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 21, 2026

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 7.01 Regulation FD Disclosure.

On May 21, 2026, Denali Therapeutics Inc. (the "Company") and Biogen Inc. issued a press release announcing topline results from the Phase 2b LUMA study evaluating BIIB122 (DNL151) in individuals with early-stage Parkinson's disease. A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

The information in this Item 7.01 (including Exhibit 99.1) shall not be deemed "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 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 21, 2026
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 21, 2026

By: /s/ Ryan J. Watts
Ryan J. Watts, Ph.D.
President and Chief Executive Officer

Biogen and Denali Therapeutics Provide Update on Phase 2b LUMA Study of BIIB122 (DNL151) in Early-Stage Parkinson's Disease

- *The Phase 2b LUMA study of BIIB122 in early-stage Parkinson's disease did not meet its primary or secondary endpoints*
- *Based on data from the Phase 2b LUMA study, Biogen and Denali will discontinue development of BIIB122 in idiopathic Parkinson's disease*
- *Denali continues to independently conduct the Phase 2a BEACON study in carriers of a pathogenic LRRK2 variant*

CAMBRIDGE, Mass. and SOUTH SAN FRANCISCO, Calif., — May 21, 2026 — Biogen Inc. (Nasdaq: BIIB) and Denali Therapeutics Inc. (Nasdaq: DNLI) today announced topline results from the Phase 2b LUMA study evaluating BIIB122 (DNL151), an investigational small molecule inhibitor of LRRK2 (leucine-rich repeat kinase 2), in individuals with early-stage Parkinson's disease. Results from the study show that BIIB122 did not slow the progression of Parkinson's disease versus placebo, as measured by the primary endpoint of Time to Confirmed Worsening in the modified Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part II and III combined score. Secondary endpoints also did not show a benefit with BIIB122. Exploratory biomarker endpoints demonstrated >90% kinase inhibition of peripheral LRRK2 (phosphoserine 935) and, in a cerebrospinal fluid (CSF) sub-study, up to approximately 30% reduction observed in a biomarker of LRRK2 activity (phosphorylated Rab10). Expected levels of BIIB122 in the blood and CSF were sustained across the study. BIIB122 was generally well tolerated with an acceptable safety profile. Based on these results, Biogen and Denali will discontinue further development of BIIB122 in idiopathic Parkinson's disease. Denali will continue to independently conduct the Phase 2a BEACON study evaluating the small molecule inhibitor in carriers of a pathogenic LRRK2 variant.

"While these are not the results we hoped for, these data provide important information to the Parkinson's community and will be presented at an upcoming scientific conference," said Diana Gallagher, MD, Senior Vice President and Head of Neurodegeneration Clinical Development at Biogen. "We are profoundly grateful to the patients, families, and investigators who participated in this study and contributed to our understanding of Parkinson's disease."

LUMA was a Phase 2b multi-center, randomized, double-blind, placebo-controlled study to evaluate the safety and efficacy of BIIB122 compared to placebo in 648 people with early-stage Parkinson's disease between the ages of 30 and 80. Participants received BIIB122 or placebo for a minimum of 48 weeks and up to 144 weeks. The study included individuals with early-stage Parkinson's disease with or without a pathogenic LRRK2 variant. The LUMA study was designed to evaluate the potential of LRRK2 inhibition to address the underlying biology of Parkinson's disease.

"While we are disappointed with these results, we believe the LUMA study was a robust test of LRRK2 inhibition using BIIB122 in idiopathic Parkinson's disease and there is more to be learned about LRRK2 as a potential therapeutic target," said Peter Chin, M.D., Chief Medical Officer and Head of Development of Denali Therapeutics. "Independently, we continue to study this small molecule inhibitor in the Phase 2a BEACON study in individuals with Parkinson's disease who are confirmed by genetic testing to be carriers of a pathogenic LRRK2 variant, which is associated with increased LRRK2 kinase activity. We look forward to further analysis of the LUMA data and the results from BEACON to inform next steps for development."

The global Phase 2a BEACON study is designed to assess safety, pharmacokinetics and biomarkers of lysosomal pathway engagement, which will inform the biomarker profile in LRRK2 pathogenic variant carriers and the impact of LRRK2 inhibition. Data from the BEACON study is anticipated in the first half of 2027. The BEACON study is being operationalized by Denali and funded under a Collaboration and Development Funding Agreement between Denali and a third party.

Biogen and Denali will share detailed findings from the LUMA study at an upcoming scientific conference to contribute to the broader understanding of Parkinson's disease and LRRK2 biology.

About Parkinson's Disease
Parkinson's disease is a progressive neurodegenerative disorder that affects movement and a wide range of non-motor functions. It is characterized by motor symptoms such as tremor, muscle stiffness, slowness of movement, and balance difficulty, as well as non-motor symptoms including sleep disturbances, mood changes, and cognitive impairment. One million people in the U.S. and more than 10 million people worldwide are estimated to have Parkinson's disease. Parkinson's disease is especially difficult to develop drugs for because of its complexity, with patients presenting differently and responding variably to treatment. The lack of reliable biomarkers, along with diverse and often unknown biological causes of the disease, also makes it challenging to track disease progression in clinical trials.

About LRRK2
Following discovery of the LRRK2 (leucine-rich repeat kinase 2) mutation as a pathogenic genetic factor for Parkinson's disease, further research has uncovered that it has the potential to be a novel therapeutic target for Parkinson's disease. Mutations in LRRK2 account for 4-5% of familial and 1-2% of sporadic Parkinson's disease.1, 2 In addition, common variants in and around LRRK2 have been identified as risk factors for sporadic Parkinson's disease.

While the exact pathogenic mechanisms remain unknown, LRRK2 is believed to play a role in intracellular trafficking in the endolysosomal system, and the endolysosomal system is overrepresented among rare and common risk gene variants for Parkinson's disease.[3,4,5] Lysosomal dysfunction is a central pathogenic driver of Parkinson's disease, characterized by failure of the cell's waste disposal system (lysosomes) to break down proteins, which then accumulate and create aggregates that can cause neuronal degeneration.[6]

About Biogen
Founded in 1978, Biogen is a leading biotechnology company that pioneers innovative science to deliver new medicines to transform patients' lives and to create value for shareholders and our communities. We apply deep understanding of human biology and leverage different modalities to advance first-in-class treatments or therapies that deliver superior outcomes. Our approach is to take bold risks, balanced with return on investment to deliver long-term growth. We routinely post information that may be important to investors on our website at www.biogen.com. Follow us on social media - Facebook, Instagram, LinkedIn, X, YouTube.

About Denali Therapeutics
Denali Therapeutics Inc. is a biotechnology company pioneering a new class of biotherapeutics designed to cross the blood-brain barrier using its proprietary TransportVehicle™ platform. With a clinically validated delivery platform and a growing portfolio of therapeutic candidates across all stages of development, Denali is advancing toward its goal of delivering effective medicines to transform life for people with neurodegenerative diseases, lysosomal storage disorders and other serious diseases. For more information, please visit www.denalitherapeutics.com.

Biogen Safe Harbor
This press release contains forward-looking statements including, among others, relating to the potential benefits and results that may be achieved through Biogen's collaboration with Denali; our efforts to contribute to and advance the understanding of Parkinson's disease; the clinical development program, clinical trials, data readouts and presentations related to BIIB122; the treatment of Parkinson's disease and the relation between LRRK2 biology and Parkinson's disease; the potential of Biogen's commercial business and pipeline programs; and risks and uncertainties associated with drug development and commercialization. These forward-looking statements may be accompanied by words such as "aim," "anticipate," "believe," "could," "estimate," "expect," "forecast," "goal," "intend," "may," "plan," "potential," "possible," "will," "would" and other words and terms of similar meaning. Drug development and commercialization involve a high degree of risk, and only a small number of research and development programs result in commercialization of a product. Results in early stage clinical trials may not be indicative of full results or results from later stage or larger scale clinical trials and do not ensure regulatory approval. You should not place undue reliance on these statements or the scientific data presented. Given their forward-looking nature, these statements involve substantial risks and uncertainties that may be based on inaccurate assumptions and could cause actual results to differ materially from those reflected in such statements.

These forward-looking statements are based on management's current beliefs and assumptions and on information currently available to management. Given their nature, we cannot assure that any outcome expressed in these forward-looking statements will be realized in whole or in part. We caution that these statements are subject to risks and uncertainties, many of which are outside of our control and could cause future events or results to differ materially from those stated or implied in this document, including, among others, uncertainty of our long-term

success in developing, licensing, or acquiring other product candidates or additional indications for existing products; expectations, plans, prospects and timing of actions relating to product approvals, approvals of additional indications for our existing products, sales, pricing, growth, reimbursement and launch of our marketed and pipeline products; the potential impact of increased product competition in the biopharmaceutical and healthcare industry, as well as any other markets in which we compete, including increased competition from new originator therapies, generics, prodrugs and biosimilars of existing products and products approved under abbreviated regulatory pathways; our ability to effectively implement our corporate strategy; difficulties in obtaining and maintaining adequate coverage, pricing, and reimbursement for our products; the drivers for growing our business, including our dependence on collaborators and other third parties for the development, regulatory approval, and commercialization of products and other aspects of our business, which are outside of our full control; risks related to commercialization of biosimilars, which is subject to such risks related to our reliance on third-parties, intellectual property, competitive and market challenges and regulatory compliance; the risk that positive results in a clinical trial may not be replicated in subsequent or confirmatory trials or success in early stage clinical trials may not be predictive of results in later stage or large scale clinical trials or trials in other potential indications; risks associated with clinical trials, including our ability to adequately manage clinical activities, unexpected concerns that may arise from additional data or analysis obtained during clinical trials, regulatory authorities may require additional information or further studies, or may fail to approve or may delay approval of our drug candidates; and the occurrence of adverse safety events, restrictions on use with our products, or product liability claims; and any other risks and uncertainties that are described in other reports we have filed with the U.S. Securities and Exchange Commission, which are available on the SEC's website at www.sec.gov.

These statements speak only as of the date of this press release and are based on information and estimates available to us at this time. Should known or unknown risks or uncertainties materialize or should underlying assumptions prove inaccurate, actual results could vary materially from past results and those anticipated, estimated or projected. Investors are cautioned not to put undue reliance on forward-looking statements. A further list and description of risks, uncertainties and other matters can be found in our Annual Report on Form 10-K for the fiscal year ended December 31, 2025, and in our subsequent reports on Form 10-Q. Except as required by law, we do not undertake any obligation to publicly update any forward-looking statements whether as a result of any new information, future events, changed circumstances or otherwise.

Digital Media Disclosure
From time to time we have used, or expect in the future to use, our investor relations website (investors.biogen.com), the Biogen LinkedIn account (linkedin.com/company/biogen-) and the Biogen X account (https://x.com/biogen) as a means of disclosing information to the public in a broad, non-exclusionary manner, including for purposes of the SEC's Regulation Fair Disclosure (Reg FD). Accordingly, investors should monitor our investor relations website and this social media channel in addition to our press releases, SEC filings, public conference calls and webcasts, as the information posted on them could be material to investors.

Denali Safe Harbor
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 by Denali Therapeutics Inc. ("Denali" or the "Company") regarding plans, timelines and expectations related to the ongoing Phase 2a BEACON study of BIIB122 in LRRK2-associated Parkinson's disease, including the timing and availability of clinical data; the presentation of data related to the Phase 2b LUMA study; the discontinuation of development of DNL151 in idiopathic Parkinson's disease; the continued evaluation of DNL151 based on its safety profile; the potential of LRRK2 as a therapeutic target; Denali's plans to share detailed findings from the LUMA study at an upcoming scientific conference; and statements by Denali's Chief Medical Officer and Head of Development. Actual results may differ materially from those expressed or implied by these forward-looking statements due to a variety of risks and uncertainties. These include, but are not limited to, uncertainties related to the FDA's policies; risks arising from adverse economic conditions and their impact on Denali's business and operations; the possibility of events or changes that could lead to the termination of Denali's collaboration agreements; challenges associated with Denali's transition to a commercial company; the ability of Denali and its collaborators to complete the development and, if approved, the commercialization of product candidates; difficulties in patient enrollment for ongoing and future clinical trials; reliance on third-party manufacturers and suppliers for clinical trial materials; potential delays or failures in meeting expected clinical trial timelines; discrepancies between preclinical, early-stage or preliminary clinical results and outcomes from later-stage trials; the risk that interim or topline clinical results may not be predictive of final study results or longer-term outcomes; the occurrence of significant adverse events or other undesirable side effects; the uncertainty surrounding regulatory approvals required for commercialization in the U.S., Europe or other international jurisdictions; Denali's ability to advance a pipeline of product candidates or develop commercially successful products; developments relating to Denali's

competitors and competing product candidates; Denali's ability to obtain, maintain or protect intellectual property rights related to its product candidates; the implementation and success 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 in the current environment; and other risks and uncertainties, including those described in Denali's most recent Annual and Quarterly Reports on Forms 10-K and 10-Q filed with the Securities and Exchange Commission (SEC) on February 26, 2026 and May 7, 2026, respectively, and Denali's future reports to be filed with the SEC. Except for AVLAYAH™ (tividenofusp alfa-eknm), Denali's product candidates are investigational, and their safety and efficacy profiles have not yet been established. 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.

References:

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2. Hernandez DG, Reed X, Singleton AB. Genetics in Parkinson disease: Mendelian versus non-Mendelian inheritance. *J Neurochem*. 2016;139 Suppl 1:59-74. Epub 2016/04/18.
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4. Robak, Laurie A et al. "Excessive burden of lysosomal storage disorder gene variants in Parkinson's disease." *Brain : a journal of neurology* vol. 140,12 (2017): 3191-3203. doi:10.1093/brain/awx285
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6. Moors, Tim et al. "Lysosomal Dysfunction and α-Synuclein Aggregation in Parkinson's Disease: Diagnostic Links." Movement disorders : official journal of the Movement Disorder Society vol. 31,6 (2016): 791-801. doi:10.1002/mds.26562

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