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):

January 13, 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) 866-8548
(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))

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. ☐

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

Item 7.01 Regulation FD Disclosure.

On January 13, 2025, Denali Therapeutics Inc. (the "Company") issued a press release announcing an update on its programs and expected milestones for 2025 and the Company's participation in the 43rd Annual J.P. Morgan Healthcare Conference.

A copy of the press release is attached hereto as Exhibit 99.1 and incorporated herein by reference.

The information furnished in this Item 7.01 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 (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, 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 January 13, 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: January 13, 2024

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

Denali Therapeutics Announces Key Anticipated 2025 Milestones and Priorities to Further Advance Its Therapeutics Portfolio for Neurodegeneration and Lysosomal Storage Diseases

- FDA Breakthrough Therapy Designation received for tividenofusp alfa for Hunter syndrome (MPS II); on track to submit biologics license application (BLA) in early 2025
- Preparing for commercial launch of tividenofusp alfa for Hunter syndrome in late 2025 or early 2026
- Enable accelerated approval pathway for DNL126 for Sanfilippo syndrome Type A (MPS IIIA)
- Expand and advance portfolio of multiple TransportVehicle™ (TV) enabled programs for delivery of enzyme, oligonucleotide, and antibody therapeutics for rare and common diseases

SOUTH SAN FRANCISCO, Calif., – Jan. 13, 2025 – Denali Therapeutics Inc. (NASDAQ: DNLI), today announced key anticipated milestones for 2025 across its portfolio. Chief Executive Officer, Ryan Watts, Ph.D., will highlight these priorities during a corporate presentation at the 43rd Annual J.P. Morgan Healthcare Conference on Tuesday, January 14, at 11:15 a.m. PDT.

"In 2025, we are on track to submit our first BLA for tividenofusp alfa for Hunter syndrome and prepare for commercial launch. In addition, we will seek alignment with the FDA on an accelerated approval path for our second program DNL126 for Sanfilippo syndrome. Together, we expect these two programs to be the foundation of a broad franchise of TransportVehicle™ (TV) enabled enzyme replacement therapies," said Ryan Watts, Ph.D., Chief Executive Officer of Denali. "Further, we are expanding our TV-enabled portfolio of therapeutic enzymes, oligonucleotides, and antibodies, and plan to advance one to two additional TV programs into the clinic each year for the next three years. We are excited about the validation and broad potential of the TV platform to deliver a new class of barrier-crossing therapeutics with great potential for people living with rare and common diseases that impact the brain."

2025 Outlook

Denali Therapeutics has pioneered and is delivering a new class of therapeutics using its TransportVehicle™ (TV) platform to enable and transform treatment for people living with rare and common diseases that impact the brain. The TV platform is designed to deliver large molecules – enzymes (ETV), oligonucleotides (OTV), and antibodies (ATV) – across biological barriers including the blood-brain barrier, enabling broad biodistribution into targeted tissues where treatment is needed. Expected progress and key milestones in 2025 across Denali's portfolio of TV enabled and small molecule programs are summarized below.

CLINICAL PROGRAMS

Tividenofusp alfa (DNL310, ETV:IDS) for Hunter syndrome (MPS II): On January 7, 2025, the FDA granted tividenofusp alfa Breakthrough Therapy Designation for Hunter syndrome (MPS II). Denali expects to submit a biologics license agreement (BLA) under the accelerated approval pathway in early 2025 and is preparing for the U.S. launch of tividenofusp alfa for the treatment of Hunter syndrome in late 2025 or early 2026. Denali is engaged in prelaunch activities including continued dialogue with prescribers and payers, building a suite of patient support services and capabilities to enable broad access, and building a right-sized team in commercial and medical affairs to support tividenofusp alfa and additional Enzyme TV (ETV) launches. The ongoing open-label extension of the Phase 1/2 study will generate long-term safety data, and the ongoing global Phase 2/3 COMPASS study will support global approval. Target enrollment of neuronopathic participants in Cohort A of the COMPASS study has been completed. In addition to Breakthrough Therapy Designation, the FDA previously granted tividenofusp alfa Fast Track Designation, Orphan Drug Designation, and Rare Pediatric Disease Designation for development in the treatment of MPS II. Additional Phase 1/2 results have been accepted for oral presentation at the 2025 WORLD*Symposium* conference taking place February 3-7, 2025.

DNL126 (ETV:SGSH) for Sanfilippo syndrome Type A (MPS IIIA): Preliminary data from the ongoing Phase 1/2 study of DNL126 have demonstrated a substantial reduction in cerebrospinal fluid heparan sulfate (CSF HS) levels from baseline, including normalization. Based on these results, Denali will seek alignment with the FDA on a path for accelerated approval. DNL126 has Orphan Disease designation, Fast Track status, and has been selected for the FDA "Support for clinical Trials Advancing Rare disease Therapeutics" (START) program, designed to accelerate the development of rare disease therapeutics.

TAK-594/DNL593 (PTV :PGRN) for GRN-related frontotemporal dementia: Data from the ongoing Phase 1/2 study of DNL593 have demonstrated dose-dependent increases in CSF progranulin levels, consistent with robust brain delivery of DNL593, in healthy volunteers. Dosing granulin (GRN)-related frontotemporal dementia (FTD-GRN) participants is ongoing.

BIIB122/DNL151 (small molecule LRRK2 inhibitor) for the treatment of Parkinson's disease (PD): Denali and Biogen have a strategic collaboration to jointly develop and commercialize small molecule inhibitors of LRRK2. Biogen is conducting the global Phase 2b LUMA study, which is evaluating the ability of BIIB122 to slow disease progression as compared to placebo in approximately 640 participants with early-stage Parkinson's disease; completion of enrollment is expected in 2025. In addition, Denali is conducting the complementary Phase 2a BEACON study in LRRK2-associated Parkinson's disease with the aim to generate biomarker and safety data to inform how LRRK2 inhibition may impact this disease.

DNL343 (small molecule eIF2B activator) for amyotrophic lateral sclerosis (ALS): Following previously reported topline results that the primary endpoint was not met in the HEALEY ALS platform trial (press release), further analyses are anticipated later in 2025, including neurofilament light (NfL) and other fluid biomarkers, data from pre-specified subgroups, as well as extended findings from the active treatment extension period.

IND-ENABLING STAGE PROGRAMS

Beginning in 2025, Denali expects to advance one to two additional programs to the clinic per year over the next three years across its TV-enabled franchises (ETV, OTV, and ATV). IND-enabling stage programs 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)

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

ATV
- DNL921 (ATV:Abeta) targeting amyloid beta for Alzheimer's disease
- Multiple ATV-enabled oncology programs

PARTNERSHIPS

Denali has active collaborations with Biogen for BIIB122/DNL151 in Parkinson's disease and with Takeda for TAK-594/DNL593 in FTD-GRN, both with 50/50 U.S. commercial rights. Denali also stands to receive royalty payments for SAR443122/DNL758, which is licensed to Sanofi and in development for ulcerative colitis.

FINANCIAL OUTLOOK

Cash, cash equivalents, and marketable securities were approximately $1.28 billion as of September 30, 2024. Denali anticipates its cash runway will extend into 2028.

UPCOMING INVESTOR CONFERENCES

- Oppenheimer's 35th Annual Healthcare Life Sciences Conference, February 11-12

- Leerink Partners Global Healthcare Conference, March 9 - 12
- Jefferies Biotech on the Beach, March 11 - 12
- UBS Virtual CNS Day 2025, March 17
- Stifel CNS Days 2025, March 18 - 19

Webcast details for Denali's presentation at the 43rd annual J.P. Morgan Healthcare Conference

A live and archived webcast of the Denali presentation during the J.P. Morgan Conference on Tuesday, Jan. 14, at 11:15 a.m. PDT will be available on the Events page under the Investor section of the Denali website at https://investors.denalitherapeutics.com/events.

About Denali Therapeutics

Denali Therapeutics is a biopharmaceutical company developing a broad portfolio of product candidates engineered to cross the blood-brain barrier for neurodegenerative diseases and lysosomal storage diseases. Denali pursues new treatments by rigorously assessing genetically validated targets, engineering delivery across the blood-brain barrier 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 the future results of operations and financial position of Denali Therapeutics Inc. ("Denali" or the "Company"); Denali's business strategy and business plans, including expected key milestones for Denali's therapeutic portfolio in 2025 and beyond and Denali's ability to execute on its tailored commercial strategies; plans, timelines, expectations related to Denali's TransportVehicle™ (TV) platform and its therapeutic and commercial potential; plans, timelines, and expectations relating to DNL310, including enrollment in ongoing clinical studies, the timing and availability of data in the Phase 1/2 study and Phase 2/3 COMPASS study, 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 the timing and availability of data from the Phase 1/2 study, interactions with the FDA, and the timing, likelihood, and scope of regulatory approval; plans and expectations regarding DNL593, including the ongoing the Phase 1/2 study; plans, timelines, and expectations related to DNL151, including the ongoing Phase 2a BEACON study and the Phase 2b LUMA study; plans, timelines, and expectations related to DNL343, including the timing and availability of data and further analysis related to Phase 2/3 HEALEY Platform Trial; expectations regarding Denali's preclinical studies and the timing and likelihood of advancement of additional programs to clinical studies; Denali's third-party collaborations and potential royalties; Denali's anticipated operating expenses and cash runway; and statements made by Denali's Chief Executive Officer. 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: Denali's dependence on successful development of its BBB platform technology and TV-enabled product candidates; Denali's ability to initiate and enroll patients in its current and future clinical trials; Denali's ability to conduct or complete clinical trials on expected timelines; Denali's reliance on third parties for the manufacture and supply of its product candidates for clinical trials; the potential for clinical trial results to differ from preclinical, early clinical, preliminary or expected results; the risk of significant adverse events, toxicities, or other undesirable side effects; the risk that results from early clinical biomarker studies will not translate to clinical benefit in late clinical studies; the risk that product candidates may not receive regulatory approval necessary to be commercialized; 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; and other risks and uncertainties. In light of these risks, uncertainties, and assumptions, the forward-looking statements in this press release are inherently uncertain and may not occur, and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. Accordingly, you should not rely upon forward-looking statements as predictions of future events. Denali's product candidates are investigational, and their safety and efficacy profiles have not yet been established. No Denali product candidates have been approved by any health authority for any use. Information regarding additional risks and uncertainties may be found in Denali's Annual and Quarterly Reports filed on Forms 10-K and 10-Q filed with the Securities and Exchange Commission (SEC) on February 28, 2024, and November 6, 2024, respectively, 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.

Investor Contact:

Laura Hansen, Ph.D.
Vice President, Investor Relations
(650) 452-2747
hansen@dnli.com

Media Contact
Rich Allan
FGS Global
(503) 851-0807
rich.allan@fgsglobal.com