provision of services is not linear then this assumption could impact the amount of expense recognized. For other activities, such as for certain clinical trials, expense is recorded based on information obtained from vendors as an intermediary to those performing the underlying services, such as contract research organizations. These estimates are inherently more judgmental since the quality and availability of the underlying data may vary. To date, there have been no material true ups from estimated to actual external research and development expenses. However, we expect that the level of judgment in estimating research and development expenses may increase over time as we are entering later stage, more extensive, clinical trials.

Research and development expenses also include reimbursements owed or owing to a collaboration partner to satisfy cost sharing requirements. These reimbursement amounts are estimated based, in part, on data received from our collaboration partner, which may include a certain level of estimation or judgments made by that partner. They also reflect our estimates of research and development expense as discussed above. As such, a change in estimates or judgments by either our partner or us can result in a change to a reimbursement amount. To date, there have been no material true ups from estimated to actual reimbursements owed or owing.

Where the company has entered into an R&D funding arrangement, payments received will be recorded as a liability, and recognized an offset to research and development expenses as the underlying research and development costs are incurred. The determination of whether an arrangement meets the definition of an R&D funding arrangement under ASC730 requires judgment, including an assessment of the nature of the arrangement, the funding party's rights and exposure to research and development risks. Further, the timing of recognition of the funding is also subject to the judgments of the underlying research and development costs. To date, there have been no material true ups to R&D funding recognition.

Recent Accounting Pronouncements

See Note 1 to our consolidated financial statements included in Part II, Item 8, "Financial Statements and Supplementary Data," of this Annual Report on Form 10-K for a description of recent accounting pronouncements applicable to our business.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are exposed to market risks in the ordinary course of our business, primarily related to interest rate and foreign currency sensitivities.

Interest Rate Sensitivity

We are exposed to market risk related to changes in interest rates. We had cash, cash equivalents and marketable securities of $966.2 million as of December 31, 2025, which consisted primarily of money market funds and marketable securities, largely composed of investment grade, short and 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 policy. 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 British Pound, and we therefore are subject to foreign exchange risk. The fluctuation in the value of the U.S. dollar against other currencies affects the reported amounts of expenses, assets and liabilities primarily associated with a limited number of preclinical, clinical and manufacturing activities.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

Denali Therapeutics Inc.
Index to Consolidated Financial Statements

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Denali Therapeutics Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Denali Therapeutics Inc. (the Company) as of December 31, 2025 and 2024, the related consolidated statements of operations and comprehensive loss**,** stockholders' equity and cash flows for each of the three years in the period ended December 31, 2025, and the related notes (collectively referred to as the “consolidated financial statements”). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2025 and 2024, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2025, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2025, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated February 26, 2026 expressed an unqualified opinion thereon.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company’s financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Accrued and prepaid clinical research and development costs

Description of the Matter

As more fully described in Note 1 to the consolidated financial statements, the Company records accrued and prepaid clinical research and development (R&D) costs based on information obtained from vendors including contract research organizations. Each reporting period, estimation is required to determine the costs for certain services when the Company has either not been invoiced or has not received information from vendors regarding actual costs incurred to determine the clinical research and development expenses incurred during the period, and the accrued and prepaid amounts in relation to payments for those services. As of December 31, 2025, accrued and prepaid clinical research and development costs were $13.7 million and $7.3 million, respectively. The accrued and prepaid clinical research and development costs (“Accrued and Prepaid Clinical R&D Costs”) are based in part on estimates for certain clinical research and developments costs incurred under the Company’s service agreements with vendors including contract research organizations. The Company expenses clinical research and development costs incurred based on several factors, such as information obtained from vendors and estimates of certain costs and services completed by certain vendors.

Auditing the Company's accounting for Accrued and Prepaid Clinical R&D Costs was complex due to the estimation of costs for certain services when the Company has either not been invoiced or has not received information regarding actual costs incurred.

How We Addressed the Matter in Our Audit

We evaluated and tested the design and operating effectiveness of the Company’s internal controls over management’s process to account for Accrued and Prepaid Clinical R&D Costs, including management’s controls over the completeness and accuracy of the data and the process used in determining these costs.

To test the Accrued and Prepaid Clinical R&D Costs, our audit procedures included, among others, confirmation directly with vendors of the completeness of the terms and conditions of significant clinical R&D service agreements and the data used by management in the determination of the Company’s clinical costs incurred. Additionally, we tested the completeness and accuracy of the underlying inputs used in the Company’s analyses through verification of significant inputs, such as costs incurred, invoices received prior to and after the balance sheet, and the terms and conditions of the underlying agreements. We evaluated the completeness of services rendered by the vendors, including examination of meeting materials and performing inquiries of R&D personnel outside the accounting department, to evaluate the completeness of clinical R&D service agreements and the costs incurred by the Company.

/s/ Ernst & Young LLP

We have served as the Company’s auditor since 2015.

San Mateo, California
February 26, 2026

Denali Therapeutics Inc.

Consolidated Balance Sheets
(In thousands, except share amounts)

	December 31, 2025	December 31, 2024
Assets		
Current assets:		
Cash and cash equivalents	$ 205,326	$ 174,960
Short-term marketable securities	662,553	657,371
Prepaid expenses and other current assets	32,779	32,105
Total current assets	900,658	864,436
Long-term marketable securities	98,322	359,373
Property and equipment, net	52,402	55,236
Finance lease right-of-use asset	48,531	47,533
Operating lease right-of-use asset	19,002	22,861
Other non-current assets	25,939	24,741
Total assets	$ 1,144,854	$ 1,374,180
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 3,330	$ 11,137
Accrued expenses and other current liabilities	95,021	91,071
Total current liabilities	98,351	102,208
Operating lease liability, less current portion	27,210	36,673
Finance lease liability, less current portion	5,532	5,615
Total liabilities	131,093	144,496
Commitments and contingencies (Note 7)		
Stockholders' equity:		
Convertible preferred stock, $0.01 par value; 40,000,000 shares authorized as of December 31, 2025 and December 31, 2024; 0 shares issued and outstanding as of December 31, 2025 and December 31, 2024	—	—
Common stock, $0.01 par value; 400,000,000 shares authorized as of December 31, 2025 and December 31, 2024; 156,182,177 and 144,220,986 shares issued and outstanding as of December 31, 2025 and December 31, 2024, respectively	1,888	1,768
Additional paid-in capital	3,062,715	2,764,880
Accumulated other comprehensive income	682	2,020
Accumulated deficit	(2,051,524)	(1,538,984)
Total stockholders' equity	1,013,761	1,229,684
Total liabilities and stockholders' equity	$ 1,144,854	$ 1,374,180

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,		
	2025	2024	2023
Collaboration revenue:			
Collaboration revenue from customers[1]	$ —	$ —	$ 330,531
Total collaboration revenue	—	—	330,531
Operating expenses:			
Research and development[2]	418,778	396,440	423,876
General and administration	136,564	105,438	103,354
Total operating expenses	555,342	501,878	527,230
Gain from divestiture of small molecule programs	—	14,537	—
Loss from operations	(555,342)	(487,341)	(196,699)
Interest and other income, net	42,904	64,636	51,505
Loss before income taxes	(512,438)	(422,705)	(145,194)
Income tax expense	(102)	(68)	(30)
Net loss	(512,540)	(422,773)	(145,224)
Other comprehensive income (loss):			
Net unrealized gain (loss) on marketable securities, net of tax	(1,338)	1,377	7,529
Comprehensive loss	$ (513,878)	$ (421,396)	$ (137,695)
Net loss per share, basic and diluted	$ (2.97)	$ (2.57)	$ (1.06)
Weighted average number of shares outstanding, basic and diluted	172,649,097	164,473,772	137,370,897

(1) Includes related-party collaboration revenue from customers of $295.5 million for the year ended December 31, 2023.
(2) Includes expense for cost sharing payments to a related party of $17.7 million for the year ended December 31, 2023.

See accompanying notes to consolidated financial statements.

Denali Therapeutics Inc.

Consolidated Statements of Stockholders' Equity
(In thousands, except share amounts)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2022	135,965,918	$ 1,686	$ 2,018,617	$ (6,886)	$ (970,987)	$ 1,042,430
Issuances under equity incentive plans	1,232,526	12	17,808	—	—	17,820
Vesting of restricted stock units	1,187,054	13	(13)	—	—	—
Stock-based compensation	—	—	108,399	—	—	108,399
Net loss	—	—	—	—	(145,224)	(145,224)
Other comprehensive income	—	—	—	7,529	—	7,529
Balance at December 31, 2023	138,385,498	$ 1,711	$ 2,144,811	$ 643	$ (1,116,211)	$ 1,030,954
Issuance of common stock and pre-funded warrants, net of issuance costs of $480	3,244,689	32	499,221	—	—	499,253
Issuances under equity incentive plans	1,288,609	13	17,376	—	—	17,389
Vesting of restricted stock units	1,302,190	12	(12)	—	—	—
Stock-based compensation	—	—	103,484	—	—	103,484
Net loss	—	—	—	—	(422,773)	(422,773)
Other comprehensive income	—	—	—	1,377	—	1,377
Balance at December 31, 2024	144,220,986	$ 1,768	$ 2,764,880	$ 2,020	$ (1,538,984)	$ 1,229,684
Issuance of common stock and pre-funded warrants, net of issuance costs of $728	9,142,857	91	189,158	—	—	189,249
Issuances under equity incentive plans	1,368,573	14	8,445	—	—	8,459
Vesting of restricted stock units	1,449,761	15	(15)	—	—	—
Stock-based compensation	—	—	100,247	—	—	100,247
Net loss	—	—	—	—	(512,540)	(512,540)
Other comprehensive loss	—	—	—	(1,338)	—	(1,338)
Balance at December 31, 2025	156,182,177	$ 1,888	$ 3,062,715	$ 682	$ (2,051,524)	$ 1,013,761

See accompanying notes to consolidated financial statements.

Denali Therapeutics Inc.

Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31,		
	2025	2024	2023
Operating activities			
Net loss	$ (512,540)	$ (422,773)	$ (145,224)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	11,183	7,795	16,726
Stock-based compensation expense	99,633	102,878	108,102
Net accretion of discounts on marketable securities	(10,253)	(35,117)	(43,952)
Non-cash adjustment to operating lease expense	(4,450)	(4,074)	(3,719)
Right-of-use asset amortization for finance lease	3,629	1,197	—
Non-cash gain from divestiture of small molecule programs	—	(14,537)	—
Other non-cash items	49	—	2
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	(540)	(2,480)	(4,094)
Other non-current assets	772	603	—
Accounts payable	(7,520)	1,437	2,431
Accruals and other current liabilities	465	3,248	2,648
Related party contract liability	—	—	(290,532)
Deferred research and development funding liability	6,972	14,129	—
Other non-current liabilities	—	—	(379)
Net cash used in operating activities	(412,600)	(347,694)	(357,991)
Investing activities			
Maturities of marketable securities	706,046	1,157,120	2,075,947
Purchases of marketable securities	(441,263)	(1,229,964)	(1,813,700)
Purchases of property and equipment	(9,502)	(15,912)	(12,939)
Net cash provided by (used in) investing activities	255,281	(88,756)	249,308
Financing activities			
Proceeds from issuance of common stock and pre-funded warrants, net of issuance costs of $480	—	499,253	—
Proceeds from public offering of common stock and pre-funded warrants, net of issuance costs of $728	189,249	—	—
Proceeds from exercise of awards under equity incentive plans	8,459	17,389	17,820
Payments for finance lease right-of-use asset	(8,168)	(32,338)	—
Issuance costs related to the royalty financing	(324)	—	—
Net cash provided by financing activities	189,216	484,304	17,820
Net increase (decrease) in cash, cash equivalents and restricted cash	31,897	47,854	(90,863)
Cash, cash equivalents and restricted cash at beginning of year	176,535	128,681	219,544
Cash, cash equivalents and restricted cash at end of year	$ 208,432	$ 176,535	$ 128,681
Supplemental disclosures of cash flow information			
Equity consideration received in the divestiture of small molecule programs (Note 13)	$ —	$ 15,000	$ —
Increase in right-of-use asset due to lessor assets	$ —	$ 7,051	$ —
Right-of-use asset obtained in exchange for new finance lease liabilities	$ —	$ 9,358	$ —
Property and equipment purchases accrued but not yet paid	$ —	$ 1,192	$ 553
Cash paid for finance lease interest	$ 720	$ 302	$ —
Issuance costs incurred but not yet paid	$ 482	$ —	$ —
Cash paid during the year for income taxes	$ 46	$ —	$ 3

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 neurodegenerative diseases and lysosomal storage diseases. 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”) and pursuant to the rules and regulations of the Securities and Exchange Commission (“SEC”).

Principles of Consolidation

These consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation. For the Company and its subsidiaries, the functional currency has been determined to be U.S. dollars. Monetary assets and liabilities denominated in foreign currency are remeasured at period-end exchange rates, non-monetary assets and liabilities denominated in foreign currencies are remeasured at historical rates, and transactions in foreign currencies are remeasured at average exchange rates. Foreign currency gains and losses resulting from remeasurement are recognized in interest and other income, net in the Consolidated Statements of Operations and Comprehensive Loss.

Reclassification

Certain prior period amounts in the Company’s Consolidated Statements of Cash Flows have been reclassified to conform to the current period presentation. Specifically, amounts related to the research and development funding liability that were previously included within changes in operating assets and liabilities - accruals and other current liabilities have been reclassified to changes in operating assets and liabilities - deferred research and development funding liability.

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 Balance Sheets and Consolidated Statements of Operations and Comprehensive Loss.

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 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's investment policy limits investments to certain types of securities issued by the U.S. government and its agencies, as well as 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, 2025 and 2024, the Company had no off-balance sheet concentrations of credit risk.

The Company is subject to a number of risks similar to other biopharmaceutical companies at our stage, 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 scale internal manufacturing and/or 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. Further, the company is also subject to broad market risks and uncertainties resulting from recent events, such as bank failures or instability in the financial services sector, geopolitical instability, war and armed conflicts, inflation, rising interest rates, and recession risks as well as supply chain and labor shortages.

Convertible Preferred Stock

The Company is authorized to issue 40.0 million shares of preferred stock in one or more series and to fix the powers, designations, preferences and relative participating option or other rights thereof, including dividend rights, conversion rights, voting rights, redemption terms, liquidation preferences and the number of shares constituting any series, without any further vote or action by the Company's shareholders. As of December 31, 2025 and 2024, the Company had no shares of preferred stock issued or outstanding.

Investments

The Company holds an equity investment in a venture-backed privately held company, Tenvie Therapeutics, Inc. ("Tenvie"). The privately held company is a Variable Interest Entity ("VIE"), but the Company is not the primary beneficiary. The Company does not have the power to direct the activities that most significantly impact the economic performance of the investee. The Company's maximum exposure to loss from this VIE is limited to the value of the equity investment. The equity investment held by the Company lacks a readily determinable fair value and therefore the securities are measured at cost minus impairment, if any, plus or minus changes resulting from observable price changes in orderly transactions for the identical or similar equity securities of the same issuer. The Company reviews the carrying value of its equity investment for impairment whenever events or changes in business circumstances indicate the carrying amount of such asset may not be fully recoverable. Impairments, if any, are based on the excess of the carrying amount over the recoverable amount of the asset. There were no impairments during the years ended December 31, 2025 and 2024.

Fair Value of Financial Instruments

Accounting Standards Codification ("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 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.

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, Cash Equivalents and Restricted Cash

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 are reported at fair value.

Cash, cash equivalents and restricted cash reported within the Consolidated Statements of Cash Flows is composed of cash and cash equivalents reported in the Consolidated Balance Sheets and restricted cash of $3.1 million, $1.6 million and $1.6 million as of December 31, 2025, 2024 and 2023, respectively, which is included within other non-current assets in the Consolidated Balance Sheets. Restricted cash relates to letters of credit supporting the Company’s headquarters building lease and, as of December 31, 2025, also includes a letter of credit supporting the Company’s credit card program.

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 Consolidated Balance Sheets, are considered available-for-sale, and are reported at fair value with net unrealized gains and losses included as a component of stockholders’ equity.

The Company classifies investments in securities with remaining maturities of less than one year, or where its intent is to use the investments to fund current operations or to make them available for current operations, as short-term investments. The Company classifies investments in securities with remaining maturities of over one year as long-term investments, unless intended to fund current operations. The amortized cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity, which is included in interest and other income, net in the Consolidated Statements of Operations and Comprehensive Loss. Realized gains and losses and declines in value determined to be due to credit losses on marketable securities, if any, are included in interest and other income, net.

The Company periodically evaluates the need for an allowance for credit losses. This evaluation includes consideration of several qualitative and quantitative factors, including whether it has plans to sell the security, whether it is more likely than not it will be required to sell any marketable securities before recovery of its amortized cost basis, and if the entity has the ability and intent to hold the security to maturity, and the portion of any unrealized loss that is the result of a credit loss. Factors considered in making these evaluations 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, expected cash flows from securities, other publicly available information that may affect the value of the marketable security, duration and severity of the decline in value, and the Company's strategy and intentions for holding the marketable security.

Accounts Receivable

Accounts receivable are included within prepaid expenses and other current assets on the Consolidated Balance Sheets. The accounts receivable balance represents amounts receivable from the Company's collaboration partners net of an allowance for credit losses, if required.

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.

Asset	Estimated useful life
Leasehold improvements	shorter of life of asset or lease term
Computer equipment and purchased software	three years
Laboratory equipment	five years
Furniture and fixtures	five years
Manufacturing equipment	eight 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 material impairment charges during the years presented.

Leases

The Company leases real estate and certain equipment for use in its operations. A determination is made as to whether an arrangement is a lease at inception. The Company recognizes finance and operating lease right-of-use ("ROU") assets, and finance and operating lease liabilities based on the present value of the future minimum lease payments at the commencement date. The Company adjusts ROU assets as needed for any lease incentives it receives and for assets it purchases that are regarded as landlord-owned. When determining the present value of lease payments, the Company uses its incremental borrowing rate on the date of lease commencement, or the rate implicit in the lease, if known. The Company does not assume renewals in its determination of the lease term unless the renewals are deemed by management to be reasonably certain at lease inception.

The Company recognizes amortization of the ROU assets and interest on the lease liabilities for its finance lease. Finance lease ROU assets are amortized on a straight-line basis from the commencement date to the earlier of the end of the useful life of the ROU asset or the end of the lease term. Operating lease expense is recognized on a straight-line basis over the lease term.

Leases with an initial term of twelve months or less are not recorded on the balance sheet, unless they include an option to purchase the underlying asset that the Company is reasonably certain to exercise. The Company has leases with lease and non-lease components, which the Company has elected to account for as a single lease component.

Revenue Recognition

License, Option and Collaboration Revenue

The Company analyzes its collaboration arrangements to assess whether they are within the scope of ASC 808, Collaborative Arrangements (“ASC 808”) to determine whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities. For elements of collaboration arrangements that are accounted for pursuant to ASC 808, an appropriate recognition method is determined and applied consistently, generally by analogy to Topic 606. The accounting treatment pursuant to Topic 606 is outlined below.

Each of these Payments received under license, option and collaboration agreements result in license, collaboration and other revenue, except for revenues from royalties on net sales of licensed products, which are classified as royalty revenue. The Company may also receive reimbursement or make payments to a collaboration partner to satisfy cost sharing requirements. These payments are accounted for pursuant to ASC 808 and are recorded as an offset or increase to research and development expenses, respectively.

The Company recognizes revenue as it fulfills its obligations under each of its agreements. An asset is transferred when, or as, the customer obtains control of that asset, which for a service is considered to be as the services are received and used. The Company recognizes revenue over time by measuring the progress toward complete satisfaction of the relevant performance obligation using an appropriate input or output method based on the nature of the service promised to the customer. Amounts received prior to satisfying the revenue recognition criteria are recorded as current or non-current contract liabilities in the Company’s Consolidated Balance Sheets, depending on when the performance obligation is expected to be satisfied.

Research and Development Expenses

Research and development expenses represent costs incurred to conduct research and development activities, including the discovery and development of product candidates. The Company recognizes all research and development costs as they are incurred. The Company’s research and development expenses consist primarily of:

- expenses incurred under agreements with collaborators, consultants, third-party contract research organizations (“CROs”), and investigative sites, which conduct a substantial portion of the Company’s preclinical studies and clinical trials;
- costs of acquiring laboratory supplies and originator comparator materials, and costs related to the internal and third-party manufacturing of preclinical and clinical trial supplies;
- costs associated with internal and third-party manufacturing process development activities, analytical activities and pre-launch inventory manufactured prior to regulatory approval being obtained or deemed to be probable;
- salaries and other personnel-related expenses, including stock–based compensation; and
- facility costs and other allocated expense, including direct and allocated costs for rent and maintenance of facilities, depreciation and amortization of leasehold improvements, and manufacturing and laboratory equipment.

Where the Company shares costs with collaboration partners, such as in the Biogen Collaboration Agreement and the Takeda Collaboration Agreement, research and development expenses may include cost sharing reimbursements from or payments to the collaboration partner, respectively. Where the company has entered into an R&D funding arrangement, payments received will be recorded as a liability, and recognized an offset to research and development expenses as the underlying research and development costs are incurred.

Nonrefundable advance payments for goods and services that will be used or received 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. There can be judgment involved in measuring the research and development expenses to be recognized in a particular period. In some cases, expense is recorded using an underlying assumption of the progress to completion of specific activities. For example, costs may be recognized based on the passage of time for activities that span reporting periods. If the provision of services is not linear then this assumption could impact the amount of expense recognized. The level of judgment varies based on the nature of the services being performed and the underlying support obtained. For some activities, such as for certain clinical trials, expense is recorded based on information obtained from vendors as an intermediary to those performing the underlying services, such as contract research organizations. These estimates are inherently more judgmental since the quality and availability of the underlying data may vary. The determination of whether an arrangement meets the definition of an R&D funding arrangement under ASC730 requires judgment, including an assessment of the nature of the arrangement, the funding party’s rights and exposure to research and development risks. Further, the timing of recognition of the funding is also subject to the judgments of the underlying research and development costs.

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’s stock-based compensation programs grant awards that have included stock options, restricted stock units, restricted stock awards, and shares issued under its employee stock purchase plan. Grants are awarded to employees, directors, and non-employee service providers.

The Company measures 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 subject solely to service-based vesting requirements using the Black-Scholes valuation model. The Company uses the fair value of its common stock to determine the fair value of restricted stock awards.

Income Taxes

Income taxes are accounted for using the liability method, under which deferred tax assets and liabilities are determined based on the temporary 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 calculation of our current provision for income taxes involves the use of estimates, assumptions and judgments while taking into account current tax laws, interpretation of current tax laws and possible outcomes of future tax audits. The Company has established reserves to address potential exposures related to tax positions that could be challenged by tax authorities. Any changes in tax law or interpretation of tax law and the resolutions of potential tax audits could significantly impact the amounts provided for income taxes in our consolidated financial statements.

Comprehensive Loss

Comprehensive loss is composed of net loss and certain changes in stockholders' equity that are excluded from net loss, primarily unrealized gains or 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. The weighted-average common shares outstanding as of December 31, 2025 and 2024 include the pre-funded warrants to purchase shares of common stock. Refer to discussion in Note 8 - "Common Stock".

Recently Issued Accounting Pronouncements

In December 2023, the FASB issued Accounting Standards Update No. 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures*, which requires that an entity, on an annual basis, disclose additional income tax information, primarily related to the rate reconciliation and income taxes paid. The Company has adopted this accounting standard update retrospectively on December 31, 2025. Newly required disclosures has been included in Note 11- "Income Taxes".

In November 2024, the FASB issued Accounting Standards Update No. 2024-03, *Income Statement - Reporting Comprehensive Income - Expense Disaggregation Disclosures (Subtopic 220-40):* D*isaggregation of Income Statement Expenses*, which is intended to improve the disclosures of expenses by providing more detailed information about the types of expenses in commonly presented expense captions. The amendments in this update are effective for annual reporting periods beginning after December 15, 2026, and interim reporting periods beginning after December 15, 2027. Early adoption is permitted. The amendments can be applied either prospectively or retrospectively. The Company has not early adopted this update, and is currently evaluating the impact of this new standard on its consolidated financial statements and related disclosures.

2. Fair Value Measurements

Assets and liabilities measured at fair value at each balance sheet date are as follows (in thousands):

	December 31, 2025			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ 149,874	$ —	$ —	$ 149,874
Commercial paper	—	24,899	—	24,899
Short-term marketable securities:				
U.S. government treasuries	600,084	—	—	600,084
Corporate debt securities	—	62,469	—	62,469
Long-term marketable securities:				
U.S. government treasuries	58,545	—	—	58,545
Corporate debt securities	—	39,777	—	39,777
Total	$ 808,503	$ 127,145	$ —	$ 935,648

	December 31, 2024			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents				
Money market funds	$ 126,728	$ —	$ —	$ 126,728
Short-term marketable securities:				
U.S. government treasuries	629,400	—	—	629,400
Corporate debt securities	—	21,399	—	21,399
Commercial paper	—	6,572	—	6,572
Long-term marketable securities:				
U.S. government treasuries	334,892	—	—	334,892
Corporate debt securities	—	24,481	—	24,481
Total	$ 1,091,020	$ 52,452	$ —	$ 1,143,472

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.

The Company did not transfer any assets or liabilities between the fair value measurement levels during the years ended December 31, 2025 or 2024.

3. Marketable Securities

All marketable securities were considered available-for-sale at December 31, 2025 and 2024. On a recurring basis, the Company records its marketable securities at fair value using Level 1 or Level 2 inputs as discussed in Note 2, "Fair Value Measurements". The amortized cost, gross unrealized holding gains or losses, and fair value of the Company's marketable securities by major security type at each balance sheet date are summarized in the tables below (in thousands):

	December 31, 2025			
	Amortized Cost	Unrealized Holding Gains	Unrealized Holding Losses	Aggregate Fair Value
Short-term marketable securities:				
U.S. government treasuries	$ 599,200	$ 893	$ (9)	$ 600,084
Corporate debt securities	62,407	71	(9)	62,469
Total short-term marketable securities	661,607	964	(18)	662,553
Long-term marketable securities:				
U.S. government treasuries	58,524	21	—	58,545
Corporate debt securities	39,710	69	(2)	39,777
Total long-term marketable securities	98,234	90	(2)	98,322
Total	$ 759,841	$ 1,054	$ (20)	$ 760,875

	December 31, 2024			
	Amortized Cost	Unrealized Holding Gains	Unrealized Holding Losses	Aggregate Fair Value
Short-term marketable securities:				
U.S. government treasuries	$ 627,809	$ 1,618	$ (27)	$ 629,400
Corporate debt securities	21,337	62	—	21,399
Commercial paper	6,572	—	—	6,572
Total short-term marketable securities	655,718	1,680	(27)	657,371
Long-term marketable securities:				
U.S. government treasuries	334,300	788	(196)	334,892
Corporate debt securities	24,354	127	—	24,481
Total long-term marketable securities	358,654	915	(196)	359,373
Total	$ 1,014,372	$ 2,595	$ (223)	$ 1,016,744

As of December 31, 2025 and 2024, some of the Company's marketable securities were in an unrealized loss position. The Company had not recognized an allowance for credit losses as of December 31, 2025 or 2024. The Company determined that it had the ability and intent to hold all marketable securities that have been in a continuous loss position until maturity or recovery. Further, a majority of the Company's investments were held in U.S. government securities, and the remainder were held with investment grade, high credit quality institutions. All marketable securities with unrealized losses as of each balance sheet date had been in a loss position for less than twelve months or the loss is not material.

As of December 31, 2025 all of the Company's marketable securities had an effective maturity of less than two years.

4. Acquisition, License Agreement and Research and Development Funding Collaboration Agreement

Acquisition of F-star Gamma

In May 2018, the Company exercised an option to acquire all of the outstanding shares of F-star Gamma Limited ("F-star Gamma") pursuant to a prenegotiated buy-out option agreement (the "Acquisition"). As a result of the Acquisition, F-star Gamma became a wholly-owned subsidiary of the Company and the Company changed the entity's name to Denali BBB Holding Limited. In addition, the Company became a direct licensee of certain intellectual property of F-star Biotechnology Limited ("F-Star Ltd") by way of the Company's assumption of F-star Gamma's license agreement with F-star Ltd, dated August 24, 2016, (the "F-star Gamma License"). The transaction was accounted for as an asset acquisition.

The Acquisition obligates the Company to make certain contingent payments to former shareholders and under the F-star Gamma license. In 2023, the Company incurred $30.0 million in R&D expenses upon the achievement of a clinical milestone. There was no contingent consideration expense recognized for the years ended December 31, 2025 or 2024. Under this arrangement, the Company may be required to make additional contingent consideration payments of up to $210.0 million, consisting of up to $60.0 million in regulatory contingent payments, including $36.0 million due upon regulatory approval of tividenofusp alfa in the United States, and up to $150.0 million in commercial contingent payments.

Genentech License Agreement

In June 2016, the Company entered into an Exclusive License Agreement with Genentech, Inc. ("Genentech"), giving the Company access to Genentech's LRRK2 inhibitor small molecule program for Parkinson's disease. 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, including up to $37.5 million in clinical milestone payments, $102.5 million in regulatory milestone payments and $175.0 million in commercial milestone payments. In addition, the Company may owe royalties on net sales of licensed products ranging from low to high single-digit percentages.

The Company has made a total of $25.0 million in consideration payments under the Genentech agreement. The Company did not recognize expenses under this agreement in the years ended December 31, 2025, 2024 or 2023.

Collaboration and Development Funding Agreement

In January 2024, the Company entered into a Collaboration and Development Funding Agreement with an unrelated third party, which obligates this third party to provide up to $75.0 million of funding and collaborate with the Company to conduct a global Phase 2a study of BIIB122/DNL151 in patients with Parkinson's disease and confirmed pathogenic variants of LRRK2.

Pursuant to this agreement, the Company has received payments totaling $50.0 million as of December 31, 2025, with the remainder to be paid upon achievement of operational milestones in the study. After the full $75.0 million in consideration has been paid, the third party will be eligible to receive low single-digit royalties from the Company on annual worldwide net sales of LRRK2 inhibitors for the treatment of Parkinson's disease.

The Company determined that this arrangement is an R&D funding arrangement under ASC 730. As the third party is sharing in the risk associated with research and development activities with the Company, the development funding is recognized as an obligation to perform contractual services. Accordingly, payments received are recorded as a liability, and recognized by the Company as a reduction to research and development expenses over the estimated Phase 2a study period as the underlying research and development costs are incurred. Under this arrangement, the Company recognized an offset to research and development expenses of $18.0 million and $10.9 million in the Consolidated Statements of Operations and Comprehensive Loss for the years ended December 31, 2025 and 2024, respectively. The Company recorded current deferred research and development funding liabilities of $21.1 million and $14.1 million on the Consolidated Balance Sheets as of December 31, 2025, and 2024, respectively.

5. Collaboration Agreements

Biogen

In August 2020, the Company entered into a binding Provisional Collaboration and License Agreement (“Provisional Biogen Collaboration Agreement”) with Biogen Inc.’s subsidiaries, Biogen MA Inc. (“BIMA”) and Biogen International GmbH (“BIG”) (BIMA and BIG, collectively, “Biogen”) pursuant to which the Company granted Biogen a license to co-develop and co-commercialize Denali’s small molecule LRRK2 inhibitor program (the “LRRK2 Program”), an option in respect of each of (i) the Company’s amyloid beta program utilizing the Company's TransportVehicle™ ("TV") technology to cross the blood-brain barrier ("BBB") and (ii) one other unnamed program also utilizing the Company's TV technology platform (the “Option Programs”), and a right of first negotiation with respect to two additional unnamed programs utilizing the Company's TV technology platform (the “ROFN Programs”), should the Company decide to seek a collaboration with a third party for such programs. The Provisional Biogen Collaboration Agreement was a binding agreement, which became effective on the closing of the Common Stock Purchase Agreement in September 2020, pursuant to which the Company sold 13,310,243 shares of common stock (the “Shares”) to BIMA for an aggregate purchase price of $465.0 million. The Provisional Biogen Collaboration Agreement expired in October 2020 upon the execution of a Definitive LRRK2 Collaboration and License Agreement (“LRRK2 Agreement”) with Biogen on October 4, 2020 and a Right of First Negotiation, Option and License Agreement (the “ROFN and Option Agreement”) on October 6, 2020 (collectively, the "Biogen Collaboration Agreement"). Biogen made an upfront payment of $560.0 million upon execution of the Biogen Collaboration Agreement in October 2020.

In August 2023, the Company and Biogen executed an Amendment (the “Biogen Amendment”) to the LRRK2 Agreement and ROFN and Option Agreement, pursuant to which Biogen waived its option to the second option program and its ROFN rights. In July 2024, Denali and Biogen executed a Side Letter to the ROFN and Option Agreement, pursuant to which, effective as of the date of the Side Letter, Biogen terminated its license to the Company's amyloid beta program utilizing the Company's TV technology platform, and granted Denali rights to data generated during the collaboration. The side letter also effected the immediate termination of the ROFN and Option Agreement; as such, the Company expects to receive no future milestone or royalty payments from Biogen related to the ROFN and Option Agreement.

LRRK2 Agreement

With respect to the LRRK2 Program, Biogen is required to make milestone payments up to approximately $1.125 billion upon achievement of certain development and sales milestone events. Such milestone payments include $375.0 million in development, $375.0 million upon first commercial sale, and $375.0 million in net sales-based milestones. Pursuant to the Biogen Amendment, the schedule of potential LRRK2 Agreement milestones was amended, while maintaining the same total value of milestones that Denali is eligible to receive. The Company will share 50% of the profits and losses with Biogen for LRRK2 Products in the United States, and 40% of such profits and losses in China. The Company will be entitled to receive royalties in the high teens to low twenties percentages on net sales for LRRK2 Products outside of the United States and China.

The Company and Biogen are jointly developing LRRK2 Products pursuant to a clinical development plan set forth within the LRRK2 Agreement. The parties share responsibility and costs for global development of LRRK2 Products pursuant to a mutually agreed development plan and budget ("LRRK2 Development Activities"), with Biogen funding 60% and the Company funding 40% of such costs.

The Company may opt out of development cost sharing worldwide and upon such election, from any further profit-sharing from the LRRK2 Program. The Company also has the right to opt-out of the profit sharing arrangement for the LRRK2 Program or for only those LRRK2 Products that do not penetrate the BBB (“Peripheral LRRK2 Products”), in each of the United States and China. After such an opt out, the Company will no longer be obligated to share in the development and commercialization costs for, or be entitled to share in the applicable revenues from, such LRRK2 Program (or from the Peripheral LRRK2 Products) for such country, as applicable. If the Company chooses to exercise its opt out rights, the Company will be entitled to receive tiered royalties on net sales of the applicable LRRK2 Program in the relevant country (or countries). The royalty rates for the applicable LRRK2 Program will be a percentage in the high teens to low twenties, but may increase to the mid-twenties if the Company has met certain co-funding thresholds or there has been a first commercial sale at the time of the Company's election.

Biogen Collaboration Agreement

The Company believes that the Biogen Collaboration Agreement is a collaboration arrangement as defined in ASC 808, Collaborative Arrangements, and that Biogen meets the definition of a customer as defined in ASC 606, Revenue From Contracts With Customers for all of the performance obligations identified at inception except for the LRRK2 Development Activities. Since ASC 808 does not address recognition and measurement, the Company looked to other accounting literature for guidance where the performance obligation does not fall under ASC 606, and determined that for the interim LRRK2 development activities subject to cost sharing provisions, the guidance in ASC 730, Research and Development should be applied. The LRRK2 Development Activities cost sharing reimbursements or expenses are being recognized over time as earned or incurred, since this is believed to directly correlate to the value of the services performed.

As of December 31, 2025, the Company had earned $5.0 million in option fee payments, but had not recorded milestone revenue or product sales under the Biogen Collaboration Agreement.

Sanofi

In October 2018, the Company entered into a Collaboration and License Agreement ("Sanofi Collaboration Agreement") with Genzyme Corporation, a wholly owned subsidiary of Sanofi S.A. ("Sanofi") pursuant to which certain small molecule CNS and peripheral receptor interacting serine/threonine protein kinase 1 ("RIPK1") inhibitors contributed by Sanofi and by the Company would be developed and commercialized. When the Sanofi Collaboration Agreement became effective in November 2018, Sanofi paid us $125.0 million upfront. Under the Sanofi Collaboration Agreement, Sanofi is required to make milestone payments totaling up to approximately $495.0 million upon achievement of certain clinical, regulatory and sales milestone events for the Peripheral Products. Such milestone payments include $120.0 million in clinical milestone payments, $175.0 million in regulatory milestone payments and $200.0 million in commercial milestone payments for Peripheral Products, as defined, that are developed and approved in the United States, Europe and in Japan for three indications. Sanofi has made payments of $35.0 million for Peripheral Product clinical milestones through December 31, 2025, and payments of $65.0 million for CNS Product clinical milestones through the sale date. On February 24, 2025, Denali and Sanofi executed a side letter terminating Sanofi's license to the CNS Products program including SAR443820/DNL788. Subsequent to this side letter, the Company expects to receive no future milestone or royalty payments from Sanofi related to the CNS Products program. The Company will receive variable royalties on net sales for Peripheral Products sold worldwide, each as further described below.

Sanofi will be responsible, at its cost, for conducting activities relating to the development and commercialization of all Peripheral Products. Denali will be entitled to receive tiered royalties in the low- to mid- teen percentages on net sales of Peripheral Products.

The Company believes that the Sanofi Collaboration Agreement is a collaboration arrangement as defined in ASC 808, Collaborative Arrangements.

During the year ended December 31, 2023, the Company earned a clinical milestone of $25.0 million when the associated performance obligation was satisfied, which was recognized in collaboration revenue from customers in the Consolidated Statement of Operations and Comprehensive Loss. There were no milestones recognized in collaboration revenue from customers in the Consolidated Statement of Operations and Comprehensive Loss for the years ended December 31, 2025 or 2024.

The Company has no remaining performance obligations under the Sanofi Collaboration Agreement, and no contract liability remains on the Consolidated Balance Sheets as of December 31, 2025 or 2024. As of December 31, 2025, the Company had earned milestone payments of $100.0 million. and had not recorded any product sales under the Sanofi Collaboration Agreement.

Takeda

Takeda Collaboration Agreement

In January 2018, the Company entered into a Collaboration and Option Agreement ("Takeda Collaboration Agreement") with Takeda Pharmaceutical Company Limited ("Takeda"), pursuant to which the Company granted Takeda an option to develop and commercialize, jointly with the Company, certain biologic products that are enabled by the Company's BBB delivery technology and intended for the treatment of neurodegenerative disorders, concurrent with a stock purchase agreement under which Takeda purchased 4,214,559 shares of Denali common stock for $110.0 million. The programs subject to the Takeda Collaboration Agreement were the Company's ATV:BACE1/Tau, ATV:TREM2 and PTV:PGRN programs. The Takeda Collaboration Agreement became effective in February 2018, at which time Takeda paid the Company an upfront payment of $40.0 million. In February 2019, the agreement was amended to replace the ATV:BACE1/Tau program with the ATV:Tau program, and in March 2022, Takeda and the Company agreed to terminate activity on the ATV:Tau program. Subsequent to the ATV:Tau termination, total preclinical milestone payments that Takeda owed under the Takeda Collaboration Agreement was $55.0 million for all three programs, all of which had been earned and received as of December 31, 2022.

Subsequent to Takeda exercising its option with respect to a particular target and collaboration program (i.e., the biologic products directed to the target for which Takeda has exercised its option), Takeda has the right to develop and commercialize, jointly with the Company, a specified number of biologic products enabled by its BBB delivery technology that were developed during the research period and which are directed to the relevant target, and the Company grants to Takeda a co-exclusive license under the intellectual property the Company controls related to those biologic products.

The Company did not record any product sales and there are no remaining performance obligations under the initial Takeda Collaboration Agreement. The Takeda Collaboration Agreement was superseded by the PTV:PGRN and ATV:TREM2 Collaboration Agreements subsequent to opt-in for the two programs in November and December 2021, respectively, recognition of all preclinical milestones, and termination of the ATV:Tau program. In February 2025, after mutual agreement to discontinue preclinical activities on ATV:TREM2, Takeda delivered notice of its election to terminate the ATV:TREM2 program, as per the terms of the Takeda Collaboration Agreement. Subsequent to the effective date of the termination of the ATV:TREM2 Collaboration Agreement, there are no future milestones, cost, or profit sharing related to this agreement. Prior to its termination, the ATV:TREM2 Collaboration Agreement was accounted for consistent with the treatment of the PTV:PGRN Collaboration Agreement, which is discussed in the subsequent section.

PTV:PGRN Collaboration Agreement

In November 2021, Takeda exercised its options to jointly develop and commercialize the PTV:PGRN program, triggering the option fee of $5.0 million, which formed the transaction price at contract inception, all of which was allocated to the underlying Technology License which was delivered on or around the effective date of the Collaboration Agreement. Management determined that the opt-in by Takeda on the PTV:PGRN program represents a new contract with a customer for accounting purposes (the "PTV:PGRN Collaboration Agreement"), effective in December 2021 upon payment of the option fee. From inception of the PTV:PGRN Collaboration Agreement through December 31, 2025, there was no change to the terms of the agreement.

The Company believes that the PTV:PGRN Collaboration Agreement is a collaboration arrangement as defined in ASC 808, Collaborative Arrangements. The Company also believes that Takeda meets the definition of a customer as defined in ASC 606, Revenue From Contracts With Customers for the PTV:PGRN Technology License performance obligation delivered in the collaboration agreement. Since ASC 808 does not address recognition and measurement, the Company looked to other accounting literature for the PTV:PGRN Development Activities unit of account, and determined that the guidance in ASC 730, Research and Development should be applied.

Under the PTV:PGRN Collaboration Agreement, Takeda may be obligated to pay the Company up to $140.0 million upon achievement of certain clinical milestone events and up to $100.0 million in regulatory milestone events relating to receipt of regulatory approval in the United States, certain European countries and Japan. Takeda may also be obligated to pay the Company up to $75.0 million upon achievement of a certain sales-based milestone. Further, the Company and Takeda share equally the development and commercialization costs, and, if applicable, the profits, for the PTV:PGRN program.

A $10.0 million milestone was triggered under the PTV:PGRN Collaboration Agreement upon achievement of a specified clinical milestone and recognized in collaboration revenue from customers in the Consolidated Statement of Operations and Comprehensive Loss for the year ended December 31, 2023. No product sales have been recorded under the agreement.

Collaboration Revenue

Revenue disaggregated by collaboration agreement and performance obligation is as follows (in thousands):

	Year Ended December 31,		
	2025	**2024**	**2023**
Takeda Collaboration Revenue - PTV:PGRN Program	—	—	10,000
Sanofi Collaboration Revenue - CNS Program	—	—	25,000
Biogen Collaboration Agreement:			
ATV:Abeta Program License[1]	—	—	293,912
Option Research Services[2]	—	—	1,619
Total Biogen Collaboration Revenue	—	—	295,531
Total Collaboration Revenue	$ —	$ —	$ 330,531

(1) Revenue of $288.9 million for the year ended December 31, 2023 was included in the related-party contract liability balance at the beginning of the period.
(2) Revenue was included in the contract liability balance at the beginning of the year.

Cost Sharing Payments and Reimbursements

Cost sharing payments to collaboration partners recorded as expenses in research and development expenses in the Consolidated Statements of Operations and Comprehensive Loss, and cost sharing reimbursements from collaboration partners recorded as an offset to research and development expenses in the Consolidated Statements of Operations and Comprehensive Loss are as follows (in thousands):

	Year Ended December 31,		
	2025	2024	2023
Takeda Collaboration Agreement:			
PTV:PGRN cost sharing (reimbursements)	$ (6,456)	$ (4,789)	$ (7,065)
ATV:TREM2 cost sharing (reimbursements)	(147)	(1,147)	(5,100)
Total Takeda cost sharing (reimbursements)[1]	(6,603)	(5,936)	(12,165)
Biogen Collaboration Agreement: LRRK2 cost sharing payments[2]	15,805	16,742	17,678
Net cost sharing payments (reimbursements)	$ 9,202	$ 10,806	$ 5,513

(1) Cost sharing reimbursements of $1.6 million and $1.5 million were recorded as a receivable within prepaid expenses and other current assets on the Consolidated Balance Sheets as of December 31, 2025 and 2024, respectively.

(2) Cost sharing payments due to Biogen of $2.8 million and $2.5 million were recorded within accounts payable on the Consolidated Balance Sheets as of December 31, 2025 and 2024, respectively.

6. Balance Sheet Components

Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consists of the following (in thousands):

	As of December 31,	
	2025	2024
Accounts receivable and other receivables	$ 2,177	$ 2,171
Prepaid clinical research & development costs	7,280	6,473
Prepaid manufacturing and other research & development costs	10,249	16,196
Other prepaid assets and other current assets	13,073	7,265
Total prepaid expenses and other current assets	$ 32,779	$ 32,105

Property and Equipment, Net

Property and equipment, net consists of the following (in thousands):

	As of December 31,	
	2025	2024
Leasehold improvements	$ 47,755	$ 46,905
Laboratory equipment	45,797	40,554
Manufacturing equipment	17,493	15,998
Computer equipment and purchased software	2,203	1,841
Furniture and fixtures	2,049	1,980
Total property and equipment	115,297	107,278
Less: accumulated depreciation	(62,895)	(52,042)
Total property and equipment, net	$ 52,402	$ 55,236

Depreciation expense was $11.2 million, $7.8 million and $16.7 million for the years ended December 31, 2025, 2024 and 2023, respectively. Depreciation expense for the year ended December 31, 2023 includes $7.9 million of accelerated depreciation on leasehold improvements due to the Company terminating the previous SLC Lease in March 2023.

Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consists of the following (in thousands):

	As of December 31,	
	2025	2024
Accrued compensation	$ 32,179	$ 24,728
Accrued clinical and other research & development costs	19,458	22,822
Accrued manufacturing costs	5,336	12,779
Operating lease liability, current	9,463	8,308
Finance lease liability, current	83	3,726
Deferred research and development funding liability, current	21,101	14,129
Other accrued costs and current liabilities	7,401	4,579
Total accrued expenses and other current liabilities	$ 95,021	$ 91,071

7. Commitments and Contingencies

Lease Obligations

In May 2018, the Company entered into an operating lease for its corporate headquarters in South San Francisco (the "Headquarters Lease"), a 148,020 rentable square feet building in South San Francisco, California (the "Headquarters"). The Headquarters Lease has a contractual term of 10 years which ends on March 31, 2029, after which the Company has an option to extend the lease term for a further ten years. The Company determined that this renewal was not reasonably certain at lease inception. The accounting lease commencement date was determined to be August 1, 2018.

The Headquarters Lease provides for monthly base rent amounts escalating over the term of the lease. In addition, the Headquarters Lease provided a tenant improvement allowance ("TIA") of up to $25.9 million, which was fully utilized, of which $4.4 million will be repaid to the landlord in the form of additional monthly rent. This is recorded as leasehold improvement assets and an offset to the lease ROU asset on the Consolidated Balance Sheets. The Company is also required to pay the operating expenses for the Headquarters, such as taxes and insurance, which are treated as variable lease payments.

In August 2021, the Company entered into an operating lease for laboratory, office and warehouse facilities in Salt Lake City, Utah. In March 2023, the Company terminated this operating lease, which resulted in the recognition of $7.9 million of accelerated depreciation on leasehold improvements during the year ended December 31, 2023. The lease had not commenced for accounting purposes.

In April 2023, the Company entered into a finance lease for its clinical manufacturing site in Salt Lake City (the "SLC Lease") for a 59,336 square foot laboratory, office and warehouse premises with a contractual term of approximately 15 years, and undiscounted lease payments of approximately $13.4 million, which was subsequently amended in October 2023. The Company has the option to extend the lease term for a period of ten years at the end of the lease term. The accounting lease commencement date was determined to be August 1, 2024, the date the Company was deemed to have obtained control over the property, at which time the lease was determined to be a finance lease and the lease liability and ROU asset were recorded on the Consolidated Balance Sheets. The Finance lease ROU asset includes approximately $47.4 million of lessor owned improvements funded by the Company.

Management exercised judgment in applying the requirements of ASC 842, including the determination as to whether certain contracts contain a lease, lease classification, the lease consideration, and the commencement date of the leases, and for leases identified under the standard, the discount rate used to determine the measurement of the lease liability. The discount rates of the Company's operating and finance leases are an approximation of the Company's incremental borrowing rate and are dependent upon the term and economics of the agreement. To estimate the incremental borrowing rates, management considered observable debt yields of comparable market instruments, as well as benchmarks within the lease agreement that may be indicative of the rate implicit in the lease. There were no changes to the terms of the leases recognized under ASC 842 during the year ended December 31, 2025.

The following table summarizes lease costs recognized for the periods presented (in thousands):

	Year Ended December 31,		
	2025	2024	2023
Operating lease cost	$ 7,595	$ 7,189	$ 7,983
Finance lease cost:			
Amortization of ROU assets	3,629	1,197	—
Interest	720	302	—
Variable lease cost	5,806	5,065	4,458
Total lease costs	$ 17,750	$ 13,753	$ 12,441

The following table contains a summary of other information pertaining to the Company’s leases for the periods presented (in thousands):

	Year Ended December 31,		
	2025	2024	2023
Operating cash flows from operating lease	$ 11,793	$ 11,417	$ 11,345

	As of December 31,		
	2025	2024	2023
Weighted-average remaining lease term (in years):			
Operating lease	3.3 years	4.3 years	5.3 years
Finance lease	13.3 years	14.3 years	—
Weighted-average discount rate applied (%):			
Operating lease	9.0 %	9.0 %	9.0 %
Finance lease	13.7 %	13.7 %	— %

The following table reconciles the undiscounted cash flows for the next five years and total of the remaining years to the operating and finance lease liabilities recorded in the Consolidated Balance Sheet as of December 31, 2025 (in thousands):

Year Ended December 31:	Operating Lease	Finance Lease
2026	$ 12,182	$ 794
2027	12,584	811
2028	13,001	829
2029	4,381	848
2030	—	867
Thereafter	—	7,947
Total undiscounted lease payments	42,148	12,096
Less: present value adjustment	(5,475)	—
Less: imputed interest	—	(6,481)
Total future minimum lease payments	$ 36,673	$ 5,615

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 Consolidated Balance Sheets, Consolidated Statements of Operations and Comprehensive Loss, or Consolidated Statements of Cash Flows.

Commitments

In the normal course of business, the Company enters into firm purchase commitments primarily related to supply of pre-launch commercial product, research, development and manufacturing activities. The Company had contractual obligations under certain commercial product, clinical and manufacturing agreements of $44.3 million and $60.8 million, as of December 31, 2025 and 2024, respectively. Further, the Company had other commitments of $1.5 million and $2.2 million as of both December 31, 2025 and 2024, respectively.

Royalty Pharma Funding Agreement

On December 4, 2025, the Company entered into a royalty funding arrangement (the "Royalty Agreement") with Royalty Pharma plc ("Royalty Pharma"). Pursuant to the Royalty Agreement, Royalty Pharma agreed to provide up to $275.0 million in funding to the Company in exchange for a 9.25% royalty on worldwide net sales of tividenofusp alfa. The transaction is subject to various closing conditions, including the Company achieving FDA approval of tividenofusp alfa on or before June 30, 2026. At closing, Royalty Pharma will make an initial payment of $200.0 million and Royalty Pharma will be obligated to make an additional payment of $75.0 million upon European Medicines Agency (the "EMA") approval of tividenofusp alfa on or before December 31, 2029. Royalty payments will cease upon Royalty Pharma receiving a multiple of 3.0x of the initial investment proceeds, or 2.5x if achieved by the first quarter of 2039. As of December 31, 2025, the transaction had not closed and no liability related to the Royalty Agreement was recorded in the consolidated financial statements.

Contingencies

From time to time, the Company may be involved in lawsuits, arbitration, claims, investigations and proceedings consisting of intellectual property, employment and other matters which arise in the ordinary course of business. The Company records accruals for loss contingencies to the extent that the Company concludes that it is probable that a liability has been incurred and the amount of the related loss can be reasonably estimated.

8. Common Stock

In February 2024, the Company entered into a securities purchase agreement (the "Purchase Agreement") with certain investors for the private placement of (i) 3,244,689 shares of the Company's common stock at a price of $17.07 per share and (ii) pre-funded warrants (the "Pre-Funded Warrants") to purchase an aggregate of 26,046,065 shares of the Company's common stock at a purchase price of $17.06 per pre-funded warrant, which represents the per share price for the common stock less the $0.01 exercise price. The private placement closed on February 29, 2024, at which time the Company received aggregate net proceeds of approximately $499.3 million, after deducting issuance costs of approximately $0.5 million.

On December 9, 2025, the Company entered into an underwriting agreement (the “Underwriting Agreement”) with Goldman Sachs & Co. LLC, J.P. Morgan Securities LLC and Morgan Stanley & Co. LLC as representatives of the several underwriters named therein (collectively, the “Underwriters”), relating to the public offering of (i) 9,142,857 shares of the Company’s common stock, at a public offering price of $17.50 per share, and (ii) additional Pre-Funded Warrants to purchase 2,285,714 shares of Common Stock at a public offering price of $17.49 per pre-funded warrant, which represents the per share price for the common stock less the $0.01 exercise price. The public offering closed on December 11, 2025, at which time the Company received aggregate net proceeds of approximately $189.2 million, after deducting issuance costs of approximately $0.7 million. In January 2026, the underwriters exercised their option to purchase an additional 746,468 shares of the Company’s Common Stock, on which date the Company received aggregate net proceeds of approximately $12.4 million.

All of the Pre-Funded Warrants issued in the aforementioned private placement and the public offering were outstanding as of December 31, 2025, and were classified as a component of permanent equity in the Company’s consolidated balance sheet as they are freestanding financial instruments that are immediately exercisable, do not embody an obligation for the Company to repurchase its shares and permit the holders to receive a fixed number of shares of common stock upon exercise.

9. Stock-Based Awards

Equity Incentive Plans

The Company's equity incentive plans, the 2017 Equity Incentive Plan (the “2017 Plan”), and previously, the 2015 Stock Incentive Plan (the “2015 Plan”), reserve shares of common stock for the issuance of 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. Upon adoption of the 2017 Plan, no new awards or grants are permitted under the 2015 Plan. The 2015 Plan continues to govern restricted stock awards and option awards previously granted thereunder.

Awards granted under the 2017 Plan and 2015 Plan expire no later than ten years from the date of grant. For stock options, the option price shall not be less than 100% of the estimated fair value of the Company's common stock on the day of grant. Options granted typically vest over a four-year period but may be granted with different vesting terms.

The 2017 Plan provides that the number of shares reserved and available for issuance under the 2017 Plan will automatically increase each January 1, beginning on January 1, 2019, by the lesser of (i) 10.0 million shares, (ii) 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 of the 2017 Plan. In 2025, common stock available for issuance under the 2017 Plan was increased by approximately 7.2 million shares as a result of this automatic increase provision. As of December 31, 2025 and 2024, there were approximately 14.8 million and 14.3 million common shares available for the Company to grant under the 2017 Plan, respectively.

Stock Option Activity

The following table summarizes option award activity under the 2017 Plan and 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, 2024	18,660,150	$ 25.99	5.94	$ 48,266
Granted	5,019,276	19.57		
Exercised	(773,881)	1.81		
Forfeited	(734,841)	25.16		
Expired	(844,371)	0.68		
Balance at December 31, 2025	21,326,333	$ 26.39	6.21	$ 10,658
Vested and expected to vest at December 31, 2025	21,326,333	$ 26.39	6.21	$ 10,658
Exercisable at December 31, 2025	13,674,635	$ 29.46	4.84	$ 8,497

Aggregate intrinsic value represents the difference between the fair value of the Company's common stock and the exercise price of outstanding options. The total intrinsic value of options exercised was $10.8 million, $10.6 million, and $12.1 million as of December 31, 2025, 2024 and 2023, respectively. During the years ended December 31, 2025, 2024, and 2023 the weighted-average grant-date fair value of the options vested was $16.30, $23.61, and $24.30 per share, respectively. The weighted-average grant date fair value of all options granted during the years ended December 31, 2025, 2024 and 2023 was $12.35, $12.99, and $17.95 per share, respectively.

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, which requires various assumptions, including the fair value of the Company’s common stock, expected term, expected dividend yield, expected volatility, and the risk-free interest rate. The fair value of the Company’s common stock is based on the current market price, unless an adjustment is determined to be required, through discussion with senior management, due to material non-public information known by the Company at the time of grant. The expected volatility used in valuing stock options granted in 2024 and 2025 is based solely on the historical volatility of the Company’s common stock. For 2023, because the Company did not have sufficient trading history to rely exclusively on its own stock price volatility, expected volatility was determined using a combination of the Company’s historical volatility and the historical volatility of comparable publicly traded biotechnology and pharmaceutical companies over a period consistent with the expected term of the awards. Management considers whether the Company is in possession of material non-public information at the time of grants when making certain estimates, including volatility and the fair value of the Company's common stock. The expected term of stock options represents the period that the Company’s stock-options 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). The risk-free interest rate is based on the implied yield currently available on U.S. treasury notes with terms approximately equal to the expected life of the option. The expected dividend rate is zero as the Company currently has no history or expectation of declaring cash dividends on the Company’s common stock.

The following assumptions were used in estimating the fair value of grants during the year ended:

	December 31,		
	2025	2024	2023
Expected term (in years)	5.50 - 6.08	5.50 - 6.08	5.50 - 6.08
Volatility	64.8% - 68.7%	64.5% - 66.0%	67.6% - 69.6%
Risk-free interest rate	3.6% - 4.5%	3.7% - 4.5%	3.4% - 4.8%
Dividend yield	—	—	—

Restricted Stock Activity

We grant restricted stock units ("RSUs") under the 2017 Plan. The fair value of restricted stock underlying the RSUs is determined based on the closing market price of the Company's common stock on the date of grant.

Aggregated information regarding RSUs granted under the Plan for the year ended December 31, 2025 is summarized below:

	Number of Units	Weighted-Average Fair Value at Date of Grant per Share
Unvested at December 31, 2024	4,128,514	$ 27.33
Granted	2,726,354	18.76
Vested and released	(1,449,761)	32.12
Forfeited	(280,478)	21.49
Unvested and expected to vest at December 31, 2025	5,124,629	$ 21.74

The aggregate intrinsic value of RSUs is calculated as the closing price per share of the Company's common stock on the last trading day of the fiscal period, multiplied by outstanding RSUs as of December 31, 2025. The total intrinsic value of RSUs expected to vest was $84.6 million as of December 31, 2025. During the years ended December 31, 2024 and 2023 the weighted-average grant-date fair value of RSUs granted was $21.01 and $27.38, respectively. The total fair value of RSUs that vested during the years ended December 31, 2025, 2024, and 2023 was $27.1 million, $27.6 million, and $31.6 million, respectively.

Stock-Based Compensation Expense

The Company’s stock-based compensation expense was as follows (in thousands):

	Year Ended December 31,		
	2025	2024	2023
Research and development	$ 59,490	$ 59,146	$ 62,901
General and administrative	40,143	43,732	45,201
Total	$ 99,633	$ 102,878	$ 108,102

As of December 31, 2025, total unamortized stock-based compensation expense was $161.0 million. The weighted-average period over which such stock-based compensation expense will be recognized is approximately 2.5 years.

There was no tax benefit realized related to awards vested or exercised during the years ended December 31, 2025, 2024 and 2023. There is no deferred tax benefit on total stock-based compensation expense for the years ended December 31, 2025, 2024 and 2023 since the company has recorded a full valuation allowance on all deferred tax assets.

10. Defined Contribution Plan

The Company sponsors a 401(k) retirement savings plan for the benefit of its employees, including Denali's 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 Company made contributions to the Plan for eligible participants, and recorded contribution expenses of $3.7 million, $3.0 million and $3.2 million for the years ended December 31, 2025, 2024, and 2023 respectively.

11. Income Taxes

The provision for income taxes consisted of the following (in thousands):

	Year Ended December 31,		
	2025	2024	2023
Current:			
U.S. Federal	$ —	$ —	$ —
U.S. State	—	—	—
Foreign	102	68	30
Total Current	$ 102	$ 68	$ 30
Deferred:			
U.S. Federal	$ —	$ —	$ —
U.S. State	—	—	—
Foreign	—	—	—
Total deferred	$ —	$ —	$ —
Total provision for income taxes	$ 102	$ 68	$ 30

The reconciliation of federal statutory income tax rate to our effective income tax rate is as follows:

	Year Ended December 31,					
	2025		2024		2023	
(In thousands, except percentages)	Amount	Rate	Amount	Rate	Amount	Rate
Taxes at the U.S. statutory tax rate of 21%	$ (107,612)	21.0 %	$ (88,531)	21.0 %	$ (30,490)	21.0 %
State income taxes, net of federal tax benefit	1,516	(0.3)	—	—	—	—
Foreign tax effects	51	—	15	—	27	—
Effective of cross-border tax laws	80	—	70	—	908	(0.6)
Change in valuation allowance	124,243	(24.2)	106,498	(25.3)	37,886	(26.1)
Tax Credits						
Research Tax Credit	(21,990)	4.3	(24,660)	5.9	(23,011)	15.9
Effect of changes in tax laws or rates enacted in the current period	—	—	—	—	—	—
Nontaxable or Nondeductible items						
Stock-based compensation	6,286	(1.2)	9,579	(2.3)	5,777	(4.0)
Nondeductible acquisition - related costs	—	—	—	—	5,040	(3.5)
Other	261	(0.1)	(2,930)	0.7	220	(0.2)
Changes in UTB	(1,573)	0.3	173	—	401	(0.3)
Other	(1,160)	0.2	(146)	—	3,273	(2.3)
Total provision for income taxes	$ 102	— %	$ 68	— %	$ 30	— %

On July 4, 2025, the U.S. enacted tax reform legislation through the One Big Beautiful Bill Act (“OBBBA”). Included in this legislation are provisions that allow for the immediate expensing of domestic research and development expenses, immediate expensing of certain capital expenditures, and other changes to the U.S. taxation of profits derived from foreign operations. The legislation has multiple effective dates, with certain provisions effective in the current fiscal period and others in the fiscal year ending December 31, 2026. OBBBA did not have a material impact to the Company’s consolidated financial statements for the year ended December 31, 2025.

Deferred Income Taxes

The components of the Company's net deferred tax assets are as follows (in thousands):

	December 31,	
	2025	2024
Deferred tax assets:		
Net operating loss carryforwards	$ 229,535	$ 113,397
Tax credit carryforwards	155,334	124,922
Research expense capitalization	161,588	176,094
Lease liabilities	9,819	11,760
Stock-based compensation	67,511	57,766
Fixed assets	8,588	6,671
Accruals and other	14,111	13,447
Gross deferred tax assets	646,486	504,057
Valuation allowance	(630,806)	(487,714)
Net deferred tax assets	15,681	16,343
Deferred tax liabilities:		
Lease right-of-use assets	(15,681)	(16,343)
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 full valuation allowance against its net deferred tax assets as of December 31, 2025 and 2024. There was an increase in the net valuation allowance of $143.1 million during the year ended December 31, 2025.

As of December 31, 2025, the Company has federal net operating loss ("NOL") carryforwards of approximately $964.9 million, which are available to reduce future taxable income, and has federal R&D and orphan drug tax credits of approximately $73.8 million and $75.0 million respectively, both of which may be used to offset future tax liabilities. The federal NOL and federal tax credit carryforwards will begin to expire in 2034. The Company also has state NOL carryforwards of approximately $398.4 million, which are available to reduce future taxable income, and has state tax credits of approximately $55.1 million which may be used to offset future tax liabilities. The state NOL will begin to expire in 2031 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. Annual limitations may result in expiration of net operating loss and tax credit carryforwards before some or all of such amounts have been utilized.

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,		
	2025	2024	2023
Unrecognized tax benefits at January 1	$ 33,761	$ 26,175	$ 19,371
Additions for tax positions taken in a prior year	169	162	168
Additions for tax positions taken in the current year	7,475	7,424	6,636
Reductions for tax positions taken in the prior year	(2,100)	—	—
Audit settlements	(53)	$ —	$ —
Unrecognized tax benefits at December 31	$ 39,252	$ 33,761	$ 26,175

If recognized, none of the unrecognized tax benefits would reduce the effective tax rate for the year ended December 31, 2025. The Company will recognize both accrued interest and penalties related to unrecognized benefits in income tax expense. As of December 31, 2025, 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.

The Company's 2015 to 2025 tax years remain subject to examination in the United States and California due to tax attributes and statutes of limitations. The Company remains subject to possible examination in various other jurisdictions that are not expected to result in material tax adjustments.

12. Net Loss and 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,		
	2025	2024	2023
Numerator:			
Net loss	$ (512,540)	$ (422,773)	$ (145,224)
Denominator:			
Weighted average number of:			
Common stock shares outstanding	146,471,525	142,626,390	137,370,897
Pre-funded warrants	26,177,572	21,847,382	—
Total	172,649,097	164,473,772	137,370,897
Net loss per share	$ (2.97)	$ (2.57)	$ (1.06)

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, including all options issued and outstanding, ESPP shares issuable, restricted shares subject to future vesting, and shares potentially issuable to the underwriters upon exercise of their option associated with the December 2025 public offering, that were not included in the diluted per share calculations for all periods presented because they would be anti-dilutive totaled approximately 28.8 million, 23.2 million and 20.5 million shares as of December 31, 2025, 2024, and 2023, respectively.

13. Divestiture of Preclinical Small Molecule Programs

In March 2024, the Company divested certain assets, including specified intellectual property, tangible assets, and equipment used to conduct early stage small molecule drug discovery ("Divested Assets") through an Asset Purchase and License Agreement (the "Asset Purchase Agreement") executed with Tenvie Therapeutics, Inc. ("Tenvie"). Additionally, certain of the Company's employees terminated their employment with the Company and became employees of Tenvie.

In exchange for the Divested Assets, the Company received equity consideration of $15.0 million in the form of a simple agreement for future equity ("SAFE"). In December 2024, the SAFE converted into 15.0 million shares of Tenvie's Series A Preferred Stock, par value $0.0001 per share, with a fair value of $15.0 million. Under the terms of the Asset Purchase Agreement, the Company is eligible to receive certain market valuation, development and sales based milestone payments up to approximately $1.2 billion in the form of either cash or equity at the election of Tenvie. The Company will also be entitled to receive future royalties on aggregate net sales of certain products, on a product-by-product and country-by-country basis during the periods of time commencing at the time of the first commercial sale of such product in such country, until the later of (i) the expiration of certain related patents, (ii) the expiration of Regulatory Exclusivity, or (iii) ten years after such first commercial sale.

This divestiture did not meet the criteria for reporting discontinued operations as the sale does not represent a strategic shift in the Company's business. The Company recognized a gain on divestiture of approximately $14.5 million in the Consolidated Statements of Operations and Comprehensive Loss during the year ended December 31, 2024, representing the difference between the fair value of the consideration received and the carrying amount of the Divested Assets.

The Company recorded the investment in the shares of Series A Preferred Stock at $15.0 million which represents the fair value of the shares on the date of issuance. There have been no subsequent observable price changes in orderly transactions for the identical or similar equity securities of Tenvie, and as such, the measurement of this investment remains unchanged, with the $15.0 million included within other non-current assets in the Consolidated Balance Sheet as of December 31, 2025 and 2024.

14. Segment Information

The Company has one operating segment with the goal to discover, develop and commercialize therapeutics ("Therapeutics"). The Company has not generated any revenue from product sales, and has no marketing or commercial product distribution costs. All revenue to date has been collaboration and license revenue from the Company's collaboration agreements.

The Company's chief operating decision maker ("CODM"), its Chief Executive Officer, manages the Company's operations on a consolidated basis for the purposes of allocating resources.

The CODM, in alignment with the Company's overall corporate strategy and goals, analyses a variety of data to guide segment resource allocation, including program and portfolio scientific data, product market information and projections, probability of regulatory and commercial success, and the competitive environment. The CODM also reviews certain financial results included in the segment Loss from Operations which is reported on the Consolidated Statements of Operations and Comprehensive Loss as Loss from Operations. The measure of segment assets is reported on the Consolidated Balance Sheets as Total Assets. The accounting policies of the Therapeutics segment are the same as those described in the summary of significant accounting policies.

The following table presents selected financial information with respect to the Company's single operating segment for the years ended December 31, 2025, 2024, and 2023 (in thousands):

	Therapeutics Segment Year Ended December 31,		
	2025	2024	2023
Total collaboration revenue	$ —	$ —	$ 330,531
Expenses			
External research and development expenses - TV programs, including cost sharing	154,799	138,196	139,064
External research and development expenses - small molecule programs, including cost sharing	8,800	42,623	49,850
Other research and development expenses	86,958	62,715	74,518
Personnel related research and development expenses	168,221	152,906	160,444
Total research and development expenses	418,778	396,440	423,876
Personnel related general and administrative expenses	86,234	73,505	73,668
Other general and administrative expenses	50,330	31,933	29,686
Total general and administrative expenses	136,564	105,438	103,354
Segment operating expenses	555,342	501,878	527,230
Segment gain from divestiture of small molecule programs	—	14,537	—
Segment loss from operations	(555,342)	(487,341)	(196,699)
Segment interest and other income, net	42,904	64,636	51,505
Segment loss before income taxes	$ (512,438)	$ (422,705)	$ (145,194)

There is no difference between the segment loss before income taxes and total consolidated loss before income taxes for the years ended December 31, 2025, 2024 and 2023.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Conclusions Regarding the Effectiveness of Disclosure Controls and Procedures

As of December 31, 2025, management, with the participation of our Chief Executive Officer and Chief Financial Officer, performed an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act. Our disclosure controls and procedures are designed to ensure that information required to be disclosed in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including the Chief Executive Officer and the Chief Financial Officer, to allow timely decisions regarding required disclosures.

Any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objective and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on this evaluation, our Chief Executive Officer and Chief Financial Officer concluded that, as of December 31, 2025, the design and operation of our disclosure controls and procedures were effective at a reasonable assurance level.

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the quarter ended December 31, 2025 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act). Under the supervision of and with the participation of our principal executive officer and principal financial officer, our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2025 based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in "Internal Control—Integrated Framework" (2013). Based on this assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2025.

The effectiveness of our internal control over financial reporting as of December 31, 2025 has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in their report which is included herein.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Denali Therapeutics Inc.

Opinion on Internal Control Over Financial Reporting

We have audited Denali Therapeutics Inc.'s internal control over financial reporting as of December 31, 2025, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Denali Therapeutics Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2025, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2025 and 2024, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2025, and the related notes and our report dated February 26, 2026 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Annual Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's 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 generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP
San Mateo, California
February 26, 2026

ITEM 9B. OTHER INFORMATION

Securities Trading Plans of Directors and Executive Officers

No officers or directors, as defined in Rule 16a-1(f), adopted and/or terminated of a “Rule 10b5-1 trading arrangement” or a “non-Rule 10b5-1 trading arrangement,” as defined in Regulation S-K Item 408, during the fourth quarter ended December 31, 2025.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

Information required by this item will be contained in our definitive proxy statement to be filed with the SEC on Schedule 14A in connection with our 2026 Annual Meeting of Stockholders (the "Proxy Statement"), which is expected to be filed not later than 120 days after December 31, 2025, and is incorporated herein by reference.

ITEM 11. EXECUTIVE COMPENSATION

Information required by this item will be contained in the Proxy Statement and is incorporated herein by reference.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

Information required by this item will be contained in the Proxy Statement and is incorporated herein by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS AND DIRECTOR INDEPENDENCE

Information required by this item will be contained in the Proxy Statement and is incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

Information required by this item will be contained in the Proxy Statement and is incorporated herein by reference.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a) The following documents are filed as part of this report:

1. Financial Statements

See Index to Financial Statements in Part II Item 8 of this Annual Report on Form 10-K.

2. Financial Statement Schedules

All schedules are omitted because they are not applicable or the required information is shown in the financial statements or notes thereto.

3. Exhibits

The documents listed in the Exhibit Index are incorporated by reference or are filed with this report, in each case as indicated therein (numbered in accordance with Item 601 of Regulation S-K).

EXHIBIT INDEX

Exhibit Number	Description	Incorporated by Reference			
		Form	File No.	Number	Filing Date
3.1	Amended and Restated Certificate of Incorporation of the Registrant.	8-K	001-38311	3.1	12/12/2017
3.2	Amended and Restated Bylaws of the Registrant.	8-K	001-38311	3.1	11/18/2024
4.1	Specimen Common Stock Certificate of the Registrant.	S-1/A	333-221522	4.2	11/27/2017
4.2#	Form of Pre-Funded Warrant (Amended), March 2024.	10-Q	001-38311	4.1	5/7/2024
4.3#	Form of Pre-Funded Warrant to Purchase Common Stock, December 2025.	8-K	001-38311	4.1	12/10/2025
4.4	Description of the Registrant's Common Stock.	—	—	—	Filed herewith
10.1+	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers.	S-1/A	333-221522	10.1	11/27/2017
10.2+	2015 Stock Incentive Plan, as amended, and forms of agreement thereunder.	S-1	333-221522	10.2	11/13/2017
10.3+	2017 Equity Incentive Plan and forms of agreements thereunder.	S-1/A	333-221522	10.3	11/27/2017
10.4+	2017 Employee Stock Purchase Plan and form of agreement thereunder.	S-1/A	333-221522	10.4	12/7/2017
10.5+	Offer Letter between the Registrant and Ryan J. Watts, Ph.D., dated November 10, 2017.	S-1	333-221522	10.5	11/13/2017
10.6+	Offer Letter between the Registrant and Alexander O. Schuth, M.D., dated November 10, 2017.	S-1	333-221522	10.6	11/13/2017
10.8+	Offer Letter between the Registrant and Carole Ho, M.D., dated November 10, 2017.	S-1	333-221522	10.8	11/13/2017
10.9	Lease Agreement between the Registrant and HCP Oyster Point III LLC, dated September 24, 2015.	S-1	333-221522	10.9	11/13/2017
10.10Ü	Exclusive License Agreement between the Registrant and Genentech, Inc., dated June 17, 2016.	S-1	333-221522	10.10	11/13/2017
10.11Ü	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.	S-1	333-221522	10.11	11/13/2017
10.12Ü	Development and Manufacturing Services Agreement between the Registrant and Lonza Sales AG, dated September 6, 2017.	S-1	333-221522	10.12	11/13/2017
10.12.1#	Amendment No. 2 to Development and Manufacturing Services Agreement between the Registrant and Lonza Sales AG, dated January 18, 2018.	10-K	001-38311	10.12.1	3/19/2018
10.12.2#	Amendment No. 3 to Development and Manufacturing Services Agreement between the Registrant and Lonza Sales AG, dated July 2, 2018.	10-Q	001-38311	10.1	11/8/2018
10.12.3#	Amendment No. 4 to Development and Manufacturing Services Agreement between the Registrant and Lonza Sales AG, dated August 30, 2018.	10-Q	001-38311	10.2	11/8/2018

10.12.4#	Amendment No. 5 to Development and Manufacturing Services Agreement between the Registrant and Lonza Sales AG, dated August 6, 2019.	10-K	001-38311	10.12.4	2/26/2021
10.12.5#	Amendment No. 3 to Development and Manufacturing Services Agreement between the Registrant and Lonza Sales AG, dated September 11, 2020.	10-K	001-38311	10.12.5	2/26/2021
10.12.6#	Amendment No. 6 to Development and Manufacturing Services Agreement between the Registrant and Lonza Sales AG, dated December 8, 2020.	10-K	001-38311	10.12.6	2/26/2021
10.12.7	Amendment No. 7 to Development and Manufacturing Services Agreement between the Registrant and Lonza Sales AG, dated March 29, 2021.	10-K	001-38311	10.12.7	2/27/2023
10.12.8#	Amendment No. 8 to Development and Manufacturing Services Agreement between the Registrant and Lonza Sales AG, dated September 8, 2022.	10-K	001-38311	10.12.8	2/27/2023
10.12.9	Amendment No. 9 to Development and Manufacturing Services Agreement between the Registrant and Lonza Sales AG, dated December 7, 2022.	10-K	001-38311	10.12.9	2/27/2023
10.13+	Amended and Restated Key Executive Change in Control and Severance Plan.	10-Q	001-38311	10.6	11/5/2020
10.14+	Executive Incentive Compensation Plan.	S-1	333-221522	10.14	11/13/2017
10.15+	Amended and Restated Outside Director Compensation Policy.	10-Q	001-38311	10.3	5/06/2025
10.16#	Option and Collaboration Agreement between the Registrant and Takeda Pharmaceutical Company Limited, dated January 3, 2018.	10-K/A	001-38311	10.16	7/13/2018
10.17	Common Stock Purchase Agreement between the Registrant and Takeda Pharmaceutical Company Limited, dated January 3, 2018.	10-K	001-38311	10.17	3/19/2018
10.18	Standstill and Stock Restriction Agreement between the Registrant and Takeda Pharmaceutical Company Limited, dated February 23, 2018.	10-K	001-38311	10.18	3/19/2018
10.19	First Amendment to Lease Agreement between the Registrant and HCP Oyster Point III LLC, dated May 2, 2018.	10-Q	001-38311	10.1	8/9/2018
10.20Ü	Amended and Restated Gamma IP License Agreement between the Registrant and F-star Gamma Limited, dated August 24, 2016.	10-Q/A	001-38311	10.2	12/6/2018
10.21Ü	Side Letter between the Registrant and F-star Gamma Limited, dated May 21, 2018.	10-Q	001-38311	10.3	8/9/2018
10.22Ü	Share Purchase Agreement between the Registrant and F-star Gamma Limited, dated May 30, 2018.	10-Q/A	001-38311	10.4	12/6/2018
10.23#	Collaboration and License Agreement between registrant and Genzyme Corporation ("Sanofi"), dated October 29, 2018.	10-K	001-38311	10.25	3/12/2019
10.24	Common Stock Purchase Agreement between the Registrant and Biogen Inc., dated August 5, 2020.	10-Q	001-38311	10.1	11/5/2020
10.25#	Provisional LRRK2 Collaboration and License Agreement between the Registrant and Biogen Inc., dated August 5, 2020.	10-Q	001-38311	10.2	11/5/2020

10.26	Standstill and Stock Restriction Agreement between the Registrant and Biogen Inc., dated September 22, 2020.	10-Q	001-38311	10.3	11/5/2020
10.27#	Definitive LRRK2 Collaboration and License Agreement between the Registrant and Biogen Inc., dated October 4, 2020.	10-Q	001-38311	10.4	11/5/2020
10.28#	Definitive Right of First Negotiation, Option and License Agreement between the Registrant and Biogen Inc., dated October 6, 2020.	10-Q	001-38311	10.5	11/5/2020
10.29#	Side Letter between the Registrant and F-star Gamma Limited, dated June 30, 2021.	10-Q	001-38311	10.1	8/4/2021
10.30#	Amendment to Definitive LRRK2 Agreement and Waiver of and Amendment to Right of First Negotiation, Option, and License Agreement.	10-Q	001-38311	10.1	11/7/2023
10.31	Securities Purchase Agreement, dated February 27, 2024, by and among the Company and the Purchasers named therein	8-K	001-38311	10.1	2/27/2024
10.32	Nominating Agreement by and among the Company and Investor	8-K	001-38311	10.2	2/27/2024
10.33	Compensation Recovery Policy (“Clawback Policy”)	10-K	001-38311	10.34	2/28/2024
10.34#	Denali - Biogen Side Letter	10-Q	001-38311	10.10	8/1/2024
10.35#	Notice of Partial Termination from Genzyme Corporation to the Registrant, dated February 24, 2025	10-Q	001-38311	10.1	5/06/2025
10.36#	Notice of Partial Termination from Takeda Pharmaceutical Company Limited to the Registrant, dated February 25, 2025	10-Q	001-38311	10.2	5/06/2025
10.37	Affiliate Registration Rights Agreement, dated June 3, 2025, by and among the Company, Baker Brothers Life Sciences, L.P. and 667, L.P.	8-K	001-38311	10.1	6/03/2025
19.1	Denali Insider Trading Policy and Guidelines with Respect to Certain Transactions in Securities as amended through May 20, 2025.	—	—	—	Filed herewith
21.1	Subsidiaries of the Registrant.	—	—	—	Filed herewith
23.1	Consent of Independent Registered Public Accounting Firm.	—	—	—	Filed herewith
24.1	Powers of Attorney (incorporated by reference to the signature page hereto)				
31.1	Certification of Chief Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act.	—	—	—	Filed herewith
31.2	Certification of Chief Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act.	—	—	—	Filed herewith
32.1*	Certification of Chief Executive Officer pursuant to Section 906 of the Sarbanes-Oxley Act.	—	—	—	Furnished herewith
32.2*	Certification of Chief Financial Officer pursuant to Section 906 of the Sarbanes-Oxley Act.	—	—	—	Furnished herewith
101	The following materials from the Company’s Annual Report on Form 10-K for the year ended December 31, 2025, formatted in Inline XBRL: (i) Consolidated Balance Sheets, (ii) Consolidated Statements of Operations and Comprehensive Loss, (iii) Consolidated Statements of Cash Flows (iv) Consolidated Statements of Stockholders’ Equity and (v) Notes to Consolidated Financial Statements.	—	—	—	Filed herewith

104	The cover page from the Company's Annual Report on Form 10-K for the year ended December 31, 2025, formatted in Inline XBRL (contained in Exhibit 101)	—	—	—	Filed herewith

* The certifications attached as Exhibits 32.1 and 32.2 that accompany this Annual Report on Form 10-K are deemed furnished and not filed with the Securities and Exchange Commission and are not to be incorporated by reference into any filing of the Registrant under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Annual Report on Form 10-K, irrespective any general incorporation language contained in such filing.

Ü Portions of the exhibit have been omitted pursuant to an order granted by the Securities and Exchange Commission for confidential treatment.

Certain confidential information contained in this exhibit has been omitted because it is both (i) not material and (ii) is the type that the Registrant treats private or confidential.

\+ Indicates management contract or compensatory plan.

ITEM 16. FORM 10-K SUMMARY

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this Annual Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized.

DENALI THERAPEUTICS INC.

Date: February 26, 2026

By: /s/ Ryan J. Watts
Ryan J. Watts, Ph.D.
President and Chief Executive Officer

POWER OF ATTORNEY

Each person whose signature appears below constitutes and appoints Ryan J. Watts, Ph.D. and Alexander O. Schuth, M.D., and each of them acting individually, as his or her true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them, or their or his substitutes, may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed by the following persons on behalf of the registrant and 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)*	February 26, 2026
/s/ Alexander O. Schuth Alexander O. Schuth, M.D.	Chief Operating and Financial Officer *(Principal Financial and Accounting Officer)*	February 26, 2026
/s/ Julian C. Baker Julian C. Baker	Chairperson of our Board of Directors	February 26, 2026
/s/ Jennifer Cook Jennifer Cook	Director	February 26, 2026
/s/ Jay Flatley Jay Flatley	Director	February 26, 2026
/s/ Peter Klein Peter Klein	Director	February 26, 2026
/s/ Steve E. Krognes Steve E. Krognes	Director	February 26, 2026
/s/ David Schenkein David Schenkein, M.D.	Director	February 26, 2026
/s/ Nancy A. Thornberry Nancy A. Thornberry	Director	February 26, 2026
/s/ Tim Van Hauwermeiren Tim Van Hauwermeiren	Director	February 26, 2026

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

The following summary describes our common stock and preferred stock, as well as certain provisions of our amended and restated certificate of incorporation and amended and restated bylaws. This summary does not purport to be complete and is qualified in its entirety by the provisions of our amended and restated certificate of incorporation and amended and restated bylaws, copies of which have been filed as exhibits to this Annual Report on Form 10-K, as well as to the applicable provisions of the Delaware General Corporation Law.

Authorized Capital Stock

Our authorized capital stock consists of 400,000,000 shares of common stock, par value $0.01 per share, and 40,000,000 shares of preferred stock, par value $0.01 per share. All outstanding shares of common stock are fully paid and non-assessable.

Common Stock

Our common stock is listed on the Nasdaq Global Select Market under the symbol "DNLI." The transfer agent and registrar for our common stock is Broadridge Financial Solutions, Inc. The transfer agent and registrar's address is 51 Mercedes Way, Edgewood, NY 11717.

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.

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.

Preferred Stock

Under the terms of our amended and restated certificate of incorporation, our board of directors is authorized 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 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 issuance of shares of preferred stock will affect, and may adversely affect, the rights of holders of common stock. It is not possible to state the actual effect of the issuance of any shares of preferred stock on the rights of holders of common stock until our board of directors determines the specific rights attached to that preferred stock. The effects of issuing additional preferred stock could include one or more of the following:

- restricting dividends on the common stock;
- diluting the voting power of the common stock;
- impairing the liquidation rights of the common stock; or
- delaying or preventing changes in control or management of our Company.

Preferred stock will be fully paid and nonassessable upon issuance.

Registration Rights of Certain Stockholders

Certain of our stockholders have registration rights under the investors' rights agreement, as amended (the "**Investors' Rights Agreement**"), by and among us and such stockholders. Two of our other stockholders, Takeda Pharmaceutical Company Limited ("**Takeda**") and Biogen MA, Inc. ("**BIMA**"), and Biogen International GmbH, ("**BIG**", together with BIMA, collectively, "**Biogen**"), also have registration rights under the standstill and stock restriction agreement between us and Takeda (the "**Takeda Standstill Agreement**") and the standstill and stock restriction agreement between us and Biogen (the "**Biogen Standstill Agreement**"), respectively. These stockholders (and certain of their permitted transferees) may request that we file registration statements under the Securities Act of 1933 and, upon such request and subject to certain conditions, the Company will be required to use its commercially reasonable efforts to effect any such registration. The Company is generally obligated to bear the expenses, other than underwriting discounts and sales commissions, of all of these registrations. This summary does not purport to be complete and is qualified in its entirety by the provisions of the Investors' Rights Agreement, the Takeda Standstill Agreement and the Biogen Standstill Agreement, copies of which have been filed as exhibits to this Annual Report on Form 10-K.

Effect of Certain Provisions of our Amended and Restated Certificate of Incorporation and Bylaws and the Delaware Anti-Takeover Statute

Some provisions of Delaware law and our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could make the following transactions more difficult:

- acquisition of us by means of a tender offer;
- acquisition of us by means of a proxy contest or otherwise; or

- removal of our incumbent officers and directors.

Those provisions, summarized below, are expected to discourage coercive takeover practices and inadequate takeover bids and to promote stability in our management. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors.

Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws

Classified Board of Directors

Our amended and restated certificate of incorporation provides that our board of directors is divided into three classes, designated Class I, Class II, and Class III. Each class is 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 directors in each class are elected to serve for a three-year term, one class being elected each year by our stockholders. At each annual meeting of stockholders, 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 provides 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

Vacancies and newly created directorships on our board of directors may 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.

No Cumulative Voting

Our amended and restated certificate of incorporation provides 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 provides 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.

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 Delaware General Corporation Law . 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 certain provisions, including those listed above, which would require the approval of a two-thirds majority of our then outstanding common stock. Additionally, our amended and restated certificate of incorporation provides 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 are 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 our Company by means of a proxy contest, tender offer, merger or otherwise.

Delaware Anti-Takeover Statute

We are subject to the provisions of Section 203 of the Delaware General Corporation Law regulating corporate takeovers. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging, under certain circumstances, in a business combination with an interested stockholder for a period of three years following the date the person became an interested stockholder unless:

- prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;

- upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, but not for determining the outstanding voting stock owned by the interested stockholder, (i) shares owned by persons who are directors and also officers, and (ii) shares owned 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

- at or subsequent to the date of the transaction, the business combination is approved by the board of directors of the corporation and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66-2/3% of the outstanding voting stock which is not owned by the interested stockholder.

Generally, a business combination includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns or, within three years prior to the determination of interested stockholder status, did own 15% or more of a corporation’s outstanding voting stock.

DENALI THERAPEUTICS INC.

INSIDER TRADING POLICY

and

Guidelines with Respect to Certain Transactions in Securities

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(As amended through May 20, 2025)

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INTRODUCTION

Denali Therapeutics Inc. (together with its subsidiaries, the "***Company***") opposes the unauthorized disclosure of any nonpublic information acquired in the course of your service with the Company and the misuse of material nonpublic information in securities trading. Any such actions will be deemed violations of this Insider Trading Policy (this "***Policy***").

Legal prohibitions on insider trading

The antifraud provisions of U.S. federal securities laws prohibit directors, officers, employees and other individuals who possess material nonpublic information from trading on the basis of that information. Transactions will be considered "on the basis of" material nonpublic information if the person engaged in the transaction was aware of the material nonpublic information at the time of the transaction. It is not a defense that the person did not "use" the information for purposes of the transaction.

Disclosing material nonpublic information directly or indirectly to others who then trade based on that information or making recommendations or expressing opinions as to transactions in securities while aware of material nonpublic information (which is sometime referred to as "***tipping***") is also illegal. Both the person who provides the information, recommendation or opinion and the person who trades based on it may be liable.

These illegal activities are commonly referred to as "***insider trading***". State securities laws and securities laws of other jurisdictions also impose restrictions on insider trading.

In addition, a company, as well as individual directors, officers and other supervisory personnel, may be subject to liability as "controlling persons" for failure to take appropriate steps to prevent insider trading by those under their supervision, influence or control.

Compliance Officers

Please direct any questions, requests or reports as to any of the matters discussed in this Policy to the Chief Operating and Financial Officer or Chief People Officer of the Company (each, a "***Compliance Officer***" and collectively, the "***Compliance Officers***"). The Compliance Officers are generally responsible for the administration of this Policy. The Compliance Officers may select others to assist with the execution of his or her duties.

Reporting violations

It is your responsibility to help enforce this Policy. You should be alert to possible violations and promptly report violations or suspected violations of this Policy to a Compliance Officer at or (650) 866-8547. If your situation requires that your identity be kept secret, your anonymity will be preserved to the greatest extent reasonably possible, or otherwise permitted by law. If you wish to remain anonymous, send a letter addressed to a Compliance Officer at Denali Therapeutics Inc., 161 Oyster Point Blvd., South San Francisco, CA 94080, or contact the whistleblower hotline, at https://secure.ethicspoint.com or by phone at: (844) 208-2253. If a Compliance Officer is implicated in your report, then you should report it through the whistleblower hotline. If you make an anonymous report, please provide as much detail as possible, including any evidence that you believe may be relevant to the issue.

Personal responsibility

The ultimate responsibility for complying with this Policy and applicable laws and regulations rests with you. You should use your best judgment at all times and consult with your legal and financial advisors, as needed. We advise you to seek assistance if you have any questions at all. The rules relating to insider trading can be complex, and a violation of insider trading laws can carry severe consequences.

PERSONS AND TRANSACTIONS COVERED BY THIS POLICY

Persons covered by this Policy

This Policy applies to all directors, officers, employees, consultants, contractors and advisors of the Company. References in this Policy to "you" (as well as general references to directors, officers, employees, consultants, contractors and advisors of the Company) should also be understood to include members of your immediate family, persons with whom you share a household, persons who are your economic dependents and any other individuals or entities whose transactions in securities you influence, direct or control (including, for example, a venture or other investment fund, if you influence, direct or control transactions by the fund), except that this Policy shall not apply to any such entity that engages in the investment of securities in the ordinary course of its business (e.g. an investment fund or partnership) if such entity has established its own insider trading policies and procedures in compliance with applicable securities laws. You are responsible for making sure that these other individuals and entities comply with this Policy.

Types of transactions covered by this Policy

Except as discussed in the section entitled "**Limited Exceptions**", this Policy applies to *all* transactions *involving* the securities of the Company or the securities of other companies as to which you possess material nonpublic information obtained in the course of your service with the Company. This Policy therefore applies to purchases, sales and other transfers of common stock, options, restricted stock units, warrants, preferred stock, debt securities (such as debentures, bonds and notes) and other securities of the Company and such other companies, whether direct or indirect (including transactions made on your behalf by money managers), and any offer to engage in the foregoing transactions. This Policy also applies to any disposition in the form of a gift of any securities of the Company and any distribution to holders of interests in an entity if the entity is subject to this Policy. This Policy also applies to any arrangements that affect economic exposure to changes in the prices of these securities. These arrangements may include, among other things, transactions in derivative securities (such as exchange-traded put or call options, swaps, caps and collars), hedging and pledging transactions, short sales and certain decisions with respect to participation in benefit plans, and any offer to engage in the foregoing transactions. You should note that there are no exceptions from insider trading laws or this Policy based on the size of the transaction or the type of consideration received.

Responsibilities regarding the nonpublic information of other companies

This Policy prohibits the unauthorized disclosure or other misuse of any nonpublic information of other companies, such as the Company's distributors, vendors, customers, collaborators, suppliers and competitors. This Policy also prohibits insider trading and tipping based on the material nonpublic information of other companies.

Applicability of this Policy after your departure

You are expected to comply with this Policy until such time as you are no longer affiliated with the Company *and* you no longer possess any material nonpublic information subject to this Policy. In addition, if you are subject to a trading blackout under this Policy at the time you cease to be affiliated with the Company, you must abide by the applicable trading restrictions until at least the end of the relevant blackout period.

No exceptions based on personal circumstances

There may be instances where you suffer financial harm or other hardship or are otherwise required to forego a planned transaction because of the restrictions imposed by this Policy. Personal financial emergency or other personal circumstances are not mitigating factors under securities laws and will not excuse a failure to comply with this Policy.

MATERIAL NONPUBLIC INFORMATION

“Material” information

Information should be regarded as material if there is a substantial likelihood that a reasonable investor would consider it important in deciding whether to buy, hold or sell securities or would view the information as significantly altering the total mix of information in the marketplace about the issuer of the security. In general, any information that could reasonably be expected to affect the market price of a security is likely to be material. Either positive or negative information may be material.

It is not possible to define all categories of “material” information. However, some examples of information that would often be regarded as material include information with respect to:

- Clinical trial results;
- Financial results, financial condition, earnings pre-announcements, guidance, projections or forecasts, particularly if inconsistent with the expectations of the investment community;
- Restatements of financial results, or material impairments, write-offs or restructurings;
- Changes in independent auditors, or notification that the Company may no longer rely on an audit report;
- Business plans or budgets;
- Creation of significant financial obligations, or any significant default under or acceleration of any financial obligation;
- Impending bankruptcy or financial liquidity problems;
- Significant developments involving business relationships, including execution, modification or termination of significant agreements or orders with customers, suppliers, distributors, manufacturers or other business partners;
- Product introductions, modifications, defects or recalls or significant pricing changes or other product announcements of a significant nature;
- Significant developments in research and development or relating to intellectual property;
- Significant legal or regulatory developments, whether actual or threatened;
- Major events involving the Company’s securities, including calls of securities for redemption, adoption of stock repurchase programs, option repricings, stock splits, changes in dividend policies, public or private securities offerings, modification to the rights of security holders or notice of delisting;
- Significant corporate events, such as a pending or proposed merger, joint venture or tender offer, a significant investment, the acquisition or disposition of a significant business or asset or a change in control of the company;
- Major personnel changes, such as changes in senior management or layoffs;
- Significant data breaches or other cybersecurity events;
- Updates regarding any prior material disclosure that has materially changed; and
- The existence of a special blackout period.

If you have any questions as to whether information should be considered “material”, you should consult with a Compliance Officer. In general, it is advisable to resolve any close questions as to the materiality of any information by assuming that the information is material.

“Nonpublic” information

Information is considered nonpublic if the information has not been broadly disseminated to the public for a sufficient period to be reflected in the price of the security. As a general rule, information should be considered nonpublic until the start of the second ***full trading day*** after the information is broadly distributed to the public in a press release, a public filing with the SEC, a pre-announced public webcast or another broad, non-exclusionary form of public communication. However, depending upon the form of the announcement and the nature of the information, it is possible that information may not be fully absorbed by the marketplace until a later time. Any questions as to whether information is nonpublic should be directed to a Compliance Officer.

The term “***trading day***” means a day on which national stock exchanges and the National Association of Securities Dealers, Inc. Automated Quotation System are open for trading. A “***full***” trading day has elapsed when, after the public disclosure, trading in the relevant security has opened and then closed.

POLICIES REGARDING MATERIAL NONPUBLIC INFORMATION

Confidentiality of nonpublic information

The unauthorized use or disclosure of nonpublic information relating to the Company or other companies is prohibited. All nonpublic information you acquire in the course of your service with the Company may only be used for legitimate Company business purposes. In addition, nonpublic information of other companies should be handled in accordance with the terms of any relevant nondisclosure agreements and regulatory requirements, and the use of any such nonpublic information should be limited to the purpose for which it was disclosed.

If you receive an inquiry for information from someone outside of the Company, such as a stock analyst, or a request for sensitive information outside the ordinary course of business from someone outside of the Company, such as a business partner, vendor, or supplier, then you should refer the inquiry to the Chief Operating and Financial Officer or the Company's Head of Investor Relations. Responding to a request yourself may violate this Policy and, in some circumstances, the law.

No trading on material nonpublic information

Except as discussed in the section entitled "**Limited Exceptions**", you may not, directly or indirectly through others, engage in any transaction involving the Company's securities *while aware of* material nonpublic information relating to the Company. It is not an excuse that you did not "use" the information in your transaction.

In addition, material nonpublic information about another company that you learn through your service with the Company is subject to these same restrictions around disclosure and trading and you cannot use that information to trade securities. Any such action will be deemed a violation of this Policy.

No disclosing material nonpublic information for the benefit of others

You may not disclose material nonpublic information concerning the Company or any other company to friends, family members or any other person or entity not authorized to receive such information where such person or entity may benefit by trading on the basis of such information. In addition, you may not make recommendations or express opinions on the basis of material nonpublic information as to trading in the securities of companies to which such information relates. You are prohibited from engaging in these actions whether or not you derive any profit or personal benefit from doing so.

TRADING BLACKOUT PERIODS

To limit the likelihood of trading at times when there is a significant risk of insider trading exposure, the Company has instituted quarterly trading blackout periods and may institute special trading blackout periods from time to time. It is important to note that whether or not you are subject to blackout periods, you remain subject to the prohibitions on trading on the basis of material nonpublic information and any other applicable restrictions in this Policy.

Quarterly blackout periods

Except as discussed in the section entitled "**Limited Exceptions**", directors, executive officers and those employees, consultants, contractors and advisors identified by the Company, must refrain from conducting transactions involving the Company's securities during quarterly blackout periods. Even if you are not specifically identified as being subject to quarterly blackout periods, you should exercise caution when engaging in transactions during quarterly blackout periods because of the heightened risk of insider trading exposure.

Quarterly blackout periods begin on the first calendar day of each fiscal quarter, and, in each case, end at the start of the second full trading day following the date of public disclosure of the financial results for the previous fiscal quarter. This period is a particularly sensitive time for transactions involving the Company's securities from the perspective of compliance with applicable securities laws due to the fact that, during this period, individuals may often possess or have access to material nonpublic information relevant to the expected financial results for the quarter.

Individuals subject to quarterly blackout periods will be informed by a Compliance Officer that they are listed on the covered persons list maintained by the Compliance Officers (the "***Covered Persons List***"). From time to time, the Company may identify other persons who should be subject to quarterly blackout periods, and a Compliance Officer may update and revise the Covered Persons List as appropriate.

Special blackout periods

From time to time, the Company may also prohibit directors, officers, employees, consultants, contractors and advisors from engaging in transactions involving the Company's securities when, in the judgment of a Compliance Officer, a trading blackout is warranted. The Company will generally impose special blackout periods when there are material developments known to the Company that have not yet been disclosed to the public. For example, the Company may impose a special blackout period in anticipation of announcing material clinical data results or a significant transaction or business development. However, special blackout periods may be declared for any reason.

The Company will notify those persons subject to a special blackout period by providing a notice in writing or via email. Each person who has been so identified and notified by the Company may not engage in any transaction involving the Company's securities until instructed otherwise by a Compliance Officer, and should not disclose to others the fact of such suspension of trading.

Regulation BTR blackouts

Directors and executive officers may also be subject to trading blackouts pursuant to Regulation Blackout Trading Restriction, or Regulation BTR, under U.S. federal securities laws. In general, Regulation BTR prohibits any director or executive officer from engaging in certain transactions involving Company securities during periods when 401(k) plan participants are prevented from purchasing, selling or otherwise acquiring or transferring an interest in certain securities held in individual account plans. Any profits realized from a transaction that violates Regulation BTR are recoverable by the Company, regardless of the intentions of the director or officer effecting the transaction. In addition, individuals who engage in such transactions are subject to sanction by the U.S. Securities and Exchange Commission (the "***SEC***") as well as potential criminal liability. The Company has provided, or will provide, separate memoranda and other appropriate materials to its directors and executive officers regarding compliance with Regulation BTR.

The Company will notify directors and officers if they are subject to a blackout trading restriction under Regulation BTR. Failure to comply with an applicable trading blackout in accordance with Regulation BTR is a violation of law and this Policy.

No “safe harbors”

There are no unconditional “safe harbors” for trades made at particular times, and all persons subject to this Policy should exercise good judgment at all times. Even when a quarterly blackout period is not in effect, you may be prohibited from engaging in transactions involving the Company’s securities because you possess material nonpublic information, are subject to a special blackout period or are otherwise restricted under this Policy.

PRE-CLEARANCE OF TRADES

Except as discussed in the section entitled "**Limited Exceptions**", directors, executive officers, and all other employees and agents of Company should refrain from engaging in any transaction involving the Company's securities without first obtaining pre-clearance of the transaction from a Compliance Officer. This is done by submitting a pre-clearance request on the form provided by a Compliance Officer, which is available on the Company's Explore Intranet, to a Compliance Officer and obtaining the required signature or other written notification from a Compliance Officer or designee (including, for example, an email notification by the Company's designated stock administration agent) prior to the desired transaction date. A Compliance Officer may not engage in a transaction involving the Company's securities unless the Chief Executive Officer has pre-cleared the transaction or, in the case the Compliance Officer engaging in the transaction is the Chief Executive Officer, another Compliance Officer has pre-cleared the transaction.

These pre-clearance procedures are intended to decrease insider trading risks associated with transactions by individuals with regular or special access to material nonpublic information. In addition, requiring pre**-**clearance of transactions by directors and officers facilitates compliance with Rule 144 resale restrictions under the Securities Act of 1933, as amended, the liability and reporting provisions of Section 16 under the Securities Exchange Act of 1934, as amended (the "***Exchange Act***") and Regulation BTR. Pre-clearance of a trade, however, is not a defense to a claim of insider trading and does not excuse you from otherwise complying with insider trading laws or this Policy.

A Compliance Officer is under no obligation to approve a transaction submitted for pre-clearance, and may determine not to permit the transaction.

ADDITIONAL RESTRICTIONS AND GUIDANCE

This section addresses certain types of transactions that may expose you and the Company to significant risks. You should understand that, even though a transaction may not be expressly prohibited by this section, you are responsible for ensuring that the transaction otherwise complies with other provisions in this Policy that may apply to the transaction, such as the general prohibition against insider trading as well as pre-clearance procedures and blackout periods, to the extent applicable.

Short sales

Short sales (*i.e.,* the sale of a security that must be borrowed to make delivery) and "selling short against the box" (*i.e.,* a sale with a delayed delivery) with respect to Company securities are prohibited under this Policy. Short sales may signal to the market possible bad news about the Company or a general lack of confidence in the Company's prospects, and an expectation that the value of the Company's securities will decline. In addition, short sales are effectively a bet against the Company's success and may reduce the seller's incentive to improve the Company's performance. Short sales may also create a suspicion that the seller is engaged in insider trading.

Derivative securities and hedging transactions

You are prohibited from engaging in transactions in publicly-traded options, such as puts and calls, and other derivative securities with respect to the Company's securities. This prohibition extends to any hedging or similar transaction designed to decrease the risks associated with holding Company securities. Stock options, stock appreciation rights and other securities issued pursuant to Company benefit plans or other compensatory arrangements with the Company are also subject to this prohibition; *provided*, *however*, as described in the "**Limited Exceptions**" section of this Policy, you are not prohibited from exercising any stock options issued under any of the Company's benefit plans or other compensatory arrangements in accordance with the terms of such plans or arrangements.

Transactions in derivative securities may reflect a short-term and speculative interest in the Company's securities and may create the appearance of impropriety, even where a transaction does not involve trading on inside information. Trading in derivatives may also focus attention on short-term performance at the expense of the Company's long-term objectives. In addition, the application of securities laws to derivatives transactions can be complex, and persons engaging in derivatives transactions may subject themselves to an increased risk of violating securities laws.

Using Company securities as collateral for loans

You may not pledge Company securities as collateral for loans. If you default on the loan, the lender may sell the pledged securities as collateral in a foreclosure sale. The sale, even though not initiated at your request, is still considered a sale for your benefit and, if made at a time when you are aware of material nonpublic information or otherwise are not permitted to trade in Company securities, may result in inadvertent insider trading violations, Section 16 and Regulation BTR violations (for officers and directors), violations of this Policy and unfavorable publicity for you and the Company.

Holding Company securities in margin accounts

You may not hold Company securities in margin accounts. Under typical margin arrangements, if you fail to meet a margin call, the broker may be entitled to sell securities held in the margin account without your consent. The sale, even though not initiated at your request, is still considered a sale for your benefit and, if made at a time when you are aware of material nonpublic information or are otherwise not permitted to trade, may result in inadvertent insider trading violations, Section 16 and Regulation BTR violations (for officers and directors), violations of this Policy and unfavorable publicity for you and the Company.

Placing open orders with brokers

Except in accordance with an approved trading plan (as discussed below), you should exercise caution when placing open orders, such as limit orders or stop orders, with brokers, particularly where the order is likely to remain outstanding for an extended period of time. If you are subject to the blackout window, open orders should be canceled prior to entering a blackout window, as this may result in the execution of a trade at a time when you are aware of material nonpublic information or otherwise are not permitted to trade in Company securities, which may result in inadvertent insider trading violations, Section 16 and Regulation BTR violations (for officers and directors), violations of this Policy and unfavorable publicity for you and the Company. If you are subject to blackout periods or pre-clearance requirements, you should so inform any broker with whom you place any open order at the time it is placed.

LIMITED EXCEPTIONS

The following are certain limited exceptions to the quarterly and special blackout period restrictions and pre-clearance requirements imposed by the Company under this Policy. Please be aware that even if a transaction is subject to an exception to this Policy, you will need to separately assess whether the transaction complies with applicable law. For example, even if a transaction is indicated as exempt from this Policy, you may need to comply with the "short-swing" trading restrictions under Section 16 of the Exchange Act, to the extent applicable. You are responsible for complying with applicable law at all times.

Transactions pursuant to a trading plan that complies with SEC rules

The SEC has enacted rules that provide an affirmative defense against alleged violations of U.S. federal insider trading laws for transactions pursuant to trading plans that meet certain requirements. In general, these rules, as set forth in Rule 10b5-1 under the Exchange Act, provide for an affirmative defense if you enter into a contract, provide instructions or adopt a written plan for trading securities when you are not aware of material nonpublic information. The contract, instructions or plan must (i) specify the amount, price and date of the transaction, (ii) specify an objective method for determining the amount, price and date of the transaction and/or (iii) place any subsequent discretion for determining the amount, price and date of the transaction in another person who is not, at the time of the transaction, aware of material nonpublic information.

Transactions made pursuant to a written trading plan that (i) complies with the affirmative defense set forth in Rule 10b5-1, (ii) complies with the "**Requirements for Trading Plans**" set forth in **Schedule I** and (iii) is approved by a Compliance Officer (or, if the plan is being adopted by a Compliance Officer, by the other Compliance Officer), are not subject to the restrictions in this Policy against trades made while aware of material nonpublic information or to the pre-clearance procedures or blackout periods established under this Policy. In approving a trading plan, a Compliance Officer may, in furtherance of the objectives expressed in this Policy, impose criteria in addition to those set forth in Rule 10b5-1.

The SEC rules regarding trading plans are complex and must be complied with completely to be effective. The description provided above is only a summary, and the Company strongly advises that you consult with your legal advisor if you intend to adopt a trading plan. While trading plans are subject to review and approval by the Company, the individual adopting the trading plan is ultimately responsible for compliance with Rule 10b5-1 and ensuring that the trading plan complies with this Policy.

Trading plans must be filed with a Compliance Officer and must be accompanied with an executed certificate stating that the trading plan complies with Rule 10b5-1. The Company may publicly disclose information regarding trading plans that you may enter.

Receipt and vesting of stock options, restricted stock units, and restricted stock

The restrictions under this Policy do not apply to the acceptance or purchase of stock options, restricted stock units, restricted stock or other equity compensation awards issued or offered by the Company. The restrictions under this Policy also do not apply to the vesting, cancellation or forfeiture of stock options, restricted stock units, restricted stock or other equity compensation awards from the Company in accordance with applicable plans and agreements.

Exercise of stock options for cash and tax withholding requirements

The restrictions under this Policy do not apply to the exercise of stock options where the purchase price of such stock options is paid in cash and there is no other associated market activity.

the restrictions under this Policy do not apply to net share withholding with respect to equity awards where shares are withheld by the Company in order to satisfy tax withholding requirements, (x) as required by either the Company's Board of Directors (or a committee thereof) or the award agreement governing such equity award or (y) as the individual elects, if permitted by the Company. so long as that election is irrevocable and made in writing at a time when a trading blackout is not in place and the individual is not in possession of material nonpublic information. Likewise, the restrictions under this Policy do not apply to sell to cover transactions where shares are sold on an individual's behalf upon vesting of equity awards sold in order to satisfy tax withholding requirements, (x) as required by either the Company's Board of Directors (or a committee thereof) or the award agreement governing such equity award or (y) as the individual elects, if permitted by the Company, so long as the election is irrevocable and made in writing at a time when a trading blackout is not in place and the individual is not in possession of material nonpublic information; however, this exception does not apply to any other market sale for the purposes of paying required withholdings.

Employee stock purchase plan

The restrictions in this Policy do not apply to elections with respect to participation in the Company's employee stock purchase plan or to purchases of securities under the plan; however, the restrictions do apply to any subsequent sales of any such securities. The restrictions in this Policy also do not apply to participation in the cashless participation program (as defined in the prospectus relating to the employee stock purchase plan) and, notwithstanding the prior sentence, do not apply to any automatic sales of securities triggered by the repayment of a loan (including with respect to related fees) under the cashless participation program.

Certain 401(k) plan transactions

The restrictions in this Policy do not apply to purchases of Company stock in the 401(k) plan resulting from periodic contributions to the plan based on your payroll contribution election. The restrictions do apply, however, to elections you make under the 401(k) plan to (i) increase or decrease the amount of your contributions under the 401(k) plan if such increase or decrease will increase or decrease the amount of your contributions that will be allocated to a Company stock fund, (ii) increase or decrease the percentage of your contributions that will be allocated to a Company stock fund, (iii) move balances into or out of a Company stock fund, (iv) borrow money against your 401(k) plan account if the loan will result in liquidation of some or all of your Company stock fund balance, and (v) pre-pay a plan loan if the pre-payment will result in the allocation of loan proceeds to a Company stock fund.

Stock splits, stock dividends and similar transactions

The restrictions under this Policy do not apply to a change in the number of securities held as a result of a stock split or stock dividend applying equally to all securities of a class, or similar transactions.

Estate planning

The restrictions under this Policy do not apply to transfers by will or the laws of descent or distribution and, provided that prior written notice is provided to a Compliance Officer, distributions or transfers (such as certain tax planning or estate planning transfers) that effect only a change in the form of beneficial interest without changing your pecuniary interest in the Company's securities.

Other exceptions

Any other exception from this Policy must be approved by a Compliance Officer, in consultation with the Board of Directors or an independent committee of the Board of Directors.

COMPLIANCE WITH SECTION 16 OF THE SECURITIES EXCHANGE ACT

Obligations under Section 16

All of the Company's officers and directors and certain other individuals are required to comply with Section 16 of the Securities Exchange Act of 1934, and related rules and regulations, which set forth (i) reporting obligations, (ii) limitations on "short-swing" transactions, which are certain matching purchases and sales of the Company's securities within a six-month period, and (iii) limitations on short sales. The Company has provided, or will provide, memoranda and other materials addressing these matters.

Notification requirements to facilitate Section 16 reporting

To facilitate timely reporting of transactions pursuant to Section 16 requirements, each person subject to Section 16 reporting requirements must provide, or must ensure that his or her broker provides, the Company with detailed information (*e.g.,* trade date, number of shares, exact price, *etc.*) regarding his or her transactions involving the Company's securities, including gifts, transfers, pledges and transactions pursuant to a trading plan, both prior to (to confirm compliance with pre-clearance procedures, if applicable) and promptly following execution.

Personal responsibility

The obligation to file Section 16 reports, and to otherwise comply with Section 16, is personal. The Company is not responsible for the failure to comply with Section 16 requirements.

ADDITIONAL INFORMATION

Delivery of Policy

This Policy will be delivered to all directors, officers, employees, consultants, contractors and advisors of the Company when they commence service with the Company. In addition, this Policy (or a summary of this Policy) will be circulated periodically. Each director, officer, employee, consultant, contractor and advisor of the Company is required to acknowledge that he or she understands, and agrees to comply with, this Policy.

Amendments

We are committed to continuously reviewing and updating our policies and procedures. The Company therefore reserves the right to amend, alter or terminate this Policy at any time and for any reason, subject to applicable law.

Current Version of Policy

A copy of the Company's current policies regarding insider trading may be obtained by contacting a Compliance Officer.

* * *

Nothing in this Insider Trading Policy creates or implies an employment contract or term of employment. Employment at the Company is employment at-will. Employment at-will may be terminated with or without cause and with or without notice at any time by the employee or the Company. Nothing in this Insider Trading Policy shall limit the right to terminate employment at-will. No employee of the Company has any authority to enter into any agreement for employment for a specified period of time or to make any agreement or representation contrary to the Company's policy of employment at-will. Only the Chief Executive Officer of the Company has the authority to make any such agreement, which must be in writing.

The policies in this Insider Trading Policy do not constitute a complete list of Company policies or a complete list of the types of conduct that can result in discipline, up to and including discharge.

SCHEDULE I

DENALI THERAPEUTICS INC.

REQUIREMENTS FOR TRADING PLANS

Denali recommends its Officers and Directors execute all open market transactions in Denali stock subject to a Rule 10b5-1 trading plan. For transactions under a trading plan to be exempt from (i) the prohibitions in the Company's Insider Trading Policy (the "***Policy***") with respect to transactions made while aware of material nonpublic information and (ii) the pre-clearance procedures and blackout periods established under the Policy, the trading plan must comply with the affirmative defense set forth in Exchange Act Rule 10b5-1 and must meet the following requirements:

1. The trading plan must be in writing and signed by the person adopting the trading plan. The person adopting the trading plan may not have an outstanding (and may not subsequently enter into any additional) trading plan except as permitted by Rule 10b5-1.

2. The trading plan must be adopted at a time when:

    - the person adopting the trading plan is not aware of any material nonpublic information; and

    - there is no quarterly, special or other trading blackout in effect with respect to the person adopting the plan.

3. The trading plan must be entered in good faith and not as part of a plan or scheme to evade the prohibitions of Rule 10b5-1, and the person adopting the trading plan must act in good faith with respect to the trading plan.

4. The trading plan must include representations that, on the date of adoption of the trading plan, the person adopting the trading plan:

    - is not aware of material nonpublic information about the securities or the Company; and

    - is adopting the trading plan in good faith and not as part of a plan or scheme to evade the prohibitions of Rule 10b5-1.

5. The person adopting the trading plan may not have entered into or altered a corresponding or hedging transaction or position with respect to the securities subject to the trading plan and must agree not to enter into any such transaction while the trading plan is in effect.

6. The first trade under the trading plan for directors and officers (as defined in Rule 16a-1(f) of the Securities Exchange Act of 1934) may not occur until the expiration of a cooling-off period consisting of the later of (i) 90 calendar days after the adoption of the trading plan and (ii) two business days after the filing by the Company of its financial results in a Form 10-Q or Form 10-K for the completed fiscal quarter in which the trading plan was adopted (but, in any event, this required cooling-off period is subject to a maximum of 120 days after the adoption of the trading plan). The first trade under the trading plan for all other persons (other than the Company) may not occur until the expiration of a cooling-off period that is 60 calendar days after the adoption of the trading plan.

7. The trading plan must have a minimum term of one year (starting from date of adoption of the trading plan).

8. Any modification or change to the amount, price or timing of transactions under the trading plan is deemed the termination of the trading plan, and the adoption of a new trading plan ("**Modification**"). Therefore, a Modification is subject to the same conditions as a new trading plan as set forth in Sections 1 through 8 herein.

9. Within the one year preceding the adoption or a Modification of a trading plan, a person may not have otherwise adopted or done a Modification to a plan more than once.

10. A person may adopt a trading plan designed to cover a single trade only once in any consecutive 12-month period except as permitted by Rule 10b5-1.

11. If the person that adopted the trading plan terminates the plan prior to its stated duration, he or she may not trade in the Company's securities until after the expiration of 60 calendar days following termination, and then only in accordance with the Policy.

12. The Company must be promptly notified of any Modification or termination of the trading plan and any suspension of trading under the trading plan.

13. The Company must have authority to require the suspension or cancellation of the trading plan at any time.

14. If the trading plan grants discretion to a stockbroker or other person with respect to the execution of trades under the trading plan:

    - trades made under the trading plan must be executed by someone other than the stockbroker or other person that executes trades in other securities for the person adopting the trading plan;

    - the person adopting the trading plan may not confer with the person administering the trading plan regarding the Company or its securities; and

    - the person administering the trading plan must provide prompt notice to the Company of the execution of a transaction pursuant to the plan.

15. All transactions under the trading plan must be in accordance with applicable law.

16. The trading plan (including any Modification) must meet such other requirements as the Compliance Officer may determine.

17. Any trading plans adopted or modified prior to February 27, 2023 (the "***Effective Date***") are permitted to continue in place until all trades are executed thereunder or they expire by their terms ("***Pre-effective Plans***"). If the person undertakes a Modification of a Pre-effective Plan on or after the Effective Date, then the Modification must meet all of the requirements set forth herein.

Exhibit 21.1

SUBSIDIARIES

Subsidiary Name	Jurisdiction of Incorporation or Organization
Denali BBB Holding Limited	United Kingdom
Denali Therapeutics CH GmbH	Switzerland

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the following Registration Statements:

1. Registration Statement (Form S-3 No. 333-285326) of Denali Therapeutics Inc.,
2. Registration Statement (Form S-8 No. 333-285333) pertaining to the 2017 Equity Incentive Plan and 2017 Employee Stock Purchase Plan of Denali Therapeutics Inc.,
3. Registration Statement (Form S-8 No. 333-277429) pertaining to the 2017 Equity Incentive Plan and 2017 Employee Stock Purchase Plan of Denali Therapeutics Inc.,
4. Registration Statement (Form S-8 No. 333-270040) pertaining to the 2017 Equity Incentive Plan and 2017 Employee Stock Purchase Plan of Denali Therapeutics Inc.,
5. Registration Statement (Form S-8 No. 333-263082) pertaining to the 2017 Equity Incentive Plan and 2017 Employee Stock Purchase Plan of Denali Therapeutics Inc.,
6. Registration Statement (Form S-8 No. 333-253567) pertaining to the 2017 Equity Incentive Plan and 2017 Employee Stock Purchase Plan of Denali Therapeutics Inc.,
7. Registration Statement (Form S-8 No. 333-236729) pertaining to the 2017 Equity Incentive Plan and 2017 Employee Stock Purchase Plan of Denali Therapeutics Inc., and
8. Registration Statement (Form S-8 No. 333-230223) pertaining to the 2017 Equity Incentive Plan, 2017 Employee Stock Purchase Plan and 2015 Stock Incentive Plan of Denali Therapeutics Inc.;
9. Registration Statement (Form S-8 No. 333-221946) pertaining to the 2017 Equity Incentive Plan, 2017 Employee Stock Purchase Plan and 2015 Stock Incentive Plan of Denali Therapeutics Inc.;

of our reports dated February 26, 2026, with respect to the consolidated financial statements of Denali Therapeutics Inc. and the effectiveness of internal control over financial reporting of Denali Therapeutics Inc. included in this Annual Report (Form 10-K) of Denali Therapeutics Inc. for the year ended December 31, 2025.

/s/ Ernst & Young LLP

San Mateo, California
February 26, 2026

Exhibit 31.1

CERTIFICATION OF PERIODIC REPORT UNDER SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Ryan J. Watts, Ph.D., certify that:

1. I have reviewed this Annual Report on Form 10-K of Denali Therapeutics Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

    a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

    b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our 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;

    c. Evaluated the effectiveness of the registrant’s disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

    d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting;

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

    a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

    b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 26, 2026

/s/ Ryan J. Watts
Ryan J. Watts, Ph.D.
President and Chief Executive Officer

Exhibit 31.2

CERTIFICATION OF PERIODIC REPORT UNDER SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Alexander O. Schuth, M.D., certify that:

1. I have reviewed this Annual Report on Form 10-K of Denali Therapeutics Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

    a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

    b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our 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;

    c. Evaluated the effectiveness of the registrant’s disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

    d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting;

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

    a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

    b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 26, 2026

/s/ Alexander O. Schuth

Alexander O. Schuth, M.D.
Chief Operating and Financial Officer

Exhibit 32.1

CERTIFICATION OF CHIEF EXECUTIVE OFFICER
PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), I, Ryan J. Watts, Ph.D., President and Chief Executive Officer of Denali Therapeutics Inc. (the "Company"), hereby certify that:

1. The Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2025, to which this Certification is attached as Exhibit 32.1 (the "Periodic Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

2. The information contained in the Periodic Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 26, 2026

By:	/s/ Ryan J. Watts
Name:	Ryan J. Watts, Ph.D.
Title:	President and Chief Executive Officer

Exhibit 32.2

CERTIFICATION OF CHIEF FINANCIAL OFFICER
PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), I, Alexander O. Schuth, M.D., Chief Operating and Financial Officer of Denali Therapeutics Inc. (the "Company"), hereby certify that:

1. The Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2025, to which this Certification is attached as Exhibit 32.2 (the "Periodic Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

2. The information contained in the Periodic Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 26, 2026

By: /s/ Alexander O. Schuth
Name: Alexander O. Schuth, M.D.
Title: Chief Operating and Financial Officer