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):

April 3, 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 1.02 Termination of a Material Definitive Agreement.

On April 3, 2026, Denali Therapeutics Inc. (“Denali”) received written notice from Takeda Pharmaceutical Company Limited (“Takeda”) of its decision to terminate the Collaboration Agreement (the “Agreement”), dated January 3, 2018, between the two companies to co-develop and co-commercialize DNL593 (PTV:PGRN). The decision was driven by strategic considerations and is not related to efficacy or safety data. The termination will become effective 60 days following the notice date, at which time all rights in the DNL593 program will revert to Denali. Following termination, Denali will have no further financial obligations to Takeda.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

The information furnished in this 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.

Exhibit No.	Description
99.1	Press Release dated April 3, 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: April 3, 2026

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

Denali Therapeutics Regains Full Rights to Investigational Therapy DNL593 (PTV:PGRN) for GRN-related Frontotemporal Dementia (FTD-GRN)

April 3, 2026

- *Denali plans to continue clinical development of DNL593, which is designed to deliver progranulin to the brain using TransportVehicle™ technology*

- *Results from ongoing Phase 1/2 study in patients with FTD-GRN expected by the end of 2026*

SOUTH SAN FRANCISCO, Calif., – April 03, 2026 (GLOBE NEWSWIRE) – Denali Therapeutics Inc. (Nasdaq: DNLI) today announced that it has received notification from Takeda of its decision to terminate the collaboration agreement between the two companies to co-develop and co-commercialize DNL593 (PTV:PGRN). The decision was driven by strategic considerations and is not related to efficacy or safety data. DNL593 is an investigational progranulin replacement therapy utilizing Denali's Protein TransportVehicle™ (PTV) to deliver progranulin across the blood-brain barrier to the brain for the treatment of frontotemporal dementia-granulin (FTD-GRN). Denali has led development activities and will regain full control of DNL593 and its intellectual property portfolio.

"While we have greatly valued our partnership, we are pleased to regain full ownership of DNL593. We remain confident in the scientific rationale and the data generated to date, and we look forward to advancing DNL593 independently. We plan to report results from the ongoing Phase 1/2 trial by the end of 2026," said Ryan Watts, Ph.D., Chief Executive Officer of Denali Therapeutics. "Our TransportVehicle platform is the first FDA-approved blood-brain barrier-crossing technology, enabling a robust portfolio with broad potential across neurodegenerative diseases like frontotemporal dementia, where there are no currently approved treatment options to slow the progression of this devasting disease."

As previously disclosed, data from the ongoing Phase 1/2 study of DNL593, including biomarker results, are expected by the end of 2026. Enrollment in this study is completed with a total of 40 participants with FTD-GRN. Interim results from Part A of the Phase 1/2 study in healthy volunteers demonstrated dose-dependent increases in cerebrospinal fluid progranulin levels, consistent with robust brain delivery of DNL593. DNL593 was generally well tolerated, and there have been no significant safety signals to date.

About Frontotemporal Dementia (FTD)

FTD is the most common form of dementia in people under 60 years of age. While the progression of symptoms varies by individual, FTD brings an inevitable decline in function together with changes in personality and social behaviors, and sometimes language and/or motor dysfunction. Mutations in the granulin (GRN) gene, which encodes the progranulin (PGRN) protein, generally result in reduced levels of PGRN and are amongst the most common genetic causes of FTD. There are currently no approved medications to stop or slow the progression of FTD or FTD-GRN.

About the Denali TransportVehicle™ Platform

The blood-brain barrier (BBB) is essential in maintaining the brain's microenvironment and protecting it from harmful substances and pathogens circulating in the bloodstream. Historically, the BBB has posed significant challenges to drug development for central nervous system diseases by preventing most drugs from reaching the brain in therapeutically relevant concentrations. Denali's TransportVehicle™ (TV) platform is a proprietary technology designed to effectively deliver large therapeutic molecules such as antibodies, enzymes and oligonucleotides throughout the whole body, including the brain, by crossing the BBB after intravenous administration. The TV platform is based on engineered Fc domains that bind to specific natural transport receptors, such as transferrin receptor and CD98 heavy chain amino acid transporter, which are expressed at the BBB and deliver the TV and its therapeutic cargo to the brain through receptor-mediated transcytosis. In animal models, antibodies and enzymes engineered with the TV platform demonstrate more than 10- to 30-fold greater brain exposure than similar antibodies and enzymes without this technology. Oligonucleotides engineered with the TV platform demonstrate more than a 1,000-fold greater brain exposure in primates than systemically delivered oligonucleotides without this technology. Improved exposure and broad distribution in the brain may increase therapeutic efficacy by enabling widespread achievement of therapeutically relevant concentrations of product candidates. The TV platform has been clinically validated and five TV-enabled programs are currently in clinical development.

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.

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, plans, timelines and expectations related to Denali's TransportVehicle™ platform, including its potential application across current and future product candidates and its ability to deliver therapeutics to the brain; plans, timelines and expectations related to DNL593, including the timing and availability of data readouts from the ongoing Phase 1/2 study, the significance of interim data from the Phase 1/2 study including with respect to tolerability and safety, and the potential therapeutic benefit of DNL593; and statements by Denali's Chief Executive Officer. 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 and accelerated approval program; 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; whether the current ongoing trials have been powered sufficiently to demonstrate approvability to regulatory agencies; reliance on third-party manufacturers and suppliers for clinical trial materials; dependence on the successful development of Denali's blood-brain barrier platform technology and related programs; potential delays or failures in meeting expected clinical trial timelines; the risk that promising preclinical profiles may not be replicated in clinical settings; discrepancies between preclinical, early-stage or preliminary clinical results and outcomes from later-stage trials; 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 its industry, including competing product candidates and therapies; 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 Form 10-K filed with the Securities and Exchange Commission (SEC) on February 26, 2026, 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.

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