

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

FORM S-3
REGISTRATION STATEMENT
Under
The Securities Act of 1933

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

Delaware

(State or other jurisdiction of
incorporation or organization)

46-3872213

(I.R.S. Employer
Identification No.)

**161 Oyster Point Blvd.
South San Francisco, CA, 94080
(650) 866-8548**

(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

**Ryan J. Watts, Ph.D.
President and Chief Executive Officer
Denali Therapeutics Inc.
161 Oyster Point Blvd.
South San Francisco, California 94080
(650) 866-8548**

(Name, address, including zip code, and telephone number, including area code, of agent for service)

**Copies to:
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**APPROXIMATE DATE OF COMMENCEMENT OF PROPOSED SALE TO THE PUBLIC:
From time to time after the effective date of this registration statement.**

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box:

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box:

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

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

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

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.

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 7(a)(2)(B) of Securities Act.



DENALI THERAPEUTICS INC

29,290,754 Shares of Common Stock

This prospectus relates to the offer and resale from time to time of up to 29,290,754 shares (the “**Shares**”) of our common stock, par value \$0.01 per share, by the selling stockholders identified in this prospectus, including their transferees, pledgees or donees or their respective successors (the “**selling stockholders**”), which consist of (i) 3,244,689 outstanding shares of our common stock held by the selling stockholders and (ii) 26,046,065 shares of our common stock issuable upon the exercise of outstanding pre-funded warrants to purchase shares of our common stock held by the selling stockholders. The shares of common stock and pre-funded warrants to purchase shares of common stock were issued and sold to the selling stockholders in a private placement (the “**Private Placement**”) pursuant to a securities purchase agreement among us and such selling stockholders dated February 27, 2024 (the “**Purchase Agreement**”). We are registering the Shares being offered hereunder pursuant to such Purchase Agreement on behalf of the selling stockholders, to be offered and sold by them from time to time.

The registration of the shares of our common stock covered by this prospectus does not mean that the selling stockholders will offer or sell any of the shares. Sales of the shares by the selling stockholders may occur at fixed prices, at market prices prevailing at the time of sale, at prices related to prevailing market prices or at negotiated prices. The selling stockholders may sell shares to or through underwriters, broker-dealers or agents, who may receive compensation in the form of discounts, concessions or commissions from the selling stockholders, the purchasers of the shares, or both. We are paying the cost of registering the shares of common stock covered by this prospectus as well as various related expenses. The selling stockholders will bear all fees, discounts, concessions or commissions of broker-dealers or agents, and any other expenses incurred in connection with the offering of the shares by the selling stockholders. See “*Plan of Distribution*” beginning on page [16](#) of this prospectus for more information about how the selling stockholders may sell their shares of common stock.

Our common stock is listed on the Nasdaq Global Select Market under the symbol “DNL1.” On March 21, 2024, the last reported sale price of our common stock on the Nasdaq Global Select Market was \$21.00 per share.

Investing in our securities involves risks. Please carefully read the information under the headings “[Risk Factors](#)” beginning on page [9](#) of this prospectus and “Item 1A – Risk Factors” of our most recent report on Form 10-K or 10-Q that is incorporated by reference in this prospectus before you invest in our securities.

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

The date of this prospectus is March 22, 2024.

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ABOUT THIS PROSPECTUS

This prospectus is part of an automatic shelf registration statement on Form S-3 that we filed with the United States Securities and Exchange Commission (the “**SEC**”) as a “well-known seasoned issuer” as defined in Rule 405 under the Securities Act of 1933, as amended (the “**Securities Act**”), using a “shelf” registration process. Under this shelf registration process, the selling stockholders may, from time to time, offer and sell shares of our common stock described in this prospectus in one or more offerings.

You should only rely on the information contained in or incorporated by reference into this prospectus (as supplemented and amended), along with the information contained in any free writing prospectuses we have authorized for use in connection with a specific offering. No person has been authorized to give any information or make any representations other than those contained in or incorporated by reference into this prospectus (as supplemented and amended) and, if given or made, such information or representations must not be relied upon as having been authorized by us or the selling stockholders. Your reliance on any unauthorized information or representation is at your own risk. This prospectus (as supplemented and amended) shall not constitute an offer to sell or a solicitation of an offer to buy offered securities in any jurisdiction in which it is unlawful for such person to make such an offering or solicitation.

You should read the entire prospectus (as supplemented and amended) and any related free writing prospectus, as well as the documents incorporated by reference into this prospectus, before making an investment decision. The information contained in this prospectus, and in any supplement or amendment to this prospectus or any related free writing prospectus, or the documents incorporated by reference herein and therein, are accurate only as of their respective dates, regardless of the time of delivery of this prospectus, any supplement or amendment to this prospectus or any related free writing prospectus, or any sale of a security. Our business, financial condition, results of operations and prospects may have changed since that date.

PROSPECTUS SUMMARY

This summary highlights selected information that is presented in greater detail elsewhere, or incorporated by reference, in this prospectus. It does not contain all of the information that may be important to you and your investment decision. Before investing in our securities, you should carefully read this entire prospectus, including the matters set forth in the section titled "Risk Factors" and the financial statements and related notes and other information that we incorporate by reference herein, including our Annual Report on Form 10-K and our Quarterly Reports on Form 10-Q. Unless the context indicates otherwise, references in this prospectus to "Denali Therapeutics Inc.," "we," "our" and "us" refer, collectively, to Denali Therapeutics Inc., a Delaware corporation.

Company Overview

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

We are a clinical stage biopharmaceutical company developing a broad portfolio of product candidates engineered to cross the blood-brain barrier ("**BBB**") for neurodegenerative diseases and lysosomal storage diseases ("**LSDs**"). We have a diversified and differentiated portfolio of both small molecule and biotherapeutic medicines, comprising seven product candidates in clinical development across seven indications as well as more than a dozen preclinical therapeutic candidates. Each of our programs has been engineered for efficient delivery across the BBB to increase drug exposure in the brain after systemic administration. We have discovered and developed a proprietary platform technology called the Transport Vehicle ("**TV**"), which we have used in developing our portfolio of brain-penetrant therapies based on our Enzyme Transport Vehicle ("**ETV**"), Antibody Transport Vehicle, Protein Transport Vehicle ("**PTV**"), and Oligonucleotide Transport Vehicle. 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 advance next-generation, targeted medicines for people living with neurodegenerative diseases. We plan to further grow our discovery and clinical development capabilities, focusing on TV-enabled biotherapeutics programs for neurodegenerative diseases, and intend to build internal manufacturing capabilities and commercial infrastructure in a staged manner that is aligned with the progression of our portfolio. We aim to serve patients as a fully integrated global organization.

We have three late-stage development programs: tividonofusp alfa (DNL310, ETV:IDS) for mucopolysaccharidosis II ("MPS II", or "Hunter syndrome"); BIIB122/DNL151 (LRRK2 inhibitor) for Parkinson's disease; and DNL343 (eIF2B activator) for amyotrophic lateral sclerosis ("ALS"). SAR443820/DNL788 (RIPK1 inhibitor) is being evaluated in a Phase 2 study for multiple sclerosis. In addition, we are conducting a Phase 1/2 study of TAK-594/DNL593 (PTV:PGRN) for frontotemporal dementia-granulin and a Phase 1/2 study of DNL126 (ETV:SGSH) for MPS IIIA (Sanfilippo syndrome). Eclitasertib (SAR443122/DNL758, peripheral RIPK1 inhibitor) is in a Phase 2 study for ulcerative colitis.

As our portfolio matures and our company scales, we plan to maintain a deep focus on science to guide our efforts to discover, develop, and deliver medicines to patients. Our discovery and development strategy is guided by three overarching principles that we believe will significantly increase the probability of success and accelerate the timing to bring effective therapeutics to people living with neurodegenerative diseases and LSDs:

- **Degenogenes: Genetic Pathway Realization** – each of our programs addresses a molecular target or biological pathway that is genetically validated to cause or increase the risk for neurodegenerative diseases.
- **Brain Delivery: Validation and Optionality** – we engineer our product candidates to cross the BBB and act directly in the brain. Our proprietary TV platform technology is designed to effectively deliver large therapeutic molecules, such as enzymes, proteins, antibodies, and oligonucleotides, across the BBB after intravenous administration.
- **Biomarker-Driven Development and Approval** – we discover, develop and use biomarkers to inform dose selection, assess clinical activity, and identify patients most likely to respond to our therapies. We are actively engaged in discussions with health authorities regarding the potential use of biomarkers as primary clinical endpoints to support faster paths to approval.

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) 866-8548. 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 use Denali®, the Denali Therapeutics logo, and other marks as trademarks in the United States and other countries. This prospectus and the documents incorporated herein may contain references to our trademarks and service marks and to those belonging to other entities. Solely for convenience, trademarks and trade names referred to in this prospectus and the documents incorporated herein, 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.

Private Placement

On February 27, 2024, in connection with the Private Placement, we entered into the Purchase Agreement with the selling stockholders named in this prospectus. Under the terms of the Purchase Agreement, we agreed to prepare and file a registration statement for purposes of registering the resale of the Shares and to use our commercially reasonable efforts to have such registration statement declared effective within the time period set forth in the Purchase Agreement.

At the closing of the Private Placement on February 29, 2024 we sold and issued to certain of the selling stockholders (i) 3,244,689 shares of our common stock at a purchase price of \$17.07 per share and (ii) 26,046,065 shares of our common stock issuable upon the exercise of outstanding pre-funded warrants to purchase shares of our common stock at a purchase price of \$17.06 per share and an exercise price of \$0.01 per share. The total purchase price paid by the selling stockholders in the Private Placement was approximately \$500 million.

The offer and sale of the securities in the Private Placement were not registered under the Securities Act, or any state securities laws. We relied on an exemption from the registration requirements of the Securities Act provided by Section 4(a)(2) thereof and Rule 506(b) of Regulation D promulgated thereunder. Each of the selling stockholders has represented to us that such selling stockholder is an "accredited investor," as defined in Regulation D of the Securities Act, and that the securities purchased by such selling stockholder were being acquired solely for such selling stockholder's own account and for investment purposes and not with a view to its future sale or distribution.

The description of the Purchase Agreement is not complete and is qualified in its entirety by reference to the Purchase Agreement, which was filed as an exhibit to our Current Report on Form 8-K, filed on February 27, 2024. See "*Where You Can Find More Information*" and "*Incorporation by Reference*." The representations, warranties, and covenants made by us in the Purchase Agreement were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties thereto, and should not be deemed to be a representation, warranty, or covenant to you. Moreover, such representations, warranties or covenants were made as of an earlier date. Accordingly, such representations, warranties, and covenants should not be relied on as accurately representing the current state of our affairs.

THE OFFERING

Common stock registered for sale by selling stockholders	29,290,754 Shares, consisting of 3,244,689 outstanding shares of our common stock held by the selling stockholders and 26,046,065 shares of our common stock issuable upon the exercise of outstanding pre-funded warrants to purchase shares of our common stock.
Use of proceeds	We will not receive any proceeds from the sale of shares of common stock by the selling stockholders. Upon any exercise of the pre-funded warrants by payment of cash, however, we will receive the exercise price of such pre-funded warrants. See <i>"Use of Proceeds"</i> for additional information.
Offering price	The selling stockholders may sell all or a portion of their shares through public or private transactions at prevailing market prices or at privately negotiated prices. See <i>"Plan of Distribution"</i> for additional information.
Risk factors	You should read the <i>"Risk Factors"</i> section included in or incorporated by reference in this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
Nasdaq Global Select Market symbol	"DNLI"

RISK FACTORS

An investment in our common stock involves a high degree of risk. Prior to making a decision about investing in our common stock, you should carefully consider the specific risks, uncertainties and assumptions discussed in Part I, Item 1A “Risk Factors” in our most recent Annual Report on Form 10-K and Part II, Item 1A “Risk Factors” in our Quarterly Reports on Form 10-Q, each as may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future, all of which are incorporated by reference into this prospectus in their entirety, together with other information in this prospectus, including any information incorporated or deemed to be incorporated by reference herein. The risks and uncertainties we have described are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations. See the sections titled “*Where You Can Find More Information*” and “*Incorporation by Reference*.”

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, any prospectus supplement and the information incorporated by reference herein may contain certain statements that constitute “forward-looking statements” within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. The words “believe,” “may,” “will,” “estimate,” “continue,” “anticipate,” “intend,” “expect,” “could,” “would,” “project,” “plan,” “potentially,” “likely,” and similar expressions and variations thereof are intended to identify forward-looking statements, but are not the exclusive means of identifying such statements. Such forward-looking statements include statements regarding the intent, belief or current expectations of our management that are subject to known and unknown risks, uncertainties and assumptions. You are cautioned that any such forward-looking statements are not guarantees of future performance and involve risks and uncertainties, and that actual results may differ materially from those projected in the forward-looking statements as a result of various factors. Forward-looking statements contained in this prospectus, any prospectus supplement, and the information incorporated by reference herein 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 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 BBB platform technology;
- 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, 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 COVID-19 pandemic, and related global economic disruptions and social conditions on our business;
- expectations regarding the intended use of proceeds from the Private Placement; and
- our financial performance.

Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not rely upon forward-looking statements as predictions of future events. The events and circumstances reflected in the 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, including the securities laws of the United States and the rules and regulations of the SEC, we do not plan to publicly update or revise any forward-looking statements contained herein after we distribute this prospectus, whether as a result of any new information, future events or otherwise.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus, and although 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 a thorough inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

This prospectus and the documents incorporated by reference in this prospectus may contain market data that we obtain from industry sources. These sources do not guarantee the accuracy or completeness of the information. Although we believe that our industry sources are reliable, we do not independently verify the information. The market data may include projections that are based on a number of other projections. While we believe these assumptions to be reasonable and sound as of the date of this prospectus, actual results may differ from the projections.

USE OF PROCEEDS

We are filing the registration statement of which this prospectus is a part to permit holders of the shares of our common stock described in the section entitled “*Selling Stockholders*” to resell such shares. We are not selling any securities under this prospectus and we will not receive any proceeds from the sale or other disposition of shares of our common stock held by the selling stockholders. Upon any exercise of the pre-funded warrants by payment of cash, however, we will receive the exercise price of such pre-funded warrants. The selling stockholders will receive all of the proceeds from this offering.

The selling stockholders will pay any discounts, commissions, fees of underwriters, selling brokers, or dealer managers and expenses incurred by the selling stockholders for brokerage, accounting, tax or legal services or any other expenses incurred by the selling stockholders in disposing of the shares. We will bear all other costs, fees, and expenses incurred in effecting the registration of the shares covered by this prospectus, including, without limitation, all registration and filing fees, printing fees, Nasdaq listing fees, and fees and expenses of our counsel and our accountants.

SELLING STOCKHOLDERS

This prospectus relates to the possible resale by certain of our stockholders, who we refer to in this prospectus as the “selling stockholders,” of up to 29,290,754 Shares, which consist of (i) 3,244,689 outstanding shares of our common stock held by the selling stockholders and (ii) 26,046,065 shares of our common stock issuable upon the exercise of outstanding pre-funded warrants to purchase shares of our common stock that are held by the selling stockholders. The pre-funded warrants are exercisable at any time after their original issuance and will not expire. We cannot predict when or whether any of the selling stockholders will exercise their pre-funded warrants. See “*Prospectus Summary—Private Placement.*”

The pre-funded warrants provide that a holder of pre-funded warrants does not have the right to exercise pre-funded warrants if such holder, together with its affiliates, would beneficially own in excess of 4.99% of the number of shares of our common stock outstanding immediately before or after giving effect to such exercise (the “**Beneficial Ownership Limitation**”); provided, however, that each holder may increase or decrease the Beneficial Ownership Limitation not in excess of 19.99%, in the case of an increase, by providing at least 61 days’ prior notice to the Company. Throughout this prospectus, when we refer to the shares of common stock being registered on behalf of the selling stockholders, we are referring to the outstanding shares of our common stock and the shares issuable upon the exercise of outstanding pre-funded warrants without giving effect to the Beneficial Ownership Limitation.

The following table provides the names of the selling stockholders and the number of shares of our common stock offered by such selling stockholders under this prospectus. The selling stockholders listed below have previously been granted registration rights with respect to the shares offered hereby pursuant to that Securities Purchase Agreement dated as of February 27, 2024, by and between us and certain of our securityholders. The shares offered by this prospectus may be offered from time to time by the selling stockholders listed below. The selling stockholders are not obligated to sell any of their shares offered by this prospectus, and reserve the right to accept or reject, in whole or in part, any proposed sale of shares. The selling stockholders listed below may also offer and sell less than the number of shares indicated. The selling stockholders are not making any representation that any shares covered by this prospectus will or will not be offered for sale.

The number of shares and percentages of beneficial ownership set forth below are based on 142,458,337 shares of our common stock outstanding as of March 15, 2024. Beneficial ownership is determined under the SEC rules and regulations and generally includes voting or investment power over securities. We have prepared the table based on information given to us by, or on behalf of, the selling stockholders. The selling stockholders may sell all, some or none of the shares of common stock subject to this prospectus. See “*Plan of Distribution*” as may be supplemented and amended from time to time.

The number of shares of common stock set forth below for each selling stockholder includes (i) all shares of our common stock beneficially held by such selling stockholder as of March 15, 2024, excluding shares issuable upon the exercise of outstanding pre-funded warrants above the Beneficial Ownership Limitation, (ii) the number of shares of our common stock that may be offered under this prospectus, and (iii) the number and percentage of our common stock beneficially owned by the selling stockholders assuming all of the shares of our common stock registered hereunder are sold. The table below and footnotes assume that the selling stockholders will sell all of the shares listed. However, because the selling stockholders may sell all, some or none of their shares under this prospectus from time to time, or in another permitted manner, we cannot assure you as to the actual number of shares that will be sold by the selling stockholders or that will be held by the selling stockholders after completion of any sales.

In addition, we may name additional selling stockholders from time to time. Information about such additional selling stockholders, including their identities and the securities to be registered on their behalf, will be set forth in a prospectus supplement, in a post-effective amendment or in filings that we make with the SEC under the Exchange Act that are incorporated by reference in this prospectus.

Name of Selling Stockholder	Shares of Common Stock Beneficially Owned Prior to Offering		Shares of Common Stock Being Offered ⁽¹⁾	Shares of Common Stock to be Beneficially Owned After Offering ⁽²⁾	
	Number	Percentage	Number	Number	Percentage
Entities Affiliated with Baker Bros. Advisors LP ⁽³⁾	7,286,032	4.99 %	26,046,065	3,731,695	2.62 %
Entities Affiliated Wellington ⁽⁴⁾	104,260	*	104,260	—	*
Entities Affiliated with Capital ⁽⁵⁾	3,140,429	2.20 %	3,140,429	—	*

* Indicates beneficial ownership of less than 1% of the total outstanding common stock.

- (1) The number of shares of our common stock in the column “Shares of Common Stock Being Offered” represents all of the shares of our common stock that a selling stockholder may offer and sell from time to time under this prospectus, without giving effect to the Beneficial Ownership Limitation.
- (2) We do not know when or in what amounts a selling stockholder may offer Shares for sale. The selling stockholders might not sell any or might sell all of the shares offered by this prospectus. Because the selling stockholders may offer all, some or none of the Shares pursuant to this offering, and because, except as set forth elsewhere in this prospectus, there are currently no agreements, arrangements or understandings with respect to the sale of any of the Shares, we cannot estimate the number of the Shares that will be held by the selling stockholders after completion of the offering. However, for purposes of this table, we have assumed that, after completion of the offering, none of the shares covered by this prospectus will be held by the selling stockholders.
- (3) The shares reported under “Shares of Common Stock Beneficially Owned Prior to Offering” consist of (i) 326,302 shares of common stock and 294,973 shares of common stock issuable upon the exercise of pre-funded warrants purchased in the Private Placement held directly by 667, L.P. (“**667**”) and (ii) 3,405,393 shares of common stock and 3,259,364 shares of Common Stock issuable upon the exercise of pre-funded warrants purchased in the Private Placement held directly by Baker Brothers Life Sciences, L.P. (“**Life Sciences**”, and together with 667, the “**Funds**”). In accordance with the Beneficial Ownership Limitation of the pre-funded warrants, 667 and Life Sciences are prohibited from exercising such pre-funded warrants to the extent that, immediately prior to or as a result of such exercise, 667 and Life Sciences would, together with affiliates and any persons who are members of a Section 13(d) group with these funds or their affiliates, beneficially own more than 4.99% of the total number of shares of common stock then issued and outstanding immediately after giving effect to the exercise. As a result, the “Shares of Common Stock Beneficially Owned Prior to Offering” excludes an aggregate of 22,491,728 shares of common stock issuable upon the exercise of the pre-funded warrants due to the Beneficial Ownership Limitation. By written notice to the Issuer, the Funds may from time to time increase or decrease the Beneficial Ownership Limitation applicable to that Fund to any other percentage not in excess of 19.99%. Any such increase will not be effective until the 61st day after such notice is delivered to the Issuer. Baker Bros. Advisors LP (the “**Advisor**”) is the investment advisor to the Funds and has the sole voting and investment power with respect to the securities held by the Funds and thus may be deemed to beneficially own such securities. Baker Bros. Advisors (GP) LLC (the “**Advisor GP**”) is the sole general partner of the Advisor and thus may be deemed to beneficially own the securities held by the Funds. The managing members of the Advisor GP are Julian C. Baker and Felix J. Baker, who may be deemed to beneficially own the securities held by the Funds. Julian C. Baker, Felix J. Baker, the Advisor and the Advisor GP disclaim beneficial ownership of all shares held by the Funds, except to the extent of their indirect pecuniary interest therein. The business address of the Advisor, the Advisor GP, Julian C. Baker and Felix J. Baker is 860 Washington Street, 3rd Floor, New York, NY 10014.
- (4) The shares reported under “Shares of Common Stock Beneficially Owned Prior to Offering” consist of (i) 4,250 shares of common stock purchased by Fiducian Technology Fund (“**Fiducian**”) in the Private Placement, (ii) 33,100 shares of common stock purchased by Salthill Investors (Bermuda) L.P. (“**Salthill Investors**”) in the Private Placement, (iii) 44,000 shares of common stock purchased by Salthill Partners, L.P. (“**Salthill Partners**”) in the Private Placement, (iv) 22,910 shares of common stock purchased by Wellington Trust Company, National Association Multiple Collective Investment Funds Trust, Biotechnology Portfolio (“**Wellington Trust**,” and together with Fiducian, Salthill Investors, and Salthill Partners, the “**Wellington Selling Stockholders**”) in the Private Placement, and (v) an aggregate of 104,260 shares of common stock held by the Wellington Selling Shareholders. Wellington Management Company LLP (“**WMC**”) has the power to dispose of the securities pursuant to WMC’s capacity as investment advisor on behalf of the Wellington Selling Stockholders. WMC is a subsidiary of Wellington Management Group LLP (“**WMG**”). WMG is a Massachusetts limited liability partnership, privately held by 204 partners (as of January 1, 2024). There are no external entities with any ownership interest in the firm. No single partner owns or has the right to vote more than 5% of WMC’s capital. Additional information about WMC is available in its Form ADV filed with the SEC. The address of the Wellington Selling Stockholders is 280 Congress Street, Boston, MA 02210.

(5) The shares reported under “Shares of Common Stock Beneficially Owned Prior to Offering” consist of (i) 1,756,500 shares of common stock purchased by SMALLCAP World Fund, Inc. (“**SMALLCAP**”) in the Private Placement, (ii) 201,200 shares of common stock purchased by American Funds Insurance Series – Global Small Capitalization Fund (“**American Funds Insurance**”) in the Private Placement, (iii) 1,141,800 shares of common stock purchased by The New Economy Fund (“**New Economy**”) in the Private Placement, (iv) 20,407 shares of common stock purchased by Capital Group New Economy Trust (US) (“**Capital Group US**”) in the Private Placement, (v) 20,522 shares of common stock purchased by Capital Group New Economy Fund (LUX) (“**Capital Group LUX**,” and together with SMALLCAP, American Funds Insurance, New Economy, and Capital Group US, the “**Capital Selling Stockholders**”) in the Private Placement, and (vi) an aggregate of 3,140,429 shares of common stock held by the Capital Selling Stockholders. Capital Research and Management Company (“**CRMC**”) is the investment advisor for the Capital Selling Stockholders. Michael Beckwith, Bradford F. Freer, Harold H. La, Shlok Melwani, Aidan O’Connell, Renaud H. Samyn and Gregory W. Wendt, as portfolio managers (the “**AFI Portfolio Managers**”), have voting or investment control over the shares of common stock held by American Funds Insurance. CRMC or Capital Research Global Investors (“**CRGI**”) may be deemed to be the beneficial owner of the shares of common stock held by American Funds Insurance; however, each of CRMC and CRGI, and each of the AFI Portfolio Managers, expressly disclaims that it is, in fact, the beneficial owner of such securities. Paul Benjamin, Mathews Cherian, Tomoko Fortune, Caroline Jones, Harold H. La, Reed Lowenstein, Lara Pellini and Richmond Wolf, as portfolio managers (the “**New Economy Portfolio Managers**”), have voting or investment control over the shares of common stock held by New Economy, Capital Group US, and Capital Group LUX. CRMC, CRGI or Capital World Investors (“**CWI**”) may be deemed to be the beneficial owner of the shares of common stock held by New Economy, Capital Group US, and Capital Group LUX; however, each of CRMC, CRGI and CWI, and each of the New Economy Portfolio Managers, expressly disclaims that it is, in fact, the beneficial owner of such securities. Julian N. Abdey, Peter Eliot, Brady L. Enright, Bradford F. Freer, Peter Gusev, Leo Hee, M. Taylor Hinshaw, Roz Hongsaranagon, Akira Horiguchi, Shlok Melwani, Dimitrije Mitrinovic, Aidan O’Connell, Samir Parekh, Piyada Phanaphat, Andraz Razen, Renaud H. Samyn, Arun Swaminathan, Thatcher Thompson and Gregory W. Wendt, as portfolio managers (the “**SMALLCAP Portfolio Managers**”), have voting or investment control over the shares of common stock held by SMALLCAP. CRMC, Capital International Investors (“**CII**”), CRGI or CWI may be deemed to be the beneficial owner of the shares of common stock held by SMALLCAP; however, each of CRMC, CII, CRGI and CWI, and each of SMALLCAP Portfolio Managers, expressly disclaims that it is, in fact, the beneficial owner of such securities. The address of SMALLCAP, American Funds Insurance, New Economy, and Capital Group US is 333 South Hope Street, 55th Floor, Los Angeles, CA 90071. The address of Capital Group Lux is 6C, Route de Trèves, Senningerberg, L- 2633, Luxembourg.

Relationships with Selling Stockholders

In connection with the Private Placement, the Company entered into a nominating agreement (the “**Nominating Agreement**”) with the Funds. Pursuant to the Nominating Agreement, at such time beginning 60 days after the Funds, together with their affiliates, beneficially own more than 10% of the outstanding Common Stock, and ending at such time as the Funds and their affiliates beneficially own at least 65% of the number of pre-funded warrants purchased pursuant to the Purchase Agreement, the Funds shall have the right to appoint one individual designated by the Funds (the “**Board Designee**”) to the Board of Directors of the Company; thereafter, the Company shall (if the Funds have exercised their right) include the Board Designee in the slate of nominees recommended to the Company’s stockholders for election as directors of the Company at each annual or special meeting of the Company’s stockholders at which directors of the same class as the Board Designee are to be elected, subject to certain exceptions.

The description of the Nominating Agreement is not complete and is qualified in its entirety by reference to the Nominating Agreement, which was filed as an exhibit to our Current Report on Form 8-K, filed on February 27, 2024. See “*Where You Can Find More Information*” and “*Incorporation by Reference*.”

PLAN OF DISTRIBUTION

The selling stockholders may sell securities under this prospectus:

- through underwriters;
- through dealers;
- through agents;
- directly to purchasers; or
- through a combination of any of these methods of sale.

The selling stockholders, including their transferees, pledgees, or donees or their respective successors, may, from time to time, sell, transfer or otherwise dispose of any or all of their shares of common stock or interests in shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These dispositions may be at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices.

The selling stockholders may use any one or more of the following methods when disposing of shares or interests therein:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent, but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- short sales effected after the date the registration statement of which this prospectus is a part is declared effective by the SEC;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share;
- a combination of any such methods of sale; and
- any other method permitted by applicable law.

The selling stockholders may, from time to time, pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock, from time to time, under this prospectus, or under an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act, amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus. The selling stockholders also may transfer the shares of common stock in other circumstances, in which case the transferees, pledgees or other successors in interest will be the selling stockholders for purposes of this prospectus.

In connection with the sale of our common stock or interests therein, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the common stock in the course of hedging the positions they assume. The selling stockholders may also sell shares of our common stock short and deliver these securities to close out their short positions, or loan or pledge the common stock to broker-dealers that in turn may sell these securities. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The aggregate proceeds to the selling stockholders from the sale of the common stock offered by them will be the purchase price of the common stock less discounts or commissions, if any. Each of the selling stockholders reserves the right to accept and, together with their agents from time to time, to reject, in whole or in part, any proposed purchase of common stock to be made directly or through agents. We will not receive any of the proceeds from this offering. Upon any exercise of the pre-funded warrants by payment of cash, however, we will receive the exercise price of such pre-funded warrants.

The selling stockholders also may resell all or a portion of the shares in open market transactions in reliance upon Rule 144 under the Securities Act, provided that they meet the criteria and conform to the requirements of that rule, or another available exemption from the registration requirements of the Securities Act.

The selling stockholders and any underwriters, broker-dealers, or agents that participate in the sale of the common stock or interests therein may be "underwriters" within the meaning of Section 2(a)(11) of the Securities Act. Any discounts, commissions, concessions or profit they earn on any resale of the shares may be underwriting discounts and commissions under the Securities Act. Selling stockholders who are "underwriters" within the meaning of Section 2(a)(11) of the Securities Act will be subject to the prospectus delivery requirements of the Securities Act.

To the extent required, the shares of our common stock to be sold, the names of the selling stockholders, the respective purchase prices and public offering prices, the names of any agents, dealer, or underwriter, and any applicable commissions or discounts with respect to a particular offer will be set forth in an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the registration statement that includes this prospectus.

In order to comply with the securities laws of some states, if applicable, the common stock may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the common stock may not be sold unless it has been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

We have advised the selling stockholders that the anti-manipulation rules of Regulation M under the Exchange Act may apply to sales of shares in the market and to the activities of the selling stockholders and their affiliates. In addition, to the extent applicable, we will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the selling stockholders for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The selling stockholders may indemnify any broker-dealer that participates in transactions involving the sale of the shares against certain liabilities, including liabilities arising under the Securities Act.

We have agreed to indemnify the selling stockholders against liabilities, including liabilities under the Securities Act and state securities laws, relating to the registration of the shares offered by this prospectus.

We have agreed with the selling stockholders to use commercially reasonable efforts to cause the registration statement of which this prospectus constitutes a part to be effective and to remain continuously effective until such time as all of the shares covered by this prospectus (A) have been disposed of pursuant to and in accordance with such registration statement or (B) become eligible for resale by non-affiliates without any restrictions pursuant to Rule 144(b)(1)(i) under the Securities Act.

LEGAL MATTERS

The validity of the securities offered hereby will be passed upon for us by Wilson Sonsini Goodrich & Rosati, Professional Corporation, Palo Alto, California. Additional legal matters may be passed on for us, or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2023, and the effectiveness of our internal control over financial reporting as of December 31, 2023, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly, and current reports, proxy statements, and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at www.sec.gov. Copies of certain information filed by us with the SEC are also available on our website at www.denalitherapeutics.com. Information accessible on or through our website is not a part of this prospectus.

This prospectus and any prospectus supplement is part of a registration statement that we filed with the SEC and do not contain all of the information in the registration statement. You should review the information and exhibits in the registration statement for further information on us and our consolidated subsidiaries and the securities that we are offering. Forms of any documents establishing the terms of the offered securities are filed as exhibits to the registration statement of which this prospectus forms a part or under cover of a Current Report on Form 8-K and incorporated in this prospectus by reference. Statements in this prospectus or any prospectus supplement about these documents are summaries and each statement is qualified in all respects by reference to the document to which it refers. You should read the actual documents for a more complete description of the relevant matters.

INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference much of the information that we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus is considered to be part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated by reference in this prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus incorporates by reference the documents listed below and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (in each case, other than those documents or the portions of those documents furnished pursuant to Items 2.02 or 7.01 of any Current Report on Form 8-K and, except as may be noted in any such Form 8-K, exhibits filed on such form that are related to such information), until the offering of the securities under the registration statement of which this prospectus forms a part is terminated or completed:

- our Annual Report on Form 10-K for the year ended December 31, 2023, filed with the SEC on [February 28, 2024](#);
- the portions of our Definitive Proxy Statement on Schedule 14A, filed with the SEC on [April 18, 2023](#) (other than information furnished rather than filed), that are incorporated by reference into our Annual Report on Form 10-K;
- our Current Report on Form 8-K filed with the SEC on [February 27, 2024](#); and
- the description of our common stock contained in the Registration Statement on Form 8-A relating thereto, filed with the SEC on [November 30, 2017](#), including any amendment or report filed for the purpose of updating such description.

You may request a copy of these filings, at no cost, by making a written or oral request at the following address and telephone number:

Denali Therapeutics Inc.
161 Oyster Point Blvd.
South San Francisco, California 94080
(650) 866-8548

PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution

The following table sets forth fees and expenses to be paid by us in connection with the issuance and distribution of the securities being registered, other than discounts and commissions to be paid to agents or underwriters. All amounts shown are estimates except for the Securities and Exchange Commission, or the SEC, registration fee.

	Amount to be Paid
SEC registration fee	\$ 86,510
Legal fees and expenses	549,500
Accounting fees and expenses	25,000
Miscellaneous fees and expenses	3,500
Total	\$ 664,510

Item 15. Indemnification of Directors and Officers

We are a Delaware corporation. Section 145(a) of the Delaware General Corporation Law (the “DGCL”) provides that a Delaware corporation may indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative, other than an action by or in the right of the corporation, by reason of the fact that such person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorney fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with such action, suit or proceeding if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful.

Section 145(b) of the DGCL provides that a Delaware corporation may indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to procure a judgment in its favor by reason of the fact that such person acted in any of the capacities set forth above, against expenses (including attorney fees) actually and reasonably incurred by such person in connection with the defense or settlement of such action or suit if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interests of the corporation, except that no indemnification shall be made in respect of any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation, unless and only to the extent that the Court of Chancery or the court in which such action or suit was brought shall determine that, despite the adjudication of liability but in view of all the circumstances of the case, such person is fairly and reasonably entitled to indemnification for such expenses which the court shall deem proper.

Further subsections of DGCL Section 145 provide that:

(1) to the extent a present or former director or officer of a corporation has been successful on the merits or otherwise in the defense of any action, suit or proceeding referred to in subsections (a) and (b) of Section 145 or in the defense of any claim, issue or matter therein, such person shall be indemnified against expenses, including attorneys’ fees, actually and reasonably incurred by such person in connection therewith;

(2) the indemnification and advancement of expenses provided for pursuant to Section 145 shall not be deemed exclusive of any other rights to which those seeking indemnification or advancement of expenses may be entitled under any bylaw, agreement, vote of stockholders or disinterested directors or otherwise; and

(3) the corporation shall have the power to purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against any liability asserted against such person and incurred by such person in any such capacity, or arising out of such person's status as such, whether or not the corporation would have the power to indemnify such person against such liability under Section 145.

As used in this Item 15, the term "proceeding" means any threatened, pending, or completed action, suit, or proceeding, whether or not by or in the right of the registrant, and whether civil, criminal, administrative, investigative or otherwise.

Section 145 of the DGCL makes provision for the indemnification of officers and directors in terms sufficiently broad to indemnify our officers and directors under certain circumstances from liabilities (including reimbursement for expenses incurred) arising under the Securities Act. Our amended and restated certificate of incorporation provides, in effect, that, to the fullest extent and under the circumstances permitted by Section 145 of the DGCL, we will indemnify any and all of our executive officers and directors. We may, in our discretion, similarly indemnify our employees and agents. Our amended and restated certificate of incorporation also relieves our directors from monetary damages to us or our stockholders for breach of such director's fiduciary duty as a director to the fullest extent permitted by the DGCL. Under Section 102(b)(7) of the DGCL, a corporation may relieve its directors from personal liability to such corporation or its stockholders for monetary damages for any breach of their fiduciary duty as directors except (1) for a breach of the duty of loyalty, (2) for failure to act in good faith, (3) for intentional misconduct or knowing violation of law, (4) for willful or negligent violations of certain provisions in the DGCL imposing certain requirements with respect to stock repurchases, redemptions and dividends, or (5) for any transactions from which the director derived an improper personal benefit.

We have entered into indemnification agreements with our directors and executive officers that provide, in general, that we will indemnify them to the fullest extent permitted by law in connection with their service to us or on our behalf. We intend to enter into indemnification agreements with any new directors and executive officers in the future.

We have purchased and intend to maintain insurance on behalf of each and any person who is or was a director or officer of the Company against any loss arising from any claim asserted against him or her and incurred by him or her in any such capacity, subject to certain exclusions.

See also the undertakings set out in response to Item 17 herein.

Item 16. Exhibits

Exhibit Number	Description	Incorporated by Reference			
		Form	File No.	Exhibit	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	3.2	12/12/2017
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.	8-K	001-38311	4.1	2/27/2024
5.1	Opinion of Wilson Sonsini Goodrich & Rosati, Professional Corporation.	—	—	—	Filed Herewith
10.1	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
10.2	Nominating Agreement by and among the Company and Investor.	8-K	001-38311	10.2	2/27/2024
23.1	Consent of Independent Registered Public Accounting Firm.	—	—	—	Filed Herewith
23.2	Consent of Wilson Sonsini Goodrich & Rosati, Professional Corporation (included in the opinion filed as Exhibit 5.1 to this Registration Statement).	—	—	—	Filed Herewith
24.1	Power of Attorney (included on the signature page to this Registration Statement).	—	—	—	Filed Herewith
107	Filing Fee Table.	—	—	—	Filed Herewith

Item 17. Undertakings

(a) The undersigned registrant hereby undertakes:

(1) to file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) to include any prospectus required by Section 10(a)(3) of the Securities Act;

(ii) to reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

(iii) to include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to Section 13 or Section 15(d) of the Exchange Act that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

(2) that, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(3) to remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) that, for the purpose of determining liability under the Securities Act to any purchaser:

(i) each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(ii) each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii) or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof. *Provided, however*, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

(5) that, for the purpose of determining liability of the registrant under the Securities Act to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

(i) any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;

(ii) any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;

(iii) the portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and

(iv) any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

(6) that, for purposes of determining any liability under the Securities Act, each filing of the registrant's annual report pursuant to Section 13(a) or 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Exchange Act) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(b) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

Signature	Title	Date
<hr/> <i>/s/ Ryan J. Watts</i> Ryan J. Watts, Ph.D.	President, Chief Executive Officer and Director <i>(Principal Executive Officer)</i>	March 22, 2024
<hr/> <i>/s/ Alexander O. Schuth</i> Alexander O. Schuth, M.D.	Chief Operating and Financial Officer <i>(Principal Financial and Accounting Officer)</i>	March 22, 2024
<hr/> <i>/s/ Vicki Sato</i> Vicki Sato, Ph.D.	Chairperson of our Board of Directors	March 22, 2024
<hr/> <i>/s/ Jennifer Cook</i> Jennifer Cook	Director	March 22, 2024
<hr/> <i>/s/ Jay Flatley</i> Jay Flatley	Director	March 22, 2024
<hr/> <i>/s/ Erik Harris</i> Erik Harris	Director	March 22, 2024
<hr/> <i>/s/ Peter Klein</i> Peter Klein	Director	March 22, 2024
<hr/> <i>/s/ Steve E. Krognes</i> Steve E. Krognes	Director	March 22, 2024
<hr/> <i>/s/ David Schenkein</i> David Schenkein, M.D.	Director	March 22, 2024
<hr/> <i>/s/ Marc Tessier-Lavigne</i> Marc Tessier-Lavigne, Ph.D.	Director	March 22, 2024
<hr/> <i>/s/ Nancy A. Thornberry</i> Nancy A. Thornberry	Director	March 22, 2024

Calculation of Filing Fee Table

Form S-3
(Form Type)

Denali Therapeutics Inc.
(Exact name of registrant as specified in its charter)

Table 1 – Newly Registered Securities

Security Type	Security Class Title	Fee Calculation Rule	Amount Registered⁽¹⁾	Proposed Maximum Offering Price Per Unit⁽³⁾	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee
Equity	Common Stock, par value \$0.01 per share	457(c)	29,290,754	\$20.01 ⁽¹⁾	\$586,107,988	0.0001476	\$86,510
Total Offering Amounts					\$586,107,988		\$86,510
Total Fees Previously Paid							—
Total Fee Offsets							—
Net Fee Due							\$86,510

- (1) Pursuant to Rule 416(a) of the Securities Act of 1933, as amended, this registration statement shall also cover any additional shares of the registrant's common stock that become issuable by reason of any stock dividend, stock split, recapitalization or other similar transaction effected without receipt of consideration that increases the number of the registrant's outstanding shares of common stock.
- (2) This registration statement registers 3,244,689 outstanding shares of common stock of the registrant and 26,046,065 shares of common stock of the registrant issuable upon the exercise of pre-funded warrants issued by the registrant at an exercise price of \$0.01 per share.
- (3) Represents shares that may be sold by the selling stockholders identified in the registration statement. Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(c) under the Securities Act based on the average of the high and low prices of the registrant's common stock on the Nasdaq Global Select Market on March 15, 2024.



Wilson Sonsini Goodrich & Rosati
Professional Corporation

650 Page Mill Road
Palo Alto, California 94304-1050

O: 650.493.9300
F: 866.974.7329

March 22, 2024

Denali Therapeutics Inc.

161 Oyster Point Blvd.

South San Francisco, California 94080

Re: Registration Statement on Form S-3ASR

Ladies and Gentlemen:

At your request, we have examined the Registration Statement on Form S-3ASR (the “**Registration Statement**”), filed by Denali Therapeutics Inc., a Delaware corporation (the “**Company**”), with the Securities and Exchange Commission (the “**Commission**”) in connection with the registration pursuant to the Securities Act of 1933, as amended (the “**Act**”), of the offer and resale of an aggregate of 29,290,754 shares (the “**Shares**”) of the Company’s common stock, \$0.01 par value per share (the “**Common Stock**”).

All of the Shares are being registered for resale on behalf of certain stockholders of the Company, including their transferees, pledgees or donees or their respective successors (the “**Selling Stockholders**”), pursuant to that certain Securities Purchase Agreement, dated February 27, 2024, by and among the Company and the Selling Stockholders (the “**Purchase Agreement**”). The Shares consist of (i) 3,244,689 outstanding shares of Common Stock (the “**Common Shares**”) that are held by certain of the Selling Stockholders and (ii) 26,046,065 shares of Common Stock issuable upon the exercise of outstanding pre-funded warrants (the “**Warrants**”) to purchase shares of Common Stock (the “**Warrant Shares**”) that are held by certain of the Selling Stockholders.

AUSTIN BEIJING BOSTON BRUSSELS HONG KONG LONDON LOS ANGELES NEW YORK PALO ALTO
SAN DIEGO SAN FRANCISCO SEATTLE SHANGHAI WASHINGTON, DC WILMINGTON, DE

We have examined instruments, documents, certificates and records that we have deemed relevant and necessary for the basis of our opinions hereinafter expressed. In such examination, we have assumed: (a) the authenticity of original documents and the genuineness of all signatures; (b) the conformity to the originals of all documents submitted to us as copies; (c) the truth, accuracy and completeness of the information, representations and warranties contained in the instruments, documents, certificates and records we have reviewed; (d) that the Registration Statement, and any amendments thereto (including post effective amendments), will have become effective under the Act; (e) that the Shares will be issued and sold in compliance with applicable U.S. federal and state securities laws and in the manner stated in the Registration Statement and the accompanying prospectus, including any supplement thereto; (f) that any applicable definitive purchase, underwriting or similar agreement with respect to any Shares offered will have been duly authorized and validly executed and delivered by the Selling Stockholders and the other parties thereto; and (g) the legal capacity of all natural persons. As to any facts material to the opinions expressed herein that were not independently established or verified, we have relied upon oral or written statements and representations of officers and other representatives of the Company.

Based on such examination, we are of the opinion that:

- (1) The Common Shares have been duly authorized and are validly issued, fully paid and nonassessable.
- (2) The Warrant Shares have been duly authorized and, when issued in accordance with the terms of the Warrants, will be validly issued, fully paid and nonassessable.

Our opinion that any document is legal, valid and binding is qualified as to:

- (a) limitations imposed by bankruptcy, insolvency, reorganization, arrangement, fraudulent transfer, moratorium or other similar laws relating to or affecting the rights of creditors generally;
- (b) rights to indemnification and contribution, which may be limited by applicable law or equitable principles; and
- (c) the effect of general principles of equity, including without limitation concepts of materiality, reasonableness, good faith and fair dealing, and the possible unavailability of specific performance or injunctive relief, whether considered in a proceeding in equity or at law.

We express no opinion as to the laws of any other jurisdiction, other than the federal laws of the United States of America and the General Corporation Law of the State of Delaware.

We hereby consent to the filing of this opinion as an exhibit to the above-referenced Registration Statement and to the use of our name wherever it appears in the Registration Statement, the Prospectus, and in any amendment or supplement thereto. In giving such consent, we do not thereby admit that we are in the category of persons whose consent is required under Section 7 of the Act or the rules and regulations of the Commission thereunder.

Sincerely,

/s/ Wilson Sonsini Goodrich & Rosati

WILSON SONSINI GOODRICH & ROSATI
Professional Corporation

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption "Experts" in the Registration Statement (Form S-3) and related Prospectus of Denali Therapeutics Inc. for the registration of 29,290,754 shares of its common stock and to the incorporation by reference therein of our reports dated February 27, 2024, 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 its Annual Report (Form 10-K) for the year ended December 31, 2023, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

San Mateo, California
March 22, 2024