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):

August 11, 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 August 11, 2025, Denali Therapeutics Inc. (the "Company") issued a press release announcing its financial results for the second quarter ended June 30, 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 August 11 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: August 11, 2025

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

Denali Therapeutics Reports Second Quarter 2025 Financial Results and Business Highlights

- Tividenofusp alfa BLA for Hunter syndrome accepted for priority review and assigned PDUFA target action date of January 5, 2026; company preparing for commercial launch
- DNL126 accelerated approval path for Sanfilippo syndrome Type A aligned with FDA; Phase 1/2 study nearing completion of enrollment; planning underway for a global Phase 3 confirmatory study
- On track to submit regulatory applications in 2025 to begin clinical testing of one to two additional TransportVehicle™ (TV)-enabled programs
- Preclinical research on ATV:Abeta program for Alzheimer's disease published in the journal *Science*

SOUTH SAN FRANCISCO, Calif., – August 11, 2025 – Denali Therapeutics Inc. (Nasdaq: DNLI) today reported financial results for the second quarter ended June 30, 2025, and provided business highlights.

"The FDA's priority review of our BLA for tividenofusp alfa and alignment on an accelerated approval path for DNL126 are key milestones highlighting the potential of our Transport Vehicle (TV) platform to catalyze a new class of blood-brain barrier-crossing therapeutics," said Ryan Watts, Ph.D., CEO of Denali Therapeutics. "With launch readiness in motion and a growing portfolio of TV-enabled enzyme, antibody, and oligonucleotide programs, Denali is poised to deliver meaningful treatments for people living with lysosomal, neurodegenerative, and other serious diseases."

Second Quarter 2025 and Recent Program Updates

CLINICAL PROGRAMS

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

In July 2025, Denali announced that the U.S. Food and Drug Administration (FDA) accepted its Biologics License Application (BLA) for tividenofusp alfa for priority review, assigning a Prescription Drug User Fee Act (PDUFA) target action date of January 5, 2026. The BLA seeks accelerated approval based on a data package including results from the Phase 1/2 study in individuals with Hunter syndrome. Tividenofusp alfa is an investigational, next-generation enzyme replacement therapy designed to cross the blood-brain barrier (BBB) and deliver the iduronate-2-sulfatase (IDS) enzyme throughout the body and brain. The FDA previously granted tividenofusp alfa Breakthrough Therapy, Fast Track, Orphan Drug, and Rare Pediatric Disease designations. Denali continues to prepare for commercial launch and is conducting the Phase 2/3 COMPASS study to support global regulatory submissions.

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

Today, Denali announced that it has reached alignment with the FDA's Center for Drug Evaluation and Research (CDER) that cerebrospinal fluid heparan sulfate (CSF HS) may be considered a reasonably likely surrogate endpoint to predict clinical benefit and may therefore be used to support accelerated approval of DNL126 for MPS IIIA. Additional 49-week data from the ongoing open-label Phase 1/2 study are consistent with previously announced 25-week data, demonstrating a significant reduction in CSF HS from baseline, including normalization, and a safety profile that supports continued development. Enrollment in the Phase 1/2 study is nearly complete, and planning is underway for a confirmatory global Phase 3 study.

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

Denali and Takeda continue their collaboration to develop DNL593, an investigational therapeutic designed to deliver progranulin across the BBB for the treatment of granulin (GRN) mutation-associated frontotemporal dementia (FTD-GRN). A Phase 1/2 study is ongoing.

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

Denali and Biogen are co-developing LRRK2 inhibitors for Parkinson's disease. In May 2025, Biogen announced that the Phase 2b LUMA study of BIIB122 completed enrollment, with a readout expected in 2026. Denali is also conducting the Phase 2a BEACON study focused on LRRK2-associated PD.

IND-ENABLING STAGE PROGRAMS

Denali expects to submit regulatory applications to begin clinical testing of one to two TV-enabled programs each year over the next three years across its Enzyme TV (ETV), Antibody TV (ATV), and Oligonucleotide TV (OTV) franchises. The most advanced programs include: DNL952 (ETV:GAA) for Pompe disease; DNL111 (ETV:GCase) for Parkinson's/Gaucher disease; DNL622 (ETV:IDUA) for MPS I; DNL921 (ATV:Abeta) for Alzheimer's disease; DNL628 (OTV:MAPT) for Alzheimer's disease; and DNL422 (OTV:SNCA) for Parkinson's disease.

Denali announced publication of preclinical data on ATV:Abeta in the August 7, 2025, issue of the journal *Science.* The research demonstrated that delivering an anti-amyloid beta antibody across the BBB using Denali's TV platform improved brain distribution and reduced the risk of amyloid-related imaging abnormality (ARIA) in a mouse model of Alzheimer's disease, compared to conventional antibody treatment. The findings suggest that TV platform-enabled brain delivery of immunotherapy bypasses amyloid-laden large vessels by traveling through smaller capillaries, offering a potential strategy to mitigate ARIA risk seen with first-generation anti-amyloid therapies. The *Science* article can be accessed here.

Participation in Upcoming Investor Conferences

- Cantor Global Healthcare Conference 2025, September 3 - 5 (New York City)
- Morgan Stanley 23rd Annual Global Healthcare Conference, September 8 - 10 (New York City)
- Baird 2025 Global Healthcare Conference, September 9 - 10 (New York City)
- H.C. Wainwright 27th Annual Global Investment Conference, September 8 - 10 (New York City)
- Deutsche Bank BioPharm Corporate Day, September 18 - 19 (Austria)
- Stifel 2025 Healthcare Conference, November 11 - 13 (New York City)
- Jefferies Global Healthcare Conference, November 17 - 20 (London)

Second Quarter 2025 Financial Results

Net loss was $124.1 million for the quarter ended June 30, 2025, compared to net loss of $99.0 million for the quarter ended June 30, 2024.

Total research and development expenses were $102.7 million for the quarter ended June 30, 2025, compared to $91.4 million for the quarter ended June 30, 2024. The increase of approximately $11.3 million was attributable to an increase of $7.3 million in TV program external research and development expenses, primarily driven by increased spend on multiple preclinical programs, and increases of $7.6 million and $6.2 million in other research and development expenses and personnel-related expenses, respectively, both driven by the commencement of operations at Denali's large molecule manufacturing facility in Salt Lake City, Utah. These increases were partially offset by a $9.8 million decrease in small molecule programs, primarily due to the winding down of activities related to the Phase 2/3 HEALEY ALS Platform Trial.

General and administrative expenses were $32.3 million for the quarter ended June 30, 2025, compared to $25.2 million for the quarter ended June 30, 2024. The increase of $7.1 million was primarily driven by activities related to preparations for a potential commercial launch for tividenofusp alfa.

Cash, cash equivalents, and marketable securities were approximately $977.4 million as of June 30, 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 for 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 the PDUFA target action date and the timing, likelihood of, and scope of regulatory approval, the ongoing global Phase 2/3 COMPASS study and the likelihood of global approvals, and planned commercial launch; plans, timelines, and expectations related to DNL126, including enrollment in the ongoing Phase 1/2 study, plans regarding the confirmatory global Phase 3 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 study and the timing and likelihood of readout, and the ongoing Phase 2a BEACON study; plans and expectations for Denali's preclinical programs, including the timing of advancement to clinical studies; the findings from Denali's recent Science publication and their therapeutic potential regarding ARIA risk; Denali's participation in upcoming investor conferences; and Denali's future operating expenses and anticipated cash runway. 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 and Quarterly Reports on Forms 10-K and 10-Q filed with the Securities and Exchange Commission (SEC) on February 27, 2025 and May 6, 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 June 30,		Six Months Ended June 30,	
	2025	**2024**	**2025**	**2024**
Operating expenses:				
Research and development	$ 102,696	$ 91,399	$ 218,923	$ 198,415
General and administrative	32,267	25,194	61,620	50,430
Total operating expenses	134,963	116,593	280,543	248,845
Gain from divestiture of small molecule programs	—	—	—	14,537
Loss from operations	(134,963)	(116,593)	(280,543)	(234,308)
Interest and other income, net	10,844	17,567	23,454	33,480
Net loss	$ (124,119)	$ (99,026)	$ (257,089)	$ (200,828)
Net loss per share, basic and diluted	$ (0.72)	$ (0.59)	$ (1.50)	$ (1.26)
Weighted average number of shares outstanding, basic and diluted	171,449,847	168,831,329	171,336,568	159,117,759

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

	June 30, 2025	December 31, 2024
Assets		
Current assets:		
Cash and cash equivalents	$ 141,207	$ 174,960
Short-term marketable securities	757,745	657,371
Prepaid expenses and other current assets	35,754	32,105
Total current assets	934,706	864,436
Long-term marketable securities	78,463	359,373
Property and equipment, net	58,717	55,236
Finance lease right-of-use asset	50,363	47,533
Operating lease right-of-use asset	21,022	22,861
Other non-current assets	22,970	24,741
Total assets	$ 1,166,241	$ 1,374,180
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 10,844	$ 11,137
Accrued compensation	12,068	24,728
Accrued clinical and other research & development costs	23,379	22,822
Accrued manufacturing costs	9,028	12,779
Operating lease liability, current	8,871	8,308
Deferred research and development funding liability, current	19,861	14,129
Other accrued costs and current liabilities	7,006	8,305
Total current liabilities	91,057	102,208
Operating lease liability, less current portion	32,110	36,673
Finance lease liability, less current portion	5,577	5,615
Deferred research funding and development liability, less current portion	10,444	—
Total liabilities	139,188	144,496
Total stockholders' equity	1,027,053	1,229,684
Total liabilities and stockholders' equity	$ 1,166,241	$ 1,374,180

Investor Contact:
Laura Hansen, Ph.D.
hansen@dnli.com

Media Contact:
Erin Patton
epatton@dnli.com