UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported):

May 6, 2025

Denali Therapeutics Inc.

(Exact name of registrant as specified in its charter)

Delaware	001-38311	46-3872213
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

161 Oyster Point Blvd.
South San Francisco, California 94080
(Address of principal executive offices, including zip code)

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

Not Applicable
(Former name or former address, if changed since last reports)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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

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

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 2.02 Results of Operations and Financial Condition.

On May 6, 2025, Denali Therapeutics Inc. (the "Company") issued a press release announcing its financial results for the first quarter ended March 31, 2025. The full text of the press release is attached hereto as Exhibit 99.1 and is incorporated herein by reference.

All of the information furnished in this Item 2.02 and Item 9.01 (including Exhibit 99.1) shall not be deemed to be “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and shall not be incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, except as shall be expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release dated May 6, 2025.
104	Cover Page Interactive Data File (formatted as Inline XBRL)

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

DENALI THERAPEUTICS INC.

Date: May 6, 2025

By: /s/ Alexander O. Schuth
Alexander O. Schuth, M.D.
Chief Operating and Financial Officer

Denali Therapeutics Reports First Quarter 2025 Financial Results and Business Highlights Including Completion of BLA Rolling Submission for Tividenofusp Alfa for Hunter Syndrome

SOUTH SAN FRANCISCO, Calif., – May 6, 2025 – Denali Therapeutics Inc. (Nasdaq: DNLI) today reported financial results for the first quarter ended March 31, 2025, and provided business highlights.

“The completion of our BLA submission for tividenofusp alfa represents a pivotal milestone—not only in our commitment to delivering a potentially transformative therapy to individuals living with Hunter syndrome, but also in Denali’s evolution as a fully integrated, late-stage development and commercial organization,” said Ryan Watts, Ph.D., CEO of Denali Therapeutics. “We are now preparing for commercial launch in late 2025 or early 2026. If approved, tividenofusp alfa would be the first FDA-approved enzyme replacement therapy engineered to cross the blood-brain barrier to treat body and brain manifestations of Hunter syndrome. Our broader TransportVehicle-enabled pipeline continues to advance, including the DNL126 program for Sanfilippo syndrome Type A for which we have an ongoing and productive collaboration with the FDA through the START program. Additionally, the recent launch of our in-house clinical biomanufacturing facility in Salt Lake City further enhances our ability to scale efficiently in the U.S. and supply future programs across lysosomal and neurodegenerative diseases.”

First Quarter 2025 and Recent Program Updates

CLINICAL PROGRAMS

Tividenofusp alfa (DNL310, ETV:IDS) for Hunter syndrome (MPS II)

Today, Denali announced completion of submission of a Biologics License Application (BLA) for tividenofusp alfa under the U.S. Food and Drug Administration's (FDA's) accelerated approval pathway based on data from the Phase 1/2 study in participants with Hunter syndrome. The submission of the final BLA modules initiates the FDA’s 60-day filing review process and, upon acceptance of the application, the FDA will communicate the Prescription Drug User Fee Act (PDUFA) target action date. In January 2025, the FDA granted Breakthrough Therapy Designation for tividenofusp alfa for the treatment of individuals with Hunter syndrome (MPS II). Tividenofusp alfa was previously granted Fast Track, Orphan Drug and Rare Pediatric Disease designations. In February 2025, at the WORLD Symposium conference, Denali presented the primary analysis of the Phase 1/2 study in 47 participants with Hunter syndrome in the 24-week treatment period and additional long-term follow-up. Denali continues preparation for the commercialization of tividenofusp alfa with a focus on launch readiness across access, education, and community engagement. Denali is conducting the ongoing global Phase 2/3 COMPASS study to support global regulatory approvals.

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

In April 2025, Denali announced productive collaboration and discussions with the FDA under the START program (“Support for clinical Trials Advancing Rare Disease Therapeutics”) around the potential for an accelerated development and approval path for DNL126 in the treatment of Sanfilippo syndrome Type A. DNL126 has FDA Fast Track, Orphan Drug, and Rare Pediatric Disease designations. Denali is conducting the Phase 1/2 study of DNL126 in Sanfilippo syndrome Type A.

TAK-594/DNL593 (PTV:PGRN) for GRN-related frontotemporal dementia

Denali and Takeda have an ongoing collaboration for the co-development and co-commercialization of DNL593, a therapeutic candidate engineered for the delivery of progranulin (PGRN) across the blood brain barrier (BBB) and into lysosomes for the treatment of frontotemporal dementia (FTD) associated with a mutation in the granulin (GRN) gene. Denali is conducting the ongoing Phase 1/2 study of DNL593 in FTD-GRN.

BIIB122/DNL151 (small molecule LRRK2 inhibitor) for the treatment of Parkinson's disease (PD)

Denali and Biogen are jointly developing LRRK2 small molecule inhibitors for Parkinson's disease (PD), with Biogen leading the global Phase 2b LUMA study evaluating the effect of BIIB122 on disease progression in early-stage PD. In May 2025, Biogen announced the Phase 2b LUMA study was fully enrolled with a readout expected in 2026. Denali is conducting the Phase 2a BEACON study specifically enrolling participants with LRRK2-associated PD to assess how LRRK2 inhibition in this population may impact disease and inform development within and across the broad PD population.

DNL343 (small molecule eIF2B agonist) for the treatment of amyotrophic lateral sclerosis (ALS)

In January 2025, Denali announced topline results that the primary endpoint was not met in Regimen G of the Phase 2/3 HEALEY ALS Platform Trial evaluating DNL343 in the treatment of ALS. In March 2025, Denali provided an update that additional analyses did not demonstrate a treatment effect on neurofilament light (NfL), a biomarker of neuronal damage, over the 24-week, double-blind period and in a subset of participants that completed an additional 28 weeks in the open-label active treatment extension. Based on these outcomes, the active treatment extension in Regimen G was discontinued. Overall, DNL343 was found to be generally well tolerated.

IND-ENABLING STAGE PROGRAMS

Denali is advancing additional candidates across its TransportVehicle™ (TV) franchises, i.e., Enzyme TV (ETV), Antibody TV (ATV), and Oligonucleotide TV (OTV), with programs for lysosomal storage diseases, Alzheimer's disease and Parkinson's disease. Programs in the Investigational New Drug (IND)-enabling stage include:

ETV
- DNL952 (ETV:GAA) for Pompe disease
- DNL111 (ETV:GCase) for Parkinson's disease and Gaucher disease
- DNL622 (ETV:IDUA) for Hurler syndrome (MPS I)

ATV
- DNL921 (ATV:Abeta) targeting amyloid beta for Alzheimer's disease

OTV
- DNL628 (OTV:MAPT) targeting tau for Alzheimer's disease
- DNL422 (OTV:SNCA) targeting alpha synuclein for Parkinson's disease

Corporate Updates

In March, Denali officially opened its clinical biomanufacturing facility in Salt Lake City, Utah, expanding its U.S. manufacturing capabilities and strengthening supply chain control and operational efficiency. Denali has begun manufacturing drug supply for clinical trials as the company expands its TV-enabled therapeutic portfolio.

Participation in Upcoming Investor Conferences
- Bank of America Healthcare Conference 2025, May 13-15 (Las Vegas)
- Jefferies Global Healthcare Conference, June 3-5 (New York City)
- Goldman Sachs 46th Annual Global Healthcare Conference, June 9-11 (Miami)
- BTIG Virtual Biotechnology Conference, July 29

First Quarter 2025 Financial Results

Net loss was $133.0 million for the quarter ended March 31, 2025, compared to net loss of $101.8 million for the quarter ended March 31, 2024.

Total research and development expenses were $116.2 million for the quarter ended March 31, 2025, compared to $107.0 million for the quarter ended March 31, 2024. The increase of approximately $9.2 million was primarily attributable to an increase of $6.3 million related to the company's TV programs, driven by increased spend on both clinical programs such as DNL126 and preclinical programs, such as the OTV franchise, as well as an increase of $9.2 million in other research and development expenses, including lab consumables, consultants and general facilities costs, driven in part by the commencement of operations at Denali's large molecule manufacturing facility in Salt Lake City, Utah. These increases were partially offset by a $2.1 million decrease in personnel-related expenses, including lower salaries and stock-based compensation, and a reduction in expenses related to small molecule programs.

General and administrative expenses were $29.4 million for the quarter ended March 31, 2025, compared to $25.2 million for the quarter ended March 31, 2024. The increase of $4.1 million was primarily driven by activities related to the submission of the BLA for tividenofusp alfa, which was completed in May 2025, and preparations for a commercial launch.

Cash, cash equivalents, and marketable securities were approximately $1.05 billion as of March 31, 2025.

About Denali Therapeutics

Denali Therapeutics is a biopharmaceutical company developing a broad portfolio of product candidates engineered to cross the blood-brain barrier (BBB) for the treatment of neurodegenerative diseases and lysosomal storage diseases. Denali pursues new treatments by rigorously assessing genetically validated targets, engineering delivery across the BBB, and guiding development through biomarkers that demonstrate target and pathway engagement. Denali is based in South San Francisco. For additional information, please visit www.denalitherapeutics.com.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements expressed or implied in this press release include, but are not limited to, statements regarding expectations regarding Denali's TV platform and its therapeutics and commercial potential; statements made by Denali's Chief Executive Officer; plans, timelines, and expectations relating to DNL310, including enrollment in the ongoing global Phase 2/3 COMPASS study and the likelihood of global approvals, the timing of planned regulatory filings, and the timing, likelihood, and scope of regulatory approvals and commercial launch; plans, timelines, and expectations related to DNL126, including enrollment in the ongoing Phase 1/2 study, planned engagement with the FDA, and the likelihood and scope of regulatory approvals; plans regarding DNL593 and the ongoing Phase 1/2 study; plans, timelines, and expectations regarding DNL151, including with respect to the ongoing Phase 2b LUMA and Phase 2a BEACON studies; plans and expectations for Denali's preclinical programs, including the timing of advancement to clinical studies; the impact and scalability of Denali's in-house manufacturing operations; Denali's future operating expenses and anticipated cash runway; and Denali's participation in upcoming investor conferences. All drugs currently being developed by Denali are investigational and have not received regulatory approval for any indication. Actual results are subject to risks and uncertainties and may differ materially from those indicated by these forward-looking statements as a result of these risks and uncertainties, including but not limited to, risks related to: the impact of adverse economic conditions, tariffs, and inflation on Denali's business and operations; the occurrence of any event, change, or other circumstance that could give rise to the termination of Denali's agreements with Sanofi, Takeda, Biogen, or other collaborators; Denali's transition to a late-stage clinical drug development company; Denali's and its collaborators' ability to complete the development and, if approved, commercialization of its product candidates; Denali's and its collaborators' ability to enroll patients in its ongoing and future clinical trials; Denali's reliance on third parties for the manufacture and supply of its product candidates for clinical trials; Denali's dependence on successful development of its blood-brain barrier platform technology and its programs and product candidates; Denali's and its collaborators' ability to conduct or complete clinical trials on expected timelines; the risk that preclinical profiles of Denali's product candidates may not translate in clinical trials; the potential for clinical trials to differ from preclinical, early clinical, preliminary or expected results; the risk of significant adverse events, toxicities, or other undesirable side effects; the uncertainty that product candidates will receive regulatory approval necessary to be commercialized; Denali's ability to continue to create a pipeline of product candidates or commercialize products; developments relating to Denali's competitors and its industry, including competing product candidates and therapies; Denali's ability to obtain, maintain, or protect intellectual property rights related to its product candidates; implementation of Denali's strategic plans for its business, product candidates, and blood-brain barrier platform technology; Denali's ability to obtain additional capital to finance its operations, as needed; Denali's ability to accurately forecast future financial results and hedge against financial risk in the current environment; and other risks and uncertainties, including those described in Denali's most recent Annual Report on Forms 10-K filed with the Securities and Exchange Commission (SEC) on February 27, 2025, and Denali's future reports to be filed with the SEC. Denali does not undertake any obligation to update or revise any forward-looking statements, to conform these statements to actual results, or to make changes in Denali's expectations, except as required by law.

Denali Therapeutics Inc.
Condensed Consolidated Statements of Operations
(Unaudited)
(In thousands, except share and per share amounts)

	Three Months Ended March 31,	
	2025	**2024**
Operating expenses:		
Research and development	$ 116,227	$ 107,016
General and administrative	29,353	25,236
Total operating expenses	145,580	132,252
Gain from divestiture of small molecule programs	—	14,537
Loss from operations	(145,580)	(117,715)
Interest and other income, net	12,610	15,913
Net loss	$ (132,970)	$ (101,802)
Net loss per share, basic and diluted	$ (0.78)	$ (0.68)
Weighted average number of shares outstanding, basic and diluted	171,222,030	149,404,188

Denali Therapeutics Inc.
Condensed Consolidated Balance Sheets
(Unaudited)
(In thousands)

	March 31, 2025	December 31, 2024
Assets		
Current assets:		
Cash and cash equivalents	$ 56,947	$ 174,960
Short-term marketable securities	760,979	657,371
Prepaid expenses and other current assets	60,712	32,105
Total current assets	878,638	864,436
Long-term marketable securities	235,844	359,373
Property and equipment, net	57,765	55,236
Finance lease right-of-use asset	50,199	47,533
Operating lease right-of-use asset	21,963	22,861
Other non-current assets	26,934	24,741
Total assets	$ 1,271,343	$ 1,374,180
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 8,458	$ 11,137
Accrued compensation	7,655	24,728
Accrued clinical and other research & development costs	27,908	22,822
Accrued manufacturing costs	14,579	12,779
Operating lease liability, current	8,585	8,308
Deferred research and development funding liability, current	17,338	14,129
Other accrued costs and current liabilities	7,354	8,305
Total current liabilities	91,877	102,208
Operating lease liability, less current portion	34,449	36,673
Finance lease liability, less current portion	5,598	5,615
Deferred research funding and development liability, less current portion	16,733	—
Total liabilities	148,657	144,496
Total stockholders' equity	1,122,686	1,229,684
Total liabilities and stockholders' equity	$ 1,271,343	$ 1,374,180

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