



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

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- 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 devastating 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™ (tividenufusp 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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