

PROSPECTUS SUPPLEMENT
(To prospectus dated February 27, 2025)**9,142,857 Shares of Common Stock**
Pre-Funded Warrants to Purchase 2,285,714 Shares of Common Stock

We are offering up to 9,142,857 shares of our common stock and, in lieu of common stock to certain investors, pre-funded warrants to purchase up to 2,285,714 shares of our common stock in this offering.

The purchase price of each pre-funded warrant equals the price per share at which shares of our common stock are being sold to the public in this offering, minus \$0.01, which is the exercise price of each pre-funded warrant. The pre-funded warrants do not expire, and each pre-funded warrant will be exercisable at any time after the date of issuance. This prospectus supplement also relates to the offering of the shares of our common stock issuable upon the exercise of such pre-funded warrants.

Our common stock is quoted on the Nasdaq Global Select Market under the symbol "DNL". On December 9, 2025, the last reported sale price of our common stock on the Nasdaq Global Select Market was \$19.66 per share. There is no established public trading market for the pre-funded warrants, and we do not expect a market to develop. We do not intend to list the pre-funded warrants on the Nasdaq Global Select Market or any other national securities exchange or nationally recognized trading system.

Investing in our securities involves risks. See "[Risk Factors](#)" beginning on page [S-7](#) of this prospectus supplement and in the documents incorporated by reference.

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

	Per Share		Per Pre-Funded Warrant		Total
Public offering price	\$ 17.50	\$	17.49	\$	199,977,135.36
Underwriting discounts and commissions ⁽¹⁾	\$ 0.875	\$	0.875	\$	9,999,999.63
Proceeds, before expenses, to Denali Therapeutics Inc.	\$ 16.625	\$	16.615	\$	189,977,135.73

⁽¹⁾ See "Underwriting" for a description of the compensation payable to the underwriters.

The underwriters have the option to purchase up to 1,714,285 additional shares of common stock from us at the initial price to the public less the underwriting discount.

The underwriters expect to deliver the shares and the pre-funded warrants against payment in New York on or about December 11, 2025.

Goldman Sachs & Co. LLC**J.P. Morgan****Morgan Stanley****Jefferies****H.C. Wainwright & Co.****B. Riley Securities****Prospectus supplement dated December 9, 2025.**

TABLE OF CONTENTS

	<u>Page</u>
Prospectus Supplement	
ABOUT THIS PROSPECTUS SUPPLEMENT	i
SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS	S-1
PROSPECTUS SUPPLEMENT SUMMARY	S-4
THE OFFERING	S-5
RISK FACTORS	S-7
USE OF PROCEEDS	S-15
DILUTION	S-16
DIVIDEND POLICY	S-18
DESCRIPTION OF CAPITAL STOCK	S-19
DESCRIPTION OF PRE-FUNDED WARRANTS	S-24
MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR HOLDERS OF OUR COMMON STOCK AND PRE-FUNDED WARRANTS	S-26
UNDERWRITING	S-33
LEGAL MATTERS	S-42
EXPERTS	S-42
WHERE YOU CAN FIND ADDITIONAL INFORMATION	S-42
INCORPORATION BY REFERENCE	S-43
Prospectus	
ABOUT THIS PROSPECTUS	1
THE COMPANY	2
RISK FACTORS	3
USE OF PROCEEDS	4
DESCRIPTION OF SECURITIES	5
PLAN OF DISTRIBUTION	6
LEGAL MATTERS	7
EXPERTS	7
WHERE YOU CAN FIND MORE INFORMATION	7
INCORPORATION BY REFERENCE	8

We have not authorized anyone to provide any information or to make any representations other than those contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or in any free writing prospectuses we have prepared. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus supplement and the accompanying prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus supplement and the accompanying prospectus is current only as of the date of the document in which it is contained.

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is part of the registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a "shelf" registration process and consists of two parts. The first part is this prospectus supplement, including the documents incorporated by reference, which describes the specific terms of this offering. The second part, the accompanying prospectus, including the documents incorporated by reference, gives more general information, some of which may not apply to this offering. Generally, when we refer to the "prospectus", we are referring to both parts combined. This prospectus supplement may add to, update or change information in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement or the accompanying prospectus.

If information in this prospectus supplement is inconsistent with the accompanying prospectus or with any document incorporated by reference that was filed with the SEC before the date of this prospectus supplement, you should rely on this prospectus supplement. This prospectus supplement, the accompanying prospectus and the documents incorporated by reference into each include important information about us, the securities being offered and other information you should know before investing in our securities. You should also read and consider information in the documents we have referred you to in the sections of this prospectus supplement and the accompanying prospectus entitled "Where You Can Find Additional Information" and "Incorporation of Certain Information by Reference."

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein or into the accompanying prospectus 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 to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

We take no responsibility for, and can provide no assurances as to the reliability of, any information that is in addition to or different from that contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. We are not offering to sell these securities in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained or incorporated by reference in this prospectus supplement or the accompanying prospectus is accurate as of any date other than as of the date of this prospectus supplement or the accompanying prospectus, as the case may be, or in the case of the documents incorporated by reference, the date of such documents regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or any sale of our securities. Our business, financial condition, liquidity, results of operations and prospects may have changed since those dates.

All references in this prospectus supplement or the accompanying prospectus to "Denali," the "Company," "we," "us," or "our" mean Denali Therapeutics Inc. and our subsidiaries, unless we state otherwise or the context otherwise requires. We use Denali Therapeutics®, the Denali Therapeutics logo, and other marks as trademarks in the United States and other countries. This prospectus supplement and any free writing prospectus that we may have authorized for use in connection with this offering and the information incorporated herein or therein, as the case may be, by reference 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 supplement and any free writing prospectus that we may have authorized for use in connection with this offering, 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.

No action is being taken in any jurisdiction outside the United States to permit a public offering of the securities or possession or distribution of this prospectus supplement or the accompanying prospectus in that jurisdiction. Persons who come into possession of this prospectus supplement or the accompanying prospectus in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus supplement or the accompanying prospectus applicable to that jurisdiction.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein and any free writing prospectus that we may have authorized for use in connection with this offering contain statements that are not historical facts and are considered forward-looking within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. All statements other than statements of historical facts contained in this prospectus, including statements regarding our future results of operations and financial position, business strategy, product candidates, planned preclinical studies and clinical trials, research and development costs, regulatory approvals, timing and likelihood of success, as well as plans and objectives of management for future operations, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that are in some cases beyond our control and may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “would,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “potential” or “continue” or the negative of these terms or other similar expressions. Forward-looking statements contained in this prospectus include, but are not limited to, statements about:

- *the 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, 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 (“TV”);*
- *our ability to obtain funding for our operations, including funding necessary to develop and commercialize our current and 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, changes in currency exchange rates and currency controls, and increased labor market competition;*
- *the impact of increased geopolitical uncertainty, tariffs and trade barriers, and related global economic disruptions and social conditions on our business;*
- *our financial performance; and*
- *the intended use of proceeds from this offering.*

We have based these forward-looking statements largely on our current expectations and projections about our business, the industry in which we operate, and financial trends that we believe may affect our business, financial condition, results of operations and prospects, and these forward-looking statements are not guarantees of future performance or development. These forward-looking statements speak only as of the date of the document containing the applicable statement and are subject to a number of risks, uncertainties and assumptions described in the section titled "Risk Factors" and elsewhere in this prospectus supplement and the accompanying prospectus. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Except as required by applicable law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this prospectus supplement 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 prospectus supplement or the accompanying prospectus, as the case may be, 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 prospectus supplement and the accompanying prospectus and any free writing prospectus that we may have authorized for use in connection with this offering contain estimates, projections and other information concerning our industry, our business and the markets for our product candidates. We obtained the industry, market and similar data set forth in this prospectus supplement and the accompanying prospectus or the free writing prospectus, as the case may be, 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.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus and in the documents we incorporate by reference. This summary may not contain all the information that you should consider before investing in our securities. You should read this entire prospectus supplement and the accompanying prospectus carefully, especially the risks of investing in our securities discussed under "Risk Factors" beginning on page S-7 of this prospectus supplement, along with our consolidated financial statements and notes to those consolidated financial statements and the other information incorporated by reference in this prospectus supplement and the accompanying prospectus, before making an investment decision. This prospectus supplement may add to, update or change information in the accompanying prospectus.

Overview

Our goal is to discover, develop, and deliver a new class of barrier-crossing therapeutics and to defeat degeneration.

Historically, the blood-brain barrier ("BBB") has been a major challenge to the development of medicines for diseases of the central nervous system ("CNS"). While the BBB 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 BBB challenge. 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 BBB 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 CNS 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, lysosomal, 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 tvidenofusp alfa (DNL310, ETV:IDS) for the potential treatment of mucopolysaccharidosis II ("MPS II", or Hunter syndrome). We submitted a biologics license application for tvidenofusp alfa under the FDA's accelerated approval pathway in May 2025. The Biologics License Application ("BLA") for tvidenofusp alfa remains under review with the U.S. Food and Drug Administration ("FDA"), with a Prescription Drug User Fee Act ("PDUFA") target action date of April 5, 2026. We are preparing for a potential commercial launch thereafter. Our second most advanced TV-enabled program is DNL126 (ETV:SGSH) for MPS IIIA (Sanfilippo syndrome). The Phase 1/2 study of DNL126 remains on track for completion in 2026, supporting a potential accelerated approval pathway and commercial launch by the end of 2027. Our TV-enabled portfolio also includes DNL593 (PTV:PGRN) for frontotemporal dementia-granulin ("FTD-GRN"), DNL628 (OTV:MAPT) for Alzheimer's disease, DNL952 (ETV:GAA) for Pompe disease, and other preclinical programs, including DNL921 (ATV:Abeta) for Alzheimer's disease. Our small molecule clinical development portfolio includes BIIB122/DNL151 (LRRK2 inhibitor, partnered with Biogen) for Parkinson's disease and eclitasertib (SAR443122 RIPK1 Inhibitor, partnered with Sanofi) for ulcerative colitis. 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.

Company Information

We were incorporated in Delaware in October 2013. Our principal executive offices are located at 161 Oyster Point Blvd, South San Francisco, CA and our telephone number at that address is (650) 866-8547. We maintain an Internet website at the following address: www.denalitherapeutics.com. The information on, or that can be accessed through, our website does not constitute part of this prospectus supplement or the accompanying prospectus, and you should not rely on any such information in making an investment decision.

THE OFFERING

Common stock offered by us	9,142,857 shares. We have also granted the underwriters a 30-day option to purchase up to 1,714,285 additional shares.
Pre-funded warrants offered by us	We are also offering, in lieu of common stock, to certain investors, pre-funded warrants to purchase 2,285,714 shares of common stock. The purchase price of each pre-funded warrant equals the price per share at which shares of common stock are being sold to the public in this offering, minus \$0.01, which is the exercise price of each pre-funded warrant. The pre-funded warrants do not expire, and each pre-funded warrant will be exercisable at any time after the date of issuance, subject to an ownership limitation. See "Description of Pre-Funded Warrants." This preliminary prospectus supplement also relates to the offering of the shares of common stock issuable upon the exercise of such pre-funded warrants.
Common stock to be outstanding following the offering	155,768,579 shares (or 157,482,864 shares if the underwriters exercise their option to purchase additional shares in full), in each case assuming no exercise of any pre-funded warrants offered and sold by us.
Use of proceeds	<p>We estimate that the net proceeds from this offering will be approximately \$189.3 million (or approximately \$217.8 million if the underwriters exercise their option to purchase additional shares in full).</p> <p>We intend to use the net proceeds to advance commercial readiness for DNL310, accelerate regulatory pathways for DNL310 and DNL126, support advancement of our pipeline, scale internal manufacturing capabilities, and for other general corporate purposes. See "Use of Proceeds" for more information.</p>
Nasdaq Global Select Market symbol	DNLI. We do not intend to list the pre-funded warrants on the Nasdaq Global Select Market or any other national securities exchange or any recognized trading system. Without an active market, the liquidity of the pre-funded warrants will be limited.
Risk factors	Investing in our securities involves risks. See "Risk Factors" beginning on page S-7 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus for a discussion of the factors you should carefully consider before deciding to invest in our securities.

The number of shares of our common stock to be outstanding after the offering is based on 146,625,722 shares of common stock outstanding as of September 30, 2025, and excludes:

- 21,442,215 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2025, at a weighted average exercise price of \$26.37 per share;

- 5,177,362 shares of common stock issuable upon the vesting of restricted stock units outstanding as of September 30, 2025;
- up to an aggregate of \$400.0 million of shares of common stock that may be sold under our "at-the-market" program with Goldman Sachs & Co. LLC and Leerink Partners LLC;
- 26,046,065 shares of common stock issuable up on the exercise of pre-funded warrants outstanding as of September 30, 2025 (which are immediately exercisable at an exercise price of \$0.01 per share of common stock, subject to beneficial ownership limitations) sold in our private placement in February 2024;
- 14,774,621 shares of common stock reserved for future issuance under our 2017 Equity Incentive Plan, or the 2017 Plan, as of September 30, 2025, plus any future increases in the number of shares of common stock reserved for issuance under the 2017 Plan pursuant to the evergreen provision of the 2017 Plan;
- 7,668,813 shares of common stock reserved for future issuance under our 2017 Employee Stock Purchase Plan, or the 2017 ESPP, as of September 30, 2025, plus any future increases in the number of shares of common stock reserved for issuance under the 2017 ESPP pursuant to the evergreen provision of the 2017 ESPP; and
- pre-funded warrants to purchase up to 2,285,714 shares of our common stock at an exercise price of \$0.01 per share.

Except as otherwise indicated, all information in this prospectus supplement assumes:

- no exercise by the underwriters of their option to purchase up to 1,714,285 additional shares of common stock in this offering;
- no exercise of the pre-funded warrants that we are offering in this offering in lieu of common stock to certain investors; and
- no exercise or settlement of stock options, RSUs or other equity awards described above, no grant of additional awards under our 2017 Plan, and no issuance of shares under the 2017 ESPP, in each case, after September 30, 2025.

RISK FACTORS

Investing in our securities involves a high degree of risk. Prior to making a an investment decision, you should carefully consider the risks discussed below and 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 supplement and the accompanying prospectus in their entirety, together with other information in this prospectus supplement and the accompanying 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 facing us. Additional risks and uncertainties not presently known to us, or that we currently see as immaterial, may also harm our business. If any of these risks occur, our business, financial condition and operating results could be harmed, the trading price of our common stock could decline and you could lose part or all of your investment.

Additional Risks Related to This Offering and 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 manufacture or scale production of our clinical and commercial products;
- 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;
- 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.

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, on February 27, 2024, we announced a strategic private offering transaction in which we sold 3,244,689 shares of our common stock and pre-funded warrants to purchase 26,046,065 shares of our common stock, resulting in net proceeds of approximately \$499.3 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.

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 decision to issue debt or equity securities in any future offering will depend on market conditions and other factors beyond our control, and therefore we cannot predict or estimate the amount, timing, or nature of any future offerings. To the extent that we raise additional capital through the sale of equity or debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. The incurrence of indebtedness would result in increased fixed payment obligations and could involve restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. In addition, any sales of our common stock or other securities under our shelf registration statement, including pursuant to at-the-market offerings, could put downward pressure on our stock price. 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.

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 the 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 (the "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. 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 issue 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.

We will have broad discretion in how we use the net proceeds of this offering. We may not use these proceeds effectively, which could affect our results of operations and cause our stock price to decline.

Although we currently intend to use the net proceeds from this offering in the manner described in the section entitled "Use of Proceeds" in this prospectus supplement, we will have considerable discretion in the application of the net proceeds of this offering. We may use the net proceeds for purposes that do not yield a significant return or any return at all for our stockholders. In addition, pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value. If we do not invest or apply the net proceeds from this offering in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline.

If you purchase securities in this offering, you may experience immediate and substantial dilution in the book value of your securities.

If you purchase shares of our common stock or pre-funded warrants in this offering, you will incur immediate and substantial dilution in the as adjusted net tangible book value of your common stock or the underlying pre-funded warrants purchased in this offering because the price that you pay will be substantially greater than the net tangible book value per share of the shares you acquire. To the extent outstanding options are exercised, restricted stock units vest and settle or we raise additional capital, you will incur further dilution. For a further description of the dilution that you will experience immediately after this offering, see the section in this prospectus supplement entitled "Dilution."

The pre-funded warrants are not listed on any exchange and we do not intend to list the pre-funded warrants on any exchange.

If you purchase pre-funded warrants, you may be unable to sell such warrants at the prices desired or at all. There is no existing trading market for the pre-funded warrants and there can be no assurance that a liquid market will develop or be maintained for the pre-funded warrants, or that you will be able to sell any of the pre-funded warrants at a particular time (if at all). In addition, we do not intend to apply for listing of the pre-funded warrants on Nasdaq or any other securities exchange or nationally recognized trading system. The liquidity of the trading market in the pre-funded warrants and the sale price, if any, for the pre-funded warrants, may be adversely affected by, among other things: (i) changes in the overall market for the pre-funded warrants; (ii) changes in our financial performance or prospects; (iii) changes or perceived changes in our creditworthiness; (iv) the prospects for companies in the industry generally; (v) the number of holders of the pre-funded warrants; and (vi) the interest of securities dealers in making a market for the pre-funded warrants.

Except for the right to participate in certain dividends and distributions, holders of the pre-funded warrants will have no rights as common stockholders until such holders exercise their pre-funded warrants and acquire our common stock.

Until holders of the pre-funded warrants exercise their pre-funded warrants and acquire shares of our common stock, such holders will have no rights with respect to the shares of our common stock underlying such pre-funded warrants, except that the holder of a pre-funded warrant shall be entitled to participate in certain distributions, including cash dividends, if any, to all holders of our common stock for no consideration. Upon exercise of the pre-funded warrants, the holders will be entitled to exercise the rights of a common stockholder only as to matters for which the record date occurs after the exercise date.

Significant holders or beneficial owners of our common stock may not be permitted to exercise the pre-funded warrants that they hold.

A holder of the pre-funded warrants will not be entitled to exercise any portion of such pre-funded warrants to the extent that immediately prior to or following such exercise, the aggregate number of shares of our common stock beneficially owned by the holder (together with its affiliates) to exceed 4.99% of the number of shares of our common stock outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the pre-funded warrants. Such percentage may be decreased or increased by the holder of the pre-funded warrants to any other percentage not in excess of 19.99% upon at least 61 days' prior notice from the holder to us. As a result, you may not be able to exercise your pre-funded warrants for shares of our common stock at a time when it would be financially beneficial for you to do so. In such circumstance you could seek to sell your pre-funded warrants to realize value, but you may be unable to do so in the absence of an established trading market for the pre-funded warrants.

We will not receive any meaningful amount of additional funds upon the exercise of the pre-funded warrants.

Each pre-funded warrant will be exercisable until it is fully exercised and by means of payment of the nominal cash purchase price upon exercise or by means of a "cashless exercise" according to a formula set forth in the pre-funded warrant. Accordingly, we will not receive any meaningful additional funds upon the exercise of the pre-funded warrants.

If we do not maintain a current and effective registration statement relating to the shares of common stock issuable upon exercise of the pre-funded warrants, holders will only be able to exercise such pre-funded warrants on a "cashless basis."

If we do not maintain a current and effective registration statement relating to the shares of common stock issuable upon exercise of the pre-funded warrants at the time that holders wish to exercise such pre-funded warrants, they will only be able to exercise them on a "cashless basis" provided that an exemption from registration is available. As a result, the number of ordinary shares that holders will receive upon exercise of the pre-funded warrants will be fewer than it would have been had such holder exercised his warrant for cash, and holders may be limited in their ability to immediately sell shares upon exercise subject to volume or other securities law limitations. Further, if an exemption from registration is not available, holders would not be able to exercise on a cashless basis and would only be able to exercise their pre-funded warrants for cash if a current and effective registration statement relating to the shares of common stock issuable upon exercise of the pre-funded warrants is available.

Resales of our common stock in the public market by our stockholders as a result of this offering may cause the market price of our common stock to fall.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. The issuance of these new shares of our common stock in this offering could result in resales of our common stock by our current stockholders concerned about the potential ownership dilution of their holdings. In turn, these resales could have the effect of depressing the market price for our common stock.

USE OF PROCEEDS

We estimate that the net proceeds from this offering will be approximately \$189.3 million or approximately \$217.8 million if the underwriters exercise in full their option to purchase an additional 1,714,285 shares of common stock, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We will receive nominal proceeds, if any, from any exercise of pre-funded warrants.

We intend to use the net proceeds of this offering to fund the following:

- Support for potential commercial launch activities for DNL310 in the United States and key global markets, including commercial supply, medical affairs activities, market access and reimbursement readiness, and commercial organization buildout;
- Accelerated regulatory pathways for both DNL310 (ETV:IDS) for MPS II and DNL126(ETV:SGHS) for MPS IIIA;
- Continued advancement of our other clinical-stage programs, including TAK-594/DNL593 (PTV:PGRN) for FTD-GRN, BIIB122/DNL151 (LRRK2 inhibitor) for Parkinson's disease, DNL628 (OTV:MAPT) for Alzheimer's disease and DNL952 (ETV:GAA) for Pompe Disease;
- Expansion and acceleration of our TransportVehicle™ (TV) platform, including continued optimization and clinical translation of the OTV and ATV platforms;
- Progression of our earlier-stage pipeline, including continued IND-enabling and early clinical studies for next-generation biotherapeutics enabled by the TV platform; and
- Build-out and scaling of internal process development and GMP clinical manufacturing capabilities, including production of drug substance and drug product to support clinical trials across our portfolio.

We expect to use any remaining net proceeds from this offering for general and administrative expenses, potential future development programs, early-stage research and development, capital expenditures and working capital and other general corporate purposes.

Our expected use of net proceeds from this offering represents our current intentions based upon our present plans and business condition. As of the date of this prospectus supplement, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the completion of this offering or the amounts that we will actually spend on the uses set forth above. We may also use a portion of the net proceeds to in-license, acquire or invest in complementary businesses, technologies, products or assets. Due to the many variables inherent to drug development at this time, such as the timing of patient enrollment and evolving regulatory requirements, we cannot currently predict the stage of development we expect the net proceeds of this offering to achieve for our clinical studies and product candidates.

The amount and timing of our actual expenditures will depend upon numerous factors, including our commercial activities, the results of our research and development efforts, the timing and success of preclinical studies, our ongoing clinical studies or clinical studies we may commence in the future and the timing of regulatory submissions. As a result, our management will have broad discretion over the use of the net proceeds from this offering.

Pending the use of the net proceeds from this offering, we intend to invest the net proceeds in short to intermediate-term fixed income securities.

DILUTION

If you invest in our common stock or pre-funded warrants in this offering, your ownership interest will be diluted immediately to the extent of the difference between the price per share of our common stock or pre-funded warrant in this offering and the as adjusted net tangible book value per share of our common stock immediately after this offering.

Our historical net tangible book value as of September 30, 2025 was \$926.2 million, or \$6.32 per share of our common stock. Our historical net tangible book value is the amount of our total tangible assets less our total liabilities. Historical net tangible book value per share represents historical net tangible book value divided by the number of shares of our common stock outstanding as of September 30, 2025.

After giving further effect to the sale of 9,142,857 shares of common stock in this offering at the public offering price of \$17.50 per share, and pre-funded warrants to purchase 2,285,714 shares of common stock at the public offering price of \$17.49 per pre-funded warrant (which equals the public offering price of the common stock at which shares of our common stock are being sold to the public in this offering less the \$0.01 per share exercise price of each such pre-funded warrant) (excluding shares of common stock issuable upon exercise of the pre-funded warrants, any proceeds which may be received upon exercise of the pre-funded warrants or any resulting accounting associated with the exercise of the pre-funded warrants), and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2025 would have been approximately \$1.1 billion, or approximately \$7.16 per share. This represents an immediate increase in as adjusted net tangible book value per share of \$0.84 to our existing stockholders and an immediate dilution in as adjusted net tangible book value per share of approximately \$10.34 to new investors participating in this offering. Dilution per share to new investors purchasing common stock or pre-funded warrants in this offering is determined by subtracting as adjusted net tangible book value per share after this offering from the public offering price per share paid by new investors.

The following table illustrates this per share dilution:

Public offering price per share		\$	17.50
Historical net tangible book value per share as of September 30, 2025	\$	6.32	
Increase in net tangible book value per share attributable to new investors	\$	0.84	
As adjusted net tangible book value per share after this offering	\$	7.16	
Dilution per share to new investors	\$	10.34	

The foregoing table and discussion is based on 146,625,722 shares of common stock outstanding as of September 30, 2025, and excludes:

- 21,442,215 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2025, at a weighted average exercise price of \$26.37 per share;
- 5,177,362 shares of common stock issuable upon the vesting of restricted stock units outstanding as of September 30, 2025;
- up to an aggregate of \$400.0 million of shares of common stock that may be sold under our "at-the-market" program with Goldman Sachs & Co. LLC and Leerink Partners LLC;
- 26,046,065 shares of common stock issuable up on the exercise of pre-funded warrants outstanding as of September 30, 2025 (which are immediately exercisable at an exercise price of \$0.01 per share of common stock, subject to beneficial ownership limitations) sold in our private placement in February 2024;

- 14,774,621 shares of common stock reserved for future issuance under the 2017 Plan as of September 30, 2025;
- 7,668,813 shares of common stock reserved for future issuance under our 2017 ESPP as of September 30, 2025; and
- pre-funded warrants to purchase up to 2,285,714 shares of our common stock at an exercise price of \$0.01 per share.

Assuming the pre-funded warrants issued in this offering were immediately and fully exercised, this would result in an as adjusted net tangible book value, after giving effect to this offering and warrant exercise, of \$7.06 per share. This represents a decrease in net tangible book value of \$0.10 per share to existing stockholders and dilution in net tangible book value per share of \$10.44 to new investors participating in this offering.

If the underwriters exercise in full their option to purchase up to 1,714,285 additional shares of common stock at the public offering price of \$17.50 per share, the as adjusted net tangible book value after this offering would be \$7.26 per share, representing an increase in net tangible book value of \$0.94 per share to existing stockholders and immediate dilution in net tangible book value of \$10.24 per share to investors participating in this offering at the public offering price.

To the extent that any options are exercised, any restricted stock units are settled, any new awards are issued under our equity incentive plans, or we otherwise issue additional shares of common stock in the future (including shares issued in connection with acquisitions), there will be further dilution to new investors.

In addition, we may choose to raise additional capital due to market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

DIVIDEND POLICY

We have never declared or paid cash dividends on our common stock. We currently intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination to pay dividends will be made at the discretion of our board of directors.

DESCRIPTION OF CAPITAL STOCK

The following is a summary of our capital stock and provisions of our amended and restated certificate of incorporation, amended and restated bylaws, as each is in effect as of the date of this prospectus supplement. 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, amended and restated bylaws, copies of which are incorporated by reference as exhibits to the accompanying registration statement. References in this section to "the company," "we," "us" and "our" refer to Denali Therapeutics Inc. and not to any of its subsidiaries.

Our authorized capital stock consists of 440,000,000 shares, with a par value of \$0.01 per share, of which:

- 400,000,000 shares are designated as common stock; and
- 40,000,000 shares are designated as preferred stock.

Common Stock

Outstanding Shares

As of December 4, 2025, we had 147,015,507 shares of common stock outstanding.

Voting Rights

Each holder of common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors. Our amended and restated certificate of incorporation and amended and restated bylaws do not provide for cumulative voting rights. Because of this, the holders of a plurality of the shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they should so choose. With respect to matters other than the election of directors, at any meeting of the stockholders at which a quorum is present or represented, the affirmative vote of a majority of the voting power of the shares present in person or represented by proxy at such meeting and entitled to vote on the subject matter shall be the act of the stockholders, except as otherwise required by law. The holders of a majority of the stock issued and outstanding and entitled to vote, present in person or represented by proxy, shall constitute a quorum for the transaction of business at all meetings of the stockholders.

Dividends

Subject to preferences that may be applicable to any then-outstanding preferred stock, holders of our common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then-outstanding shares of preferred stock.

Rights and Preferences

Holders of our common stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of our preferred stock that we may designate in the future.

Fully Paid and Nonassessable

All of our outstanding shares of common stock are, and the shares of common stock to be issued in this offering, upon payment and delivery in accordance with the underwriting agreement, will be fully paid and nonassessable.

Preferred Stock

Our amended and restated certificate of incorporation contains provisions that permit our board of directors to issue, without any further vote or action by the stockholders, shares of preferred stock in one or more series and, with respect to each such series, to fix the number of shares constituting the series and the designation of the series, the voting rights (if any) of the shares of the series, and the powers, preferences or relative, participation, optional and other special rights, if any, and any qualifications, limitations or restrictions, of the shares of such series.

Anti-Takeover Effects of Certain Provisions of Delaware Law, Our Amended and Restated Certificate of Incorporation and Our Amended and Restated Bylaws

Certain provisions of Delaware law and certain provisions included in our amended and restated certificate of incorporation and amended and restated bylaws summarized below may be deemed to have an anti-takeover effect and may delay, deter, or prevent a tender offer or takeover attempt that a stockholder might consider to be in its best interests, including attempts that might result in a premium being paid over the market price for the shares held by stockholders.

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. The directors in each class serve for a three-year term, one class being elected each year by our stockholders, with staggered three-year terms. Only one class of directors is elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms. Because our stockholders do not have cumulative voting rights, our stockholders holding a majority of the shares of common stock outstanding are able to elect all of our directors.

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 Nominating Agreement

In connection with the securities purchase agreement we entered into in February 2024 (the "Purchase Agreement") with the purchasers named therein, including Baker Brothers Life Sciences, L.P. and 667, L.P. (the "Baker Funds"), we entered into a nominating agreement (the "Nominating Agreement") with the Baker Funds. Pursuant to the Nominating Agreement, at such time beginning 60 days after the Baker Funds, together with their affiliates, beneficially own more than 10% of our outstanding common stock, and ending at such time as the Baker Funds and their affiliates beneficially own at least 65% of the number of securities purchased pursuant to the Purchase Agreement, the Baker Funds shall have the right to designate one individual to serve on our board of directors (the "Baker Funds Designation Right"); and if the Baker Funds have exercised this right, we shall include the designee in the slate of nominees recommended to our 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 such designee are to be elected, subject to certain exceptions. Julian C. Baker was elected as a director of the Company in June 2025.

Director Vacancies

Our amended and restated certificate of incorporation authorizes only our board of directors to fill vacant directorships.

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 provide that, except as otherwise required by law, special meetings of the stockholders may be called only by an officer at the request of a majority of our board of directors, by the chairperson of our board of directors, or by our Chief Executive Officer.

Advance Notice Procedures for Director Nominations

Our amended and restated bylaws provide that stockholders seeking to nominate candidates for election as directors at an annual or special meeting of stockholders must provide timely notice thereof in writing. To be timely, a stockholder's notice generally must be delivered to and received at our principal executive offices before notice of the meeting is issued by the secretary of the company, with such notice being served not less than 90 nor more than 120 days before the meeting. Although our amended and restated bylaws do not give our board of directors the power to approve or disapprove stockholder nominations of candidates to be elected at an annual meeting, our amended and restated bylaws may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed or may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect its own slate of directors or otherwise attempting to obtain control of the company.

Action by Written Consent

Our amended and restated certificate of incorporation and amended and restated bylaws provide that any action to be taken by the stockholders must be effected at a duly called annual or special meeting of stockholders and may not be effected by written consent.

Amending our Certificate of Incorporation and Bylaws

Our amended and restated certificate of incorporation may be amended or altered in any manner provided by the DGCL. Our amended and restated bylaws may be adopted, amended, altered, or repealed by stockholders only upon approval of at least majority of the voting power of all the then outstanding shares of the common stock, except for any amendment of the above provisions, which would require the approval of a two-thirds majority of our then outstanding common stock. Additionally, our amended and restated certificate of incorporation 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 the company by means of a proxy contest, tender offer, merger or otherwise.

Exclusive Jurisdiction

Our amended and restated certificate of incorporation provide that, unless we consent to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of fiduciary duty, any action asserting a claim arising pursuant to the DGCL, any action regarding our amended and restated certificate of incorporation or our amended and restated bylaws or any action asserting a claim against us that is governed by the internal affairs doctrine.

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

Business Combinations with Interested Stockholders

We are governed by Section 203 of the DGCL. Subject to certain exceptions, Section 203 of the DGCL prohibits a public Delaware corporation from engaging in a business combination (as defined in such section) with an "interested stockholder" (defined generally as any person who beneficially owns 15% or more of the outstanding voting stock of such corporation or any person affiliated with such person) for a period of three years following the time that such stockholder became an interested stockholder, unless (i) prior to such time the board of directors of such corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder; (ii) upon consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of such corporation at the time the transaction commenced (excluding for purposes of determining the voting stock of such corporation outstanding (but not the outstanding voting stock owned by the interested stockholder) those shares owned (A) by persons who are directors and also officers of such corporation and (B) by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer); or (iii) at or subsequent to such time the business combination is approved by the board of directors of such corporation and authorized at a meeting of stockholders (and not by written consent) by the affirmative vote of at least 66 2/3% of the outstanding voting stock of such corporation not owned by the interested stockholder.

Limitation on Liability and Indemnification

Our amended and restated certificate of incorporation and our amended and restated bylaws provide that we must indemnify our directors and officers to the fullest extent authorized by the DGCL. We are expressly authorized to carry, and we do carry, directors' and officers' insurance providing coverage for our directors, officers and certain employees for some liabilities. We believe that these indemnification provisions and insurance are useful to attract and retain qualified directors and executive officers.

The limitation on liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against directors for breach of their fiduciary duty. These provisions may also have the effect of reducing the likelihood of derivative litigation against directors and officers, even though such an action, if successful, might otherwise benefit us and our stockholders. In addition, your investment may be adversely affected to the extent we pay the costs of settlement and damage awards against directors and officers pursuant to these indemnification provisions.

Registration Rights

In connection with our private placement in February 2024, we granted an Investor, once that Investor was deemed an affiliate of the Company in June 2025, certain resale registration rights with respect to shares of the Company's common stock held by the Investor under an Affiliate Registration Rights Agreement. Under the Affiliate Registration Rights Agreement, following a request by Investor, the Company is obligated to file a resale registration statement as promptly as reasonably practicable following such request, and in any event within 60 days of such request. The Company's obligations to file such registration statement are subject to specified exceptions, and suspension and deferral rights as are set forth in the Affiliate Registration Rights Agreement. Under specified circumstances, the Company may also include securities of the Company in any such registration statement. This summary does not purport to be complete and is qualified in its entirety by the provisions of the Affiliate Registration Rights Agreement, a copy of which has been filed as an exhibit to our Form 8-K filed on June 3, 2025.

Listing

Our common stock is listed on the Nasdaq Global Select Market under the symbol "DNLI".

Transfer Agent and Registrar

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.

DESCRIPTION OF PRE-FUNDED WARRANTS

The following is a brief summary of certain terms and conditions of the pre-funded warrants being offered in this offering. The following description is subject in all respects to the provisions contained in the pre-funded warrants.

Form

The pre-funded warrants will be issued as individual warrant agreements to investors. The form of pre-funded warrant will be filed as an exhibit to a Current Report on Form 8-K that we expect to file with the SEC.

Term

The pre-funded warrants do not expire.

Exercisability

The pre-funded warrants are exercisable at any time on or after their original issuance. The pre-funded warrants are exercisable, at the option of each holder, in whole or in part by delivering to us a duly signed exercise notice and by payment in full in immediately available funds for the number of shares of common stock purchased upon such exercise. As an alternative to payment in immediately available funds, the holder may, in its sole discretion, elect to exercise the pre-funded warrant through a cashless exercise, in which case the holder would receive upon such exercise the net number of shares of common stock determined according to the formula set forth in the pre-funded warrant. No fractional shares of common stock will be issued in connection with the exercise of a pre-funded warrant. In lieu of fractional shares, we will pay the holder an amount in cash equal to the fractional amount multiplied by the fair market value of the common stock on the exercise date.

Exercise Limitations

We may not effect the exercise of any pre-funded warrant, and a holder will not be entitled to exercise any portion of any pre-funded warrant that, upon giving effect to such exercise, would cause the aggregate number of shares of our common stock beneficially owned by the holder (together with its attribution affiliates (as defined below)) to exceed 4.99% (or 9.99%) of the number of shares of our common stock that would be outstanding immediately after giving effect to the exercise. However, any holder of a pre-funded warrant may increase or decrease such percentage to any other percentage not in excess of 19.99% upon at least 61 days' prior notice from the holder to us. For purposes of the foregoing, "attribution affiliates" means, collectively, the following persons and entities with respect to any holder: (i) its direct or indirect affiliates, (ii) any person acting or who could be deemed to be acting as a Section 13(d) "group" together with the holder or any attribution parties and (iii) any other persons whose beneficial ownership of our common stock would or could be aggregated with the holder and/or any other attribution parties for purposes of Section 13(d) or Section 16 of the Exchange Act.

Exercise Price

The exercise price per whole share of our common stock purchasable upon the exercise of the pre-funded warrants is \$0.01 per share of common stock. The exercise price of the pre-funded warrants and the number of shares of our common stock issuable upon exercise of the pre-funded warrants is subject to appropriate adjustment in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting our common stock.

Transferability

Subject to applicable laws, the pre-funded warrants may be offered for sale, sold, transferred or assigned without our consent. The ownership of the pre-funded warrants and any transfers of the pre-funded warrants will be registered in a warrant register maintained by the warrant agent. We will initially act as warrant agent.

Exchange Listing

There is no established trading market for the pre-funded warrants, and we do not expect a market to develop. We do not plan on applying to list the pre-funded warrants on the Nasdaq Global Select Market or any other national securities exchange or any nationally recognized trading system.

Fundamental Transactions

In the event of a fundamental transaction, as described in the pre-funded warrants and generally including any reorganization, recapitalization or reclassification of our common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding common stock, or any person or group becoming the beneficial owner of more than 50% of the voting power represented by our outstanding common stock, the holders of the pre-funded warrants will be entitled to receive upon exercise of the pre-funded warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the pre-funded warrants immediately prior to such fundamental transaction without regard to any limitations on exercise contained in the pre-funded warrants.

Rights as a Stockholder

Except by virtue of such holder's ownership of shares of our common stock, the holder of a pre-funded warrant does not have the rights or privileges of a holder of our common stock, including any voting rights, until the holder exercises the pre-funded warrant.

MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR HOLDERS OF OUR COMMON STOCK AND PRE-FUNDED WARRANTS

The following is a summary of the material U.S. federal income tax consequences of the ownership and disposition of our common stock and pre-funded warrants acquired in this offering to a "U.S. holder" and a "non-U.S. holder" (as defined below), but does not purport to be a complete analysis of all the potential tax considerations relating thereto. This summary is based upon the provisions of the United States Internal Revenue Code of 1986, as amended (the "Code"), Treasury Regulations promulgated thereunder, administrative rulings and judicial decisions, all as of the date hereof. These authorities may be changed, possibly retroactively, so as to result in U.S. federal income tax consequences different from those set forth below. We have not sought, and do not intend to seek, any ruling from the Internal Revenue Service (the "IRS"), with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS or a court will agree with such statements and conclusions.

This summary also does not address the tax considerations arising under the laws of any non-U.S., state or local jurisdiction or under U.S. federal gift and estate tax rules. In addition, this discussion does not address tax considerations applicable to an investor's particular circumstances or to investors that may be subject to special tax rules, including, without limitation:

- banks, insurance companies, regulated investment companies, real estate investment trusts or other financial institutions;
- persons subject to any minimum tax or the tax on net investment income;
- tax-exempt organizations;
- pension plans and tax-qualified retirement plans;
- controlled foreign corporations, passive foreign investment companies and corporations that accumulate earnings to avoid U.S. federal income tax;
- brokers or dealers in securities or currencies;
- traders in securities that elect to use a mark-to-market method of tax accounting for their securities holdings;
- persons that own, or are deemed to own, more than five percent of our capital stock and/or pre-funded warrants (except to the extent specifically set forth below);
- certain former citizens or long-term residents of the United States;
- persons who hold our common stock and/or pre-funded warrants as a position in a hedging transaction, "straddle," "conversion transaction" or other risk reduction transaction;
- persons who hold or receive our common stock pursuant to the exercise of any option or otherwise as compensation;
- persons subject to special tax accounting rules under Section 451 of the Code;
- persons who do not hold our common stock or pre-funded warrants as a capital asset within the meaning of Section 1221 of the Code (generally, property held for investment); or
- persons deemed to sell our common stock or pre-funded warrants under the constructive sale provisions of the Code.

In addition, if a partnership or entity or arrangement classified as a partnership or flow-through entity for U.S. federal income tax purposes holds our common stock or pre-funded warrants, the tax treatment of a partner (or owner of such flow-through entity) generally will depend on the status of the partner (or owner) and upon the activities of the partnership or other such entity. A partner (or owner) in a partnership or other such entity that will hold our common stock and/or pre-funded warrants should consult his, her or its own tax advisor regarding the tax consequences of the ownership and disposition of our common stock and/or pre-funded warrants through a partnership or other such entity, as applicable.

You are urged to consult your tax advisor with respect to the application of the U.S. federal income tax laws to your particular situation, as well as any tax consequences of the purchase, ownership and disposition of our common stock or pre-funded warrants arising under the U.S. federal gift or estate tax rules or under the laws of any state, local, non-U.S. or other taxing jurisdiction or under any applicable tax treaty.

U.S. Holder and Non-U.S. Holder Defined

For purposes of this discussion, you are a U.S. holder if you are a beneficial owner of our common stock or pre-funded warrants that is any of the following (or treated as any of the following) and is not a partnership (or other entity classified as a partnership for U.S. federal income tax purposes):

- an individual who is a citizen or resident of the United States (for U.S. federal income tax purposes);
- a corporation or other entity taxable as a corporation created or organized in the United States or under the laws of the United States or any political subdivision thereof, or otherwise treated as such for U.S. federal income tax purposes;
- an estate whose income is subject to U.S. federal income tax regardless of its source; or
- a trust (x) whose administration is subject to the primary supervision of a U.S. court and that has one or more "U.S. persons" (within the meaning of Section 7701(a)(30) of the Code) who have the authority to control all substantial decisions of the trust or (y) that has made a valid election under applicable Treasury Regulations to be treated as a U.S. person.

For purposes of this discussion, you are a "non-U.S. holder" if you are a beneficial owner of our common stock or pre-funded warrants that is not a U.S. holder, a partnership (or other entity classified as a partnership for U.S. federal income tax purposes), or a partner in a partnership.

General Treatment of Pre-Funded Warrants

Although the law in this area is not completely settled, the pre-funded warrants are generally expected to be treated as shares of our common stock for U.S. federal income tax purposes and a holder of pre-funded warrants should generally be taxed in the same manner as a holder of common stock as described below. Accordingly, no gain or loss should be recognized upon the exercise of a pre-funded warrant (except to the extent of cash received in exchange for a fractional share, which will be treated as a sale subject to the rules described below under "Tax Considerations Applicable to U.S. Holders—Gain on Disposition of Our Common Stock or Pre-Funded Warrants," and "Tax Consequences Applicable to Non-U.S. Holders—Gain on Disposition of Our Common Stock or Pre-Funded Warrants") and, upon exercise, the holding period of a pre-funded warrant should carry over to the common shares received. Similarly, the tax basis of a pre-funded warrant should carry over to the common share received upon exercise, increased by the exercise price (if applicable). You should discuss with your tax advisor the consequences of the acquisition, ownership and disposition of the pre-funded warrants, as well as the exercise of, certain adjustments to, and any payments in respect of the pre-funded warrants (including potential alternative characterizations). The balance of this discussion generally assumes that the characterization described above is respected for U.S. federal income tax purposes.

Tax Considerations Applicable to U.S. Holders

Distributions

As described in the section titled "Dividend Policy," we have never declared or paid cash dividends on our common stock, and we do not anticipate paying any dividends on our common stock following the completion of this offering. However, if we do make distributions on our common stock, those payments will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent those distributions exceed both our current and our accumulated earnings and profits, the excess will constitute a return of capital and will first reduce your basis in our common stock, but not below zero, and then will be treated as gain from the sale of stock as described below under "Tax Considerations Applicable to U.S. Holders—Gain on Disposition of Our Common Stock or Pre-Funded Warrants." If you are a non-corporate U.S. holder, and certain requirements are met, a preferential U.S. federal income tax rate will apply to any dividends paid to you if you meet certain holding period requirements.

If you are a corporate shareholder, distributions constituting dividends for U.S. federal income tax purposes may be eligible for the dividends received deduction, or DRD. No assurance can be given that we will have sufficient earnings and profits (as determined under U.S. federal income tax principles) to cause any distributions to be eligible for a DRD. In addition, a DRD is available only if certain holding periods and other taxable income requirements are satisfied.

The taxation of a distribution received with respect to a pre-funded warrant is unclear. It is possible such a distribution would be treated as a distribution as described in this section, although other treatments may also be possible. You should consult your tax advisors regarding the proper treatment of any payments in respect of the pre-funded warrants.

Gain on Disposition of Our Common Stock or Pre-Funded Warrants

Upon a sale or other taxable disposition of our common stock or pre-funded warrants, you generally will recognize capital gain or loss in an amount equal to the difference between the amount realized and your adjusted tax basis in the common stock or pre-funded warrant. Capital gain or loss will constitute long-term capital gain or loss if your holding period for the common stock or pre-funded warrant exceeds one year. The deductibility of capital losses is subject to certain limitations. U.S. holders who recognize losses with respect to a disposition of our common stock or pre-funded warrants should consult their own tax advisors regarding the tax treatment of such losses.

Certain Adjustments to Pre-Funded Warrants

Under Section 305 of the Code, an adjustment to the number of shares of common stock that will be issued on the exercise of the pre-funded warrants, or an adjustment to the exercise price of the pre-funded warrants, may be treated as a constructive distribution to you of the pre-funded warrants if, and to the extent that, such adjustment has the effect of increasing your proportionate interest in our "earnings and profits" or assets, depending on the circumstances of such adjustment (for example, if such adjustment is to compensate for a distribution of cash or other property to our shareholders). Any such adjustment that is treated as a constructive distribution would be treated as a dividend, subject to withholding, to the extent described above under "Tax Considerations Applicable to U.S. Holders—Distributions." You should consult your tax advisor regarding the proper tax treatment of any such adjustment.

Information Reporting and Backup Withholding

Information reporting requirements generally will apply to payments of dividends (including constructive dividends) on the common stock or pre-funded warrants and to the proceeds of a sale or other disposition of common stock or pre-funded warrants paid by us to you unless you are an exempt recipient, such as certain corporations. Backup withholding at a current rate of 24% will apply to those payments if you fail to provide your taxpayer identification number, or certification of exempt status, or if you otherwise fail to comply with applicable requirements to establish an exemption.

Backup withholding is not an additional tax. Rather, any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against your U.S. federal income tax liability, if any, provided the required information is timely furnished to the IRS. You should consult your own tax advisors regarding their qualification for exemption from information reporting and backup withholding and the procedure for obtaining such exemption.

Tax Consequences Applicable to Non-U.S. Holders

Distributions

As described in the section titled "Dividend Policy," we have never declared or paid cash dividends on our common stock, and we do not anticipate paying any dividends on our common stock following the completion of this offering. However, if we do make distributions on our common stock, those payments generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent those distributions exceed both our current and our accumulated earnings and profits, the excess will constitute a return of capital and will first reduce your basis in our common stock, but not below zero, and then will be treated as gain from the sale of stock.

Subject to the discussions below on effectively connected income and Foreign Account Tax Compliance Act, or FATCA, withholding, any distribution (including constructive distributions) treated as a dividend paid to you generally will be subject to U.S. federal withholding tax either at a rate of 30% of the gross amount of the dividend or such lower rate as may be specified by an applicable income tax treaty between the United States and your country of residence. In order to receive a reduced treaty rate, you must provide the applicable withholding agent with an IRS Form W-8BEN or W-8BEN-E or other appropriate version of IRS Form W-8 certifying qualification for the reduced rate. A non-U.S. holder of shares of our common stock or pre-funded warrants eligible for a reduced rate of U.S. federal withholding tax pursuant to an income tax treaty may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. If the non-U.S. holder holds our common stock or pre-funded warrants through a financial institution or other agent acting on the non-U.S. holder's behalf, the non-U.S. holder will be required to provide appropriate documentation to the agent, which then will be required to provide certification to the applicable withholding agent, either directly or through other intermediaries.

Dividends received by you that are treated as effectively connected with your conduct of a U.S. trade or business (and, if required by an applicable income tax treaty, such dividends are attributable to a permanent establishment or fixed base maintained by you in the United States) are generally exempt from the 30% U.S. federal withholding tax, subject to the discussion below on backup withholding and FATCA withholding. In order to obtain this exemption, you must provide the applicable withholding agent with a properly executed IRS Form W-8ECI or other applicable IRS Form W-8 properly certifying such exemption. Such effectively connected dividends, although not subject to U.S. federal withholding tax, are taxed at the same rates applicable to U.S. persons, net of certain deductions and credits, subject to an applicable income tax treaty providing otherwise. In addition, if you are a corporate non-U.S. holder, dividends you receive that are effectively connected with your conduct of a U.S. trade or business may also be subject to a branch profits tax at a rate of 30% or such lower rate as may be specified by an applicable income tax treaty between the United States and your country of residence. You should consult your tax advisor regarding the tax consequences of any distribution (including constructive distributions) in respect of our common stock or pre-funded warrants, including any applicable tax treaties that may provide for different rules.

The taxation of a distribution received with respect to a pre-funded warrant is unclear. It is possible such a distribution would be treated as a distribution as described in this section, although other treatments may also be possible. You should consult your own tax advisors regarding the proper treatment of any payments in respect of the pre-funded warrants.

Gain on Disposition of Our Common Stock or Pre-Funded Warrants

Subject to the discussion below regarding backup withholding and FATCA withholding, you generally will not be required to pay U.S. federal income tax on any gain realized upon the sale or other disposition of our common stock or pre-funded warrants unless:

- the gain is effectively connected with your conduct of a U.S. trade or business (and, if an applicable income tax treaty so provides, the gain is attributable to a permanent establishment or fixed base maintained by you in the United States);
- you are an individual who is present in the United States for a period or periods aggregating 183 days or more during the calendar year in which the sale or disposition occurs and certain other conditions are met; or
- our common stock or pre-fund warrants constitute a United States real property interest by reason of our status as a “United States real property holding corporation,” or USRPHC, for U.S. federal income tax purposes at any time within the shorter of the five-year period preceding your disposition of, or your holding period for, our common stock or pre-funded warrants.

We believe that we are not currently and will not become a USRPHC for U.S. federal income tax purposes, and the remainder of this discussion so assumes. However, because the determination of whether we are a USRPHC depends on the fair market value of our U.S. real property interests relative to the fair market value of our U.S. and worldwide real property interests plus our other business assets, there can be no assurance that we will not become a USRPHC in the future. Even if we become a USRPHC, however, as long as our common stock is regularly traded on an established securities market, your common stock will be treated as U.S. real property interests only if you actually (directly or indirectly) or constructively hold more than five percent of such regularly traded common stock at any time during the shorter of the five-year period preceding your disposition of, or your holding period for, our common stock. We expect our stock to continue to be regularly traded on an established securities market; however, we cannot provide any assurance that our stock will be regularly traded on an established securities market in the future. Special rules may apply to non-U.S. holders of pre-funded warrants, who should consult their tax advisors.

If you are a non-U.S. holder described in the first bullet above, you will be required to pay tax on the gain derived from the sale (net of certain deductions and credits) under regular U.S. federal income tax rates, and a corporate non-U.S. holder described in the first bullet above also may be subject to the branch profits tax at a 30% rate, or such lower rate as may be specified by an applicable income tax treaty. If you are an individual non-U.S. holder described in the second bullet above, you will be subject to tax at 30% (or such lower rate specified by an applicable income tax treaty) on the gain derived from the sale, which gain may be offset by U.S. source capital losses for the year, provided you have timely filed U.S. federal income tax returns with respect to such losses. You should consult your tax advisor regarding any applicable income tax or other treaties that may provide for different rules.

Certain Adjustments to Pre-Funded Warrants

Under Section 305 of the Code, an adjustment to the number of shares of common stock that will be issued on the exercise of the pre-funded warrants, or an adjustment to the exercise price of the pre-funded warrants, may be treated as a constructive distribution to you of the pre-funded warrants if, and to the extent that, such adjustment has the effect of increasing your proportionate interest in our "earnings and profits" or assets, depending on the circumstances of such adjustment (for example, if such adjustment is to compensate for a distribution of cash or other property to our shareholders). Any such adjustment that is treated as a constructive distribution would be treated as a dividend, subject to withholding, to the extent described above under "Tax Consequences Applicable to Non-U.S. Holders—Distributions." You should consult your tax advisor regarding the proper tax treatment of any such adjustment.

Backup Withholding and Information Reporting

Generally, we or the applicable withholding agent must report annually to the IRS the amount of dividends paid to you, your name and address, and the amount of tax withheld, if any. A similar report will be sent to you. Pursuant to applicable income tax treaties or other agreements, the IRS may make these reports available to tax authorities in your country of residence.

Payments of dividends (including constructive dividends) on or of proceeds from the disposition of our common stock or pre-funded warrants made to you may be subject to information reporting and backup withholding at a current rate of 24% unless you establish an exemption, for example, by properly certifying your non-U.S. status on a properly completed IRS Form W-8BEN or W-8BEN-E or another appropriate version of IRS Form W-8. Notwithstanding the foregoing, backup withholding and information reporting may apply if either we or the applicable withholding agent has actual knowledge, or reason to know, that you are a U.S. person.

Backup withholding is not an additional tax; rather, the U.S. federal income tax liability of persons subject to backup withholding may be reduced by the amount of tax withheld. If withholding results in an overpayment of taxes, a refund or credit may generally be obtained from the IRS, provided that the required information is furnished to the IRS in a timely manner.

Foreign Account Tax Compliance Act (“FATCA”)

The Foreign Account Tax Compliance Act, Treasury Regulations issued thereunder and official IRS guidance, collectively “FATCA,” generally impose a U.S. federal withholding tax of 30% on dividends on, and, subject to the discussion of certain proposed Treasury Regulations below, the gross proceeds from a sale or other disposition of our common stock or pre-funded warrants, paid to a “foreign financial institution” (as specially defined under these rules), unless such institution enters into an agreement with the U.S. government to, among other things, withhold on certain payments and to collect and provide to the U.S. tax authorities substantial information regarding the U.S. account holders of such institution (which includes certain equity and debt holders of such institution, as well as certain account holders that are foreign entities with U.S. owners) or otherwise establishes an exemption. FATCA also generally imposes a U.S. federal withholding tax of 30% on dividends on and, subject to the discussion of certain proposed Treasury Regulations below, the gross proceeds from a sale or other disposition of our common stock or pre-funded warrants paid to a “non-financial foreign entity” (as specially defined under these rules) unless such entity provides the withholding agent with a certification identifying the substantial direct and indirect U.S. owners of the entity, certifies that it does not have any substantial U.S. owners, or otherwise establishes an exemption. The Treasury Secretary has issued proposed Treasury Regulations, which, if finalized in their present form, would eliminate withholding under FATCA with respect to payment of gross proceeds from a sale or other disposition of our common stock or pre-funded warrants. In its preamble to such proposed Treasury Regulations, the U.S. Treasury stated that taxpayers may generally rely on the proposed Treasury Regulations until final regulations are issued.

The withholding tax will apply regardless of whether the payment otherwise would be exempt from U.S. nonresident and backup withholding tax, including under the other exemptions described above. Under certain circumstances, a non-U.S. holder might be eligible for refunds or credits of such taxes. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this section. Prospective investors should consult with their own tax advisors regarding the application of FATCA withholding to their investment in, and ownership and disposition of, our common stock or pre-funded warrants.

The preceding discussion of U.S. federal tax considerations is for general information only. It is not tax advice to investors in their particular circumstances. Each prospective investor should consult its own tax advisor regarding the particular U.S. federal, state and local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock or pre-funded warrants, including the consequences of any proposed change in applicable laws.

UNDERWRITING

We and the underwriters named below have entered into an underwriting agreement with respect to the shares being offered. Subject to certain conditions, each underwriter has severally agreed to purchase the number of shares of our common stock and pre-funded warrants indicated in the following table. Goldman Sachs & Co. LLC, J.P. Morgan Securities LLC and Morgan Stanley & Co. LLC are the representatives of the underwriters.

Underwriters	Number of Shares	Number of Pre-Funded Warrants
Goldman Sachs & Co. LLC	3,062,858	765,714
J.P. Morgan Securities LLC	2,240,000	560,000
Morgan Stanley & Co. LLC	1,508,571	377,143
Jefferies LLC	1,508,571	377,143
H.C. Wainwright & Co., LLC	457,143	114,286
B. Riley Securities, Inc.	365,714	91,428
Total	9,142,857	2,285,714

The underwriters will be committed to take and pay for all of the shares being offered, if any are taken, other than the shares covered by the option described below unless and until this option is exercised.

The underwriters will have an option to buy up to approximately 1,714,285 additional shares from us to cover sales by the underwriters of a greater number of shares than the total number set forth in the table above. They may exercise that option for 30 days. If any shares are purchased pursuant to this option, the underwriters will severally purchase shares in approximately the same proportion as set forth in the table above.

The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters by us, and proceeds before expenses to us. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Per Share	Per Pre-Funded Warrant	Total	
			No Exercise	Full Exercise
Public offering price	\$ 17.50	\$ 17.49	\$ 199,977,135.36	\$ 229,977,122.86
Underwriting discounts and commissions to be paid by us	\$ 0.875	\$ 0.875	\$ 9,999,999.63	\$ 11,499,999.00
Proceeds, before expenses, to us	\$ 16.625	\$ 16.615	\$ 189,977,135.73	\$ 218,477,123.86

Shares sold by the underwriters to the public will be offered at the public offering price set forth on the cover of this prospectus supplement. Any shares sold by the underwriters to securities dealers may be sold at a discount of up to \$0.525 per share from the public offering price. After the initial offering of the shares, the representatives may change the offering price and the other selling terms. The offering of the shares by the underwriters is subject to receipt and acceptance and subject to the underwriters' right to reject any order in whole or in part. The underwriters have not been engaged to act as warrant agent for the pre-funded warrants or to act as underwriter or agent or otherwise participate in the issuance of the shares of our common stock upon the exercise of the pre-funded warrants.

We have agreed that, without the prior written consent of Goldman Sachs & Co. LLC, for a period of 60 days after the date of this prospectus supplement, we will not (1) offer, sell, contract to sell, pledge, grant any option to purchase, make any short sale or otherwise transfer or dispose of, directly or indirectly, or file with or confidentially submit to the SEC a registration statement under the Securities Act relating to any of our securities that are substantially similar to our common stock, including but not limited to any options or warrants to purchase shares of our common stock or any securities that are convertible into or exchangeable for, or that represent the right to receive common stock or any such substantially similar securities, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, or (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of our common stock or other securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of our common stock or other securities, in cash or otherwise. This agreement does not apply to (a) the securities to be sold in this offering, (b) shares issued upon the exercise or settlement of options pursuant to our equity incentive plans that are described in this preliminary prospectus supplement or accompanying prospectus or upon the conversion of outstanding convertible securities as described in this preliminary prospectus supplement or accompanying prospectus, (c) shares of our common stock or securities convertible into, exchangeable for or that represent the right to receive shares of common stock, in each case pursuant to our equity incentive plans that are described in this preliminary prospectus supplement or accompanying prospectus, (d) shares of our common stock or securities convertible into, exchangeable for or that represent the right to receive shares of common stock in connection with (1) our acquisition of the business, technology, not less than a majority or controlling portion of the securities, property or other assets of another person or entity or pursuant to an employee benefit plan assumed by us in connection with such acquisition and the issuance of any such securities pursuant to any such agreement, or (2) bona fide commercial transactions (including joint ventures, commercial relationships, or other strategic transactions), (e) the filing of any registration statement on Form S-8 relating to securities granted or to be granted under our equity incentive plans that are described in this preliminary prospectus supplement or accompanying prospectus or any assumed employee benefit plan contemplated by clause (d); provided, that the aggregate number of shares that we may sell or issue or agree to sell or issue in connection with a transaction described in clause (e) shall not exceed 7.5% of the total number of shares outstanding immediately following this offering; and provided, further, that each recipient of any securities described in clauses (d) and (e) shall enter into a lock-up agreement or (f) after the date 30 days after the date of the prospectus, the offer and sale by us of shares of common stock pursuant to that certain Equity Distribution Agreement by and among us, Goldman Sachs & Co. LLC and Leerink Partners LLC, dated as of February 27, 2025.

Our directors and executive officers have entered into lock-up agreements with the representatives prior to the commencement of this offering, pursuant to which each such person or entity, for a period of 45 days after the date of this prospectus supplement (the "restricted period"), may not, without the prior written consent of Goldman Sachs & Co. LLC, (i) offer, sell, contract to sell, pledge, grant any option to purchase, make any short sale, lend or otherwise dispose of any shares of common stock, or any options or warrants to purchase any shares of common stock, or any securities convertible into, exchangeable for or that represent the right to receive shares of common stock, (ii) engage in any hedging or other transaction or arrangement which is designed to or which reasonably could be expected to lead to or result in a sale, loan, pledge, other disposition or transfer of any of the economic consequences of ownership, in whole or in part, directly or indirectly, of any shares, whether any such transaction or arrangement would be settled by delivery of common stock, other securities or cash, or (iii) otherwise make any public announcement or SEC filing relating to any intention to engage in any of the foregoing transactions, other than any shares sold to the underwriters pursuant to the underwriting agreement.

The restrictions described in the immediately preceding paragraph do not prohibit:

- transfers of shares as a bona fide gift, including without limitation to a charitable organization or educational institution, or for bona fide estate planning purposes;

- transfers to any immediate family member or to a trust or other legal entity for the direct or indirect benefit of the transferor, or the immediate family of the transferor, or if the undersigned is a trust, to a trustor or beneficiary of the trust or to the estate of a beneficiary of such trust, provided that any such transfer shall not involve a disposition for value;
- transfers by will, other testamentary document or the laws of intestate succession;
- transfers in connection with the sale of the transferor's shares acquired in open market transactions on or after the offering;
- transfers from a corporation, partnership, limited liability company, trust or other business entity, (A) to another corporation, member, partner, partnership, limited liability company, trust or other business entity that is an affiliate (as defined in Rule 405 under the Securities Act), or to any investment fund or other entity controlling, controlled by, managing or managed by or under common control with the transferor or affiliates of the transferor, or (B) as part of a distribution, transfer or disposition by the transferor to its or its affiliates' directors, officers, employees, managers, managing members, members, stockholders, partners, beneficiaries (or the estates thereof) or other equity holders;
- (a) the surrender or forfeiture of shares in connection with the "net" or "cashless" exercise or settlement of stock options, other rights to purchase shares or other awards, or for the payment of tax withholdings or remittance payments due as a result of the vesting, settlement, or exercise of such options, rights or other awards, in all such cases pursuant to an equity incentive plan, stock purchase plan or other employee benefit plan, (b) surrender or forfeiture to us of shares of common stock upon the conversion of a convertible security in order to cover withholding tax obligations in connection with such conversion or (c) the sale of shares of common stock underlying restricted stock units to cover the payment of tax withholding obligations upon the vesting of such awards, in each case which securities have been issued pursuant to an equity incentive plan, stock purchase plan or other employee benefit plan;
- transfers in connection with a contractual arrangement that provides for the repurchase by us of shares from a service provider in connection with termination of service;
- transfers in connection with the conversion of any convertible security into shares of common stock;
- transfers pursuant to a bona fide third-party tender offer, merger, consolidation or similar transaction that is approved by the board of directors and made to all holders of our capital stock;
- transfers by operation of law, including pursuant to orders of a court, a qualified domestic order or in connection with a divorce settlement;
- transfers pursuant to a trading plan adopted pursuant to Rule 10b5-1 of the Exchange Act prior to the date of the underwriting agreement;
- transfer from us of shares of common stock in connection with the exercise of options or other rights granted under a stock incentive plan or other equity award plan; or
- the establishment of a trading plan adopted pursuant to Rule 10b5-1 of the Exchange Act, provided that such plan does not provide for the transfer of lock-up securities during the restricted period.

In connection with the offering, the underwriters may purchase and sell shares of common stock in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering, and a short position represents the amount of such sales that have not been covered by subsequent purchases. A "covered short position" is a short position that is not greater than the amount of additional shares for which the underwriters' option described above may be exercised. The underwriters may cover any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to cover the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase additional shares pursuant to the option described above. "Naked" short sales are any short sales that create a short position greater than the amount of additional shares for which the option described above may be exercised. The underwriters must cover any such naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of common stock made by the underwriters in the open market prior to the completion of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it, because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Purchases to cover a short position and stabilizing transactions, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of our stock, and together with the imposition of the penalty bid, may stabilize, maintain or otherwise affect the market price of the common stock. As a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. The underwriters are not required to engage in these activities and may end any of these activities at any time. These transactions may be effected on Nasdaq, in the over-the-counter market or otherwise.

Certain of the underwriters and their affiliates have provided in the past to us and our affiliates and may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates in the ordinary course of their business, for which they have received and may continue to receive customary fees and commissions. Goldman Sachs & Co. LLC is a sales agent under our equity distribution agreement dated February 27, 2025 among us, Goldman Sachs & Co. LLC and Leerink Partners LLC. Under the equity distribution agreement, we may offer and sell, from time to time, shares of our common stock through Goldman Sachs & Co. LLC and Leerink Partners LLC in an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act. Our chief executive officer provides consulting services to an affiliate of Goldman Sachs & Co. LLC, for which he is paid a fee. In addition, from time to time, certain of the underwriters and their affiliates may effect transactions for their own account or the account of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future.

Our common stock is quoted on the Nasdaq Global Select Market ("Nasdaq") under the symbol "DNL1." There is no established public trading market for the pre-funded warrants, and we do not expect a market to develop. We do not intend to list the pre-funded warrants on the Nasdaq Global Select Market, any other national securities exchange or any other recognized trading system.

Selling Restrictions

Other than in the U.S., no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus supplement in any jurisdiction where action for that purpose is required. The securities offered by this prospectus supplement may not be offered or sold, directly or indirectly, nor may this prospectus supplement or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus supplement comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus supplement. This prospectus supplement does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus supplement in any jurisdiction in which such an offer or a solicitation is unlawful.

European Economic Area

In relation to each Member State of the European Economic Area (each a "Relevant State"), no common stock or pre-funded warrants (the "Shares") have been offered or will be offered pursuant to the offering to the public in that Relevant State prior to the publication of a prospectus in relation to the Shares which has been approved by the competent authority in that Relevant State or, where appropriate, approved in another Relevant State and notified to the competent authority in that Relevant State, all in accordance with the Prospectus Regulation, except that offers of shares may be made to the public in that Relevant State at any time under the following exemptions under the Prospectus Regulation:

- (a) to any legal entity which is a qualified investor as defined under the Prospectus Regulation;
- (b) to fewer than 150 natural or legal persons (other than qualified investors as defined under the Prospectus Regulation), subject to obtaining the prior consent of the representatives for any such offer; or
- (c) in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of Shares shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

For the purposes of this provision, the expression an "offer to the public" in relation to Shares in any Relevant State means the communication in any form and by any means of sufficient information on the terms of the offer and any Shares to be offered so as to enable an investor to decide to purchase or subscribe for any Shares, and the expression "Prospectus Regulation" means Regulation (EU) 2017/1129.

United Kingdom

In relation to the United Kingdom, no shares have been offered or will be offered pursuant to the offering to the public in the United Kingdom prior to the publication of a prospectus in relation to the shares that either (i) has been approved by the Financial Conduct Authority, or (ii) is to be treated as if it had been approved by the Financial Conduct Authority in accordance with the transitional provision in Regulation 74 of the Prospectus (Amendment etc.) (EU Exit) Regulations 2019, except that offers of shares may be made to the public in the United Kingdom at any time under the following exemptions under the UK Prospectus Regulation:

- (a) to any legal entity which is a qualified investor as defined under Article 2 of the UK Prospectus Regulation;

- (b) to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the UK Prospectus Regulation), subject to obtaining the prior consent of underwriters for any such offer; or
- (c) in any other circumstances falling within Section 86 of the Financial Services and Markets Act 2000, or the FSMA; provided that no such offer of common stock and pre-funded warrants shall require us or any representatives to publish a prospectus pursuant to Section 85 of the FSMA or supplement a prospectus pursuant to Article 23 of the UK Prospectus Regulation.

For the purposes of this provision, the expression an “offer to the public” in relation to the common stock and pre-funded warrants in the United Kingdom means the communication in any form and by any means of sufficient information on the terms of the offer and any common stock and pre-funded warrants to be offered so as to enable an investor to decide to purchase or subscribe for any common stock and pre-funded warrants and the expression “UK Prospectus Regulation” means Regulation (EU) 2017/1129 as it forms part of domestic law by virtue of the European Union (Withdrawal) Act 2018.

In addition, this prospectus supplement is only being distributed to, and is only directed at, and any investment or investment activity to which this prospectus supplement relates is available only to, and will be engaged in only with, persons who are outside the United Kingdom or persons in the United Kingdom (i) having professional experience in matters relating to investments who fall within the definition of “investment professionals” in Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, or the Order; or (ii) who are high net worth entities falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as “relevant persons”). Persons who are not relevant persons should not take any action on the basis of this prospectus supplement and should not act or rely on it.

Canada

The common stock and pre-funded warrants may be sold in Canada only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the common stock and pre-funded warrants must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser’s province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser’s province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 *Underwriting Conflicts* (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Hong Kong

The common stock and pre-funded warrants have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to “professional investors” as defined in the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong), or the SFO, of Hong Kong and any rules made thereunder; or (b) in other circumstances which do not result in the document being a “prospectus” as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32) of Hong Kong, or the CO or which do not constitute an offer to the public within the meaning of the CO. No advertisement, invitation or document relating to the common stock and pre-funded warrants has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to “professional investors” as defined in the SFO and any rules made thereunder.

Singapore

Singapore SFA Product Classification—In connection with Section 309B of the SFA and the CMP Regulations 2018, unless otherwise specified before an offer of common stock and pre-funded warrants, we have determined, and hereby notify all relevant persons (as defined in Section 309A(1) of the SFA), that the common stock and pre-funded warrants are “prescribed capital markets products” (as defined in the CMP Regulations 2018) and Excluded Investment Products (as defined in MAS Notice SFA 04-N12: Notice on the Sale of Investment Products and MAS Notice FAA-N16: Notice on Recommendations on Investment Products).

Each underwriter has acknowledged that this prospectus supplement and the accompanying prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, each underwriter has represented and agreed that it has not offered or sold any common stock and pre-funded warrants or caused the common stock and pre-funded warrants to be made the subject of an invitation for subscription or purchase and will not offer or sell any common stock and pre-funded warrants or cause the common stock and pre-funded warrants to be made the subject of an invitation for subscription or purchase, and has not circulated or distributed, nor will it circulate or distribute, this prospectus supplement and the accompanying prospectus or any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the common stock and pre-funded warrants, whether directly or indirectly, to any person in Singapore other than:

In connection with Section 309B of the SFA and the Capital Markets Products (the “CMP”) Regulations 2018, the shares are prescribed capital markets products (as defined in the CMP Regulations 2018) and Excluded Investment Products (as defined in Monetary Authority of Singapore Notice SFA 04-N12: Notice on the Sale of Investment Products and Monetary Authority of Singapore Notice FAA-N16: Notice on Recommendations on Investment Products).

- (a) to an institutional investor (as defined in Section 4A of the Securities and Futures Act (Chapter 289) of Singapore, as modified or amended from time to time, or the SFA) pursuant to Section 274 of the SFA;
- (b) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA; or
- (c) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the common stock and pre-funded warrants are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- (a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, securities or securities-based derivatives contracts (each term as defined in Section 2(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:
 - (i) to an institutional investor or to a relevant person, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
 - (ii) where no consideration is or will be given for the transfer;
 - (iii) where the transfer is by operation of law;
 - (iv) as specified in Section 276(7) of the SFA; or
 - (v) as specified in Regulation 37A of the Securities and Futures (Offers of Investments) (Securities and Securities-based Derivatives Contracts) Regulations 2018.

Japan

The common stock and pre-funded warrants have not been and will not be registered pursuant to Article 4, Paragraph 1 of the Financial Instruments and Exchange Law Act. Accordingly, none of the common stock and pre-funded warrants nor any interest therein may be offered or sold, directly or indirectly, in Japan or to, or for the benefit of, any "resident" of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to or for the benefit of a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Act and any other applicable laws, regulations and ministerial guidelines of Japan in effect at the relevant time.

We estimate that our share of the total expenses of the offering, excluding underwriting discounts and commissions, will be approximately \$0.7 million. We have agreed to reimburse the underwriters for expenses related to any applicable state securities filings and to the Financial Industry Regulatory Authority incurred by them in connection with this offering in an amount up to \$10,000.

We have agreed to indemnify the several underwriters against certain liabilities, including liabilities under the Securities Act.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. Certain of the underwriters and their respective affiliates have provided, and may in the future provide, a variety of these services to the issuer and to persons and entities with relationships with the issuer, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and their respective affiliates, officers, directors and employees may purchase, sell or hold a broad array of investments and actively trade securities, derivatives, loans, commodities, currencies, credit default swaps and other financial instruments for their own account and for the accounts of their customers, and such investment and trading activities may involve or relate to assets, securities and/or instruments of the issuer (directly, as collateral securing other obligations or otherwise) and/or persons and entities with relationships with the issuer. The underwriters and their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

LEGAL MATTERS

The validity of the issuance of our securities offered in this prospectus supplement will be passed upon for us by Wilson Sonsini Goodrich & Rosati, Professional Corporation, Palo Alto, California. Davis Polk & Wardwell LLP, Redwood City, California, is acting as counsel for the underwriters.

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, 2024, and the effectiveness of our internal control over financial reporting as of December 31, 2024, as set forth in their reports, which are incorporated by reference in this prospectus supplement and the accompanying 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 ADDITIONAL INFORMATION

We have filed with the SEC a registration statement on Form S-3 under the Securities Act of 1933, as amended, or the Securities Act, with respect to the common stock offered by this prospectus supplement. This prospectus supplement, filed as part of the registration statement, does not contain all the information set forth in the registration statement and its exhibits and schedules, portions of which have been omitted as permitted by the rules and regulations of the SEC. For further information about us, we refer you to the registration statement and to its exhibits and schedules.

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, free of charge, through the Investors section of our website, which is located at www.denalitherapeutics.com. Information contained on our website is not incorporated by reference into this prospectus supplement or the accompanying prospectus and you should not consider information on our website to be part of this prospectus supplement or the accompanying prospectus.

INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference much of the information 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 supplement and the accompanying prospectus is considered to be part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus supplement is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus supplement. 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 supplement, the accompanying prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus supplement 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 Securities Exchange Act of 1934, as amended, or the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) between the date of this prospectus supplement and the termination of this offering:

- Annual Report on [Form 10-K](#) for the year ended December 31, 2024, as filed with the SEC on February 27, 2025;
- The information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2024 from our definitive proxy statement on [Schedule 14A](#) (other than information furnished rather than filed), which was filed with the SEC on April 17, 2025;
- Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2025, June 30, 2025 and September 30, 2025, as filed with the SEC on [May 6, 2025](#), [August 11, 2025](#), and [November 6, 2025](#), respectively;
- Current Reports on Form 8-K filed with the SEC on [February 27, 2025](#), [June 3, 2025](#), [December 4, 2025](#), and [December 4, 2025](#) (other than information furnished rather than filed); and
- The description of our common stock contained in our registration statement on [Form 8-A](#), which was 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 contacting us, either orally or in writing, at the following:

Denali Therapeutics Inc.
161 Oyster Point Blvd.
South San Francisco CA 94080
Phone: (650) 866-8547

PROSPECTUS

DENALI THERAPEUTICS INC.



Common Stock
Preferred Stock
Debt Securities
Warrants
Purchase Contracts
Units

We may offer and sell the securities identified above from time to time in one or more offerings. This prospectus provides you with a general description of the securities.

Each time we offer and sell securities, we will provide a supplement to this prospectus that contains specific information about the offering and the amounts, prices and terms of the securities. The supplement may also add, update or change information contained in this prospectus with respect to that offering. You should carefully read this prospectus and the applicable prospectus supplement, together with any documents we incorporated by reference, before you invest in any of our securities.

We may offer and sell the securities described in this prospectus and any prospectus supplement to or through one or more underwriters, dealers and agents, or directly to purchasers, or through a combination of these methods. If any underwriters, dealers or agents are involved in the sale of any of the securities, their names and any applicable purchase price, fee, commission or discount arrangement between or among them will be set forth, or will be calculable from the information set forth, in the applicable prospectus supplement. See the sections of this prospectus entitled "About this Prospectus" and "Plan of Distribution" for more information. No securities may be sold without delivery of this prospectus and the applicable prospectus supplement describing the method and terms of the offering of such securities.

INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE "[RISK FACTORS](#)" BEGINNING ON PAGE 3 OF THIS PROSPECTUS AND IN ANY SIMILAR SECTION CONTAINED IN OR INCORPORATED BY REFERENCE HEREIN OR IN THE APPLICABLE PROSPECTUS SUPPLEMENT CONCERNING FACTORS YOU SHOULD CONSIDER BEFORE INVESTING IN OUR SECURITIES.

Our common stock is listed on The Nasdaq Global Select Market ("Nasdaq") under the symbol "DNLI." On February 25, 2025, the last reported sale price of our common stock on Nasdaq was \$19.20 per share.

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 February 27, 2025.

TABLE OF CONTENTS

	<u>Page</u>
ABOUT THIS PROSPECTUS	1
THE COMPANY	2
RISK FACTORS	3
USE OF PROCEEDS	4
DESCRIPTION OF SECURITIES	5
PLAN OF DISTRIBUTION	6
LEGAL MATTERS	7
EXPERTS	7
WHERE YOU CAN FIND MORE INFORMATION	7
INCORPORATION BY REFERENCE	8

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the U.S. 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, using a "shelf" registration process. By using a shelf registration statement, we may sell securities from time to time and in one or more offerings as described in this prospectus. Each time that we offer and sell securities, we will provide a prospectus supplement to this prospectus that contains specific information about the securities being offered and sold and the specific terms of that offering and, to the extent appropriate, any updates to the information about us contained in this prospectus. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement may also add, update or change information contained or incorporated by reference in this prospectus with respect to that offering. If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement, you should rely on the prospectus supplement. Before purchasing any securities, you should carefully read both this prospectus and the applicable prospectus supplement, together with the additional information described under the heading "Where You Can Find More Information" and "Incorporation by Reference."

We have not authorized anyone to provide you with any information or to make any representations other than those contained or incorporated by reference in this prospectus, any applicable prospectus supplement or any free writing prospectuses prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We will not make an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus and the applicable prospectus supplement to this prospectus is accurate as of the date on its respective cover or as otherwise specified therein and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, unless we indicate otherwise. Our business, financial condition, results of operations and prospects may have changed since those dates. This prospectus incorporates by reference, and any prospectus supplement or free writing prospectus may contain and incorporate by reference, market data and industry statistics and forecasts that are based on independent industry publications and other publicly available information. Although we believe these sources are reliable, we do not guarantee the accuracy or completeness of this information and we have not independently verified this information. Although we are not aware of any misstatements regarding the market and industry data presented in this prospectus, the applicable prospectus supplement and the documents incorporated herein and therein by reference, these estimates involve risks and uncertainties and are subject to change based on various factors, including those discussed under the heading "Risk Factors" contained or incorporated by reference in this prospectus, the applicable prospectus supplement and any related free writing prospectus and under similar headings in other documents that are incorporated by reference into this prospectus. Accordingly, investors should not place undue reliance on this information.

When we refer to "Denali," "we," "our," "us" and the "Company" in this prospectus, we mean Denali Therapeutics Inc., unless the context indicates otherwise or unless otherwise specified. When we refer to "you," we mean the holders of the applicable series of securities.

THE COMPANY

Denali is 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 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.

RISK FACTORS

Investing in our securities involves a high degree of risk. Before making a decision to invest in our securities, in addition to carefully considering the other information contained in this prospectus, in any accompanying prospectus supplement and incorporated by reference herein or therein, you should carefully consider the risks described under the caption "Risk Factors" contained in the applicable prospectus supplement, and any related free writing prospectus, and the risks discussed under the caption "Risk Factors" contained in our most recent annual report on Form 10-K and in our most recent quarterly report on Form 10-Q, as well as any amendments thereto, which are incorporated by reference into this prospectus in their entirety, together with other information in this prospectus, the documents incorporated by reference, and any free writing prospectus that we may authorize for use in connection with a specific offering. See "Where You Can Find More Information; Incorporation by Reference."

USE OF PROCEEDS

We intend to use the net proceeds from the sale of the securities as set forth in the applicable prospectus supplement.

DESCRIPTION OF SECURITIES

We may issue from time to time, in one or more offerings, the following securities:

- shares of common stock, par value \$0.01 per share, of the Company;
- shares of preferred stock, par value \$0.01 per share, of the Company;
- debt securities, which may be senior or subordinated, and which may be convertible into our common stock or be non-convertible;
- warrants to purchase from us shares of our common stock or preferred stock or other securities;
- purchase contracts; and
- units representing two or more of the foregoing securities.

We will set forth in the applicable prospectus supplement and/or free writing prospectus a description of any common stock, debt securities, warrants, purchase contracts or units issued by us that may be offered or sold pursuant to this prospectus. The terms of the offering of securities, the initial offering price and the net proceeds to us will be contained in the prospectus supplement, and other offering material, relating to such offer.

PLAN OF DISTRIBUTION

We may sell the offered securities from time to time:

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

We will identify the specific plan of distribution, including any underwriters, dealers, agents or direct purchasers and their compensation in the applicable prospectus supplement.

LEGAL MATTERS

Wilson Sonsini Goodrich & Rosati, Professional Corporation, Palo Alto, California, will pass upon certain legal matters relating to the issuance and sale of the securities offered hereby on behalf of Denali Therapeutics Inc. Additional legal matters may be passed upon 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, 2024, and the effectiveness of our internal control over financial reporting as of December 31, 2024, 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 are part of a registration statement that we filed with the SEC and do not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided below. Forms of the indenture and other documents establishing the terms of the offered securities are or may be filed as exhibits to the registration statement. 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 refer to the actual documents for a more complete description of the relevant matters. You may inspect a copy of the registration statement at the SEC's Public Reference Room in Washington, D.C. or through the SEC's website, as provided above.

INCORPORATION BY REFERENCE

The SEC's rules allow us to "incorporate by reference" information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus modifies or replaces that statement.

We incorporate by reference our documents listed below and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, which we refer to as the "Exchange Act" in this prospectus, between the date of this prospectus and the termination of the offering of the securities described in this prospectus. We are not, however, incorporating by reference any documents or portions thereof, whether specifically listed below or filed in the future, that are not deemed "filed" with the SEC, including any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K.

This prospectus and any accompanying prospectus supplement incorporate by reference the documents set forth below that have previously been filed with the SEC:

- Our Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2024 filed on February 27, 2025.
- The description of our common stock, par value \$0.01 per share, contained in our registration statement on [Form 8-A](#), filed with the SEC on November 30, 2017, including any subsequent filed amendments and reports updating such description.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and documents.

You may request a free copy of any of the documents incorporated by reference in this prospectus (other than exhibits, unless they are specifically incorporated by reference in the documents) by writing or telephoning us at the following address:

Denali Therapeutics Inc.
161 Oyster Point Blvd.
South San Francisco, California 94080
(650) 866-8547

Exhibits to the filings will not be sent, however, unless those exhibits have specifically been incorporated by reference in this prospectus and any accompanying prospectus supplement.

The information accessible through any website referred to in this prospectus or any document incorporated herein is not, and should not be deemed to be, a part of this prospectus.

DENALI THERAPEUTICS INC.



Common Stock

Preferred Stock

Debt Securities

Warrants

Purchase Contracts

Units
