# Denali Therapeutics Presents Enzyme TransportVehicle™ Progress Across Three Clinical Programs for Treatment of Lysosomal Storage Disorders at 2026 WORLDSymposium™

February 5, 2026

- Analysis from continued follow-up of Phase 1/2 clinical trial data in Hunter syndrome (MPS II) reinforces potential for tividenofusp alfa (DNL310) to address full disease spectrum
- Launch readiness established in anticipation of April 5, 2026, Prescription Drug User Fee Act (PDUFA) date for tividenofusp alfa
- Preliminary Phase 1/2 study data show treatment with DNL126 (ETV:SGSH) substantially reduced disease biomarkers in cerebrospinal fluid (CSF) and peripheral tissues, including an 80% mean reduction in CSF heparan sulfate, in Sanfilippo syndrome type A (MPS IIIA); safety profile generally consistent with established enzyme replacement therapies
- Design of ongoing DNL952 (ETV:GAA) Phase 1 clinical study presented in addition to preclinical data that show therapeutic potential to treat both muscle and nervous system manifestations of Pompe disease

SOUTH SAN FRANCISCO, Calif., Feb. 05, 2026 (GLOBE NEWSWIRE) -- Denali Therapeutics Inc. (Nasdaq: DNLI) today announced data from programs in Hunter syndrome (mucopolysaccharidosis type II, MPS II), Sanfilippo syndrome type A (MPS IIIA) and Pompe disease that highlight the potential of its Enzyme TransportVehicle™ (ETV) to enable the delivery of enzyme replacement therapies (ERT) to the whole body, including the brain. Data were presented this week at the 22nd Annual WORLD*Symposium* ™ inSan Diego, California.

“The data presented at this year’s WORLD *Symposium* reflect the strong momentum of our Enzyme TransportVehicle franchise as we continue to prepare for the potential commercial launch of tividenofusp alfa for Hunter syndrome and make meaningful progress across lysosomal storage disorders,” said Peter Chin, M.D., Acting Chief Medical Officer and Head of Development of Denali Therapeutics. “From advancing our program in Sanfilippo to expanding into muscle disease with Pompe, we are continuing to broaden the reach of our ETV platform with the goal of delivering new medicines in areas of high unmet need. This progress is made possible through constructive collaboration with regulatory authorities and close partnership with the community, listening to and learning from them to better understand treatment journeys of individuals and their families living with these debilitating diseases.”

Key highlights from the presentations are summarized below.

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

An analysis from continued follow-up of the Phase 1/2 study of the investigational therapy tividenofusp alfa (DNL310) for MPS II showed that rapid, substantial reduction from baseline and normalization of cerebrospinal fluid heparan sulfate (CFS HS) and urine HS, both key biomarkers of disease, resulting from treatment was maintained through Week 201 (as of the clinical data cut-off of March 28, 2025). Stabilization or improvement in clinical endpoints including adaptive behavior, cognition and hearing, and normalization of liver volume was also observed through Week 201. Safety and tolerability data were consistent with previously reported results from the Phase 1/2 study. Data from this Phase 1/2 study support the Biologics License Application (BLA) for tividenofusp alfa that is currently under Priority Review by the U.S. Food and Drug Administration (FDA) with a target decision date of April 5, 2026.

Denali also highlighted data from a case study of two male siblings with non-neuronopathic MPS II enrolled in the Phase 1/2 trial, which further supports the potential of tividenofusp alfa to address the full disease spectrum.

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

The ongoing Phase 1/2 study of the investigational therapy DNL126 (ETV:SGSH) is fully enrolled with a total of 20 participants and is an open-label, 25-week study followed by an open-label extension period through 193 weeks. Preliminary data as of the clinical data cut-off (June 4, 2025) were presented, including biomarker results from the dose-finding cohorts (n=8) and safety data from the dose-finding and efficacy cohorts (n=14). Preliminary biomarker results from dose-finding cohorts showed treatment with DNL126 resulted in a mean reduction in CSF HS of 80% (95% CI: 43% to 93%) and 61% in CSF GM3 (95% CI: 36% to 76%), a biomarker of lysosomal function, from baseline at Week 49. Normalization of levels of CSF HS and GM3 from baseline were observed in three of seven individuals and six of seven individuals, respectively, with CSF samples available at Week 49. A mean reduction in urine HS of 83% (95% CI: 77% to 87%) from baseline was observed at Week 49, and improvement in liver volume was observed as early as Week 25. Preliminary safety data from participants who had received at least 24 weeks of treatment in the dose-finding and efficacy cohorts demonstrates that the safety profile of DNL126 is generally consistent with established ERTs. The most common treatment-related adverse events in the study were infusion-related reactions.

“These promising data show for the first time that treatment with the brain-penetrant enzyme replacement therapy DNL126 substantially reduced biomarkers of substrate accumulation in cerebrospinal fluid and peripheral tissues,” said Elizabeth Jalazo,

M.D., University of North Carolina at Chapel Hill and an investigator in the Phase 1/2 study. “Currently, there are no approved disease-modifying therapies for individuals living with Sanfilippo syndrome type A, which presents with developmental delay and behavior problems that progress to severe cognitive and motor decline. Many affected individuals do not live beyond adolescence.”

In August 2025, Denali announced that it reached alignment with the FDA that CSF HS may be considered a reasonably likely surrogate endpoint to predict clinical benefit and may therefore be used to support an accelerated approval path for DNL126 for MPS IIIA. Denali expects a BLA submission and potential approval for DNL126 for MPS IIIA in 2027. Planning for a global Phase 3 confirmatory study is ongoing.

**DNL952 (ETV:GAA) for Pompe disease**

Denali presented the Phase 1 clinical study design for the investigational therapy DNL952 (ETV:GAA) in participants with late-onset Pompe disease. The study includes planned cohorts evaluating different dose regimens of DNL952 in patients previously treated with second-generation ERTs, as well as optional additional cohorts including treatment-naïve patients. The study is intended to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of DNL952. Preclinical data also presented at WORLD*Symposium* showed improved glycogen reduction compared to a second-generation ERT in both skeletal muscle and brain in a mouse model of Pompe disease.

**About Hunter syndrome (MPS II)**

Hunter syndrome, also known as MPS II, is a rare genetic lysosomal storage disease caused by mutations in the iduronate-2-sulfatase (IDS) gene. This results in a deficiency of the IDS enzyme, which is responsible for breaking down glycosaminoglycans (GAGs) such as heparan sulfate and dermatan sulfate. The accumulation of GAGs leads to progressive damage in multiple organs and tissues, including the brain. Symptoms of Hunter syndrome include developmental delays, cognitive decline, behavioral abnormalities and physical complications such as joint stiffness, hearing loss and organ dysfunction. Current standard-of-care enzyme replacement therapies do not cross the blood-brain barrier and therefore do not address the neurological symptoms of the disease. There is a significant unmet need for therapies that address both the central nervous system (CNS) and peripheral manifestations of Hunter syndrome.

**About Tividenofusp Alfa**

Tividenofusp alfa (DNL310) is composed of the iduronate 2-sulfatase (IDS) enzyme fused to Denali’s proprietary TransportVehicle™ (TV) platform, designed to deliver IDS into the brain and the body, with the goal of addressing behavioral, cognitive and physical symptoms of Hunter syndrome (MPS II). In addition to Rare Pediatric Disease Designation and Breakthrough Therapy Designation, the U.S. Food and Drug Administration has granted Fast Track and Orphan Drug designations to tividenofusp alfa for development in the treatment of MPS II. The European Medicines Agency has granted Priority Medicines designation to tividenofusp alfa.

Denali is conducting the Phase 2/3 COMPASS study in participants with MPS II in North America, South America and Europe to support global approval. Participants are randomized 2:1 to receive either tividenofusp alfa or idursulfase, respectively. More information about the COMPASS study can be found here.

Tividenofusp alfa is an investigational therapeutic and has not been approved for use by any Health Authority.

**About Sanfilippo syndrome type A (MPS IIIA)**

Sanfilippo syndrome type A, also known as MPS IIIA, is a rare, genetic lysosomal storage disorder characterized by severe neurocognitive deterioration during childhood, with many affected individuals not living past adolescence. MPS IIIA results from a deficiency of the sulfoglucosamine sulfohydrolase (SGSH) enzyme, which is responsible for degrading heparan sulfate in the lysosome. There are no approved disease-modifying therapies for MPS IIIA.

**About DNL126 (ETV:SGSH)**

DNL126 (ETV:SGSH) is an investigational, intravenously administered, Enzyme TransportVehicle™ (ETV)-enabled N-sulfoglucosamine sulfohydrolase (SGSH) replacement therapy designed to deliver SGSH into the brain and body, with the goal of addressing the behavioral, cognitive and physical manifestations of MPS IIIA. In 2024, the U.S. Food and Drug Administration (FDA) selected DNL126 for participation in the Support for clinical Trials Advancing Rare disease Therapeutics (START) Pilot Program, with the stated purpose to further accelerate the pace of development of novel drug and biological products that are intended to address an unmet medical need as a treatment for a rare disease.

Denali is conducting a multicenter, open-label, Phase 1/2 study to assess the safety, tolerability, pharmacokinetics, pharmacodynamics and exploratory clinical efficacy of DNL126 in participants with MPS IIIA. The core study period is approximately 6 months and is followed by an open-label extension for approximately 18 months. The study has five cohorts (two dose-finding cohorts and three efficacy cohorts). The primary endpoint of the Phase 1/2 study is percent change in baseline in cerebrospinal fluid heparan sulfate (CSF HS) at Week 49. More information about the study can be found here. Planning for a global Phase 3 confirmatory study is ongoing.

**About Pompe disease**

Pompe disease is a rare, progressively debilitating genetic disorder in which the body cannot break down glycogen, a complex sugar that is stored in cells for energy. This is caused by a deficiency of the lysosomal enzyme, acid alpha-glucosidase (GAA), which is responsible for the breakdown of glycogen. As a result, glycogen builds up in cells, especially in muscle tissue, including the heart, diaphragm and skeletal muscles, leading to muscle weakness, breathing difficulties and, in some cases, life-threatening complications.

**About DNL952 (ETV:GAA)**

DNL952 (ETV:GAA) is an investigational therapy being developed by Denali. This treatment is proposed to work by using the Enzyme TransportVehicle™ (ETV) to enhance delivery of the missing enzyme, GAA, into muscle tissues and across the blood-brain barrier into the brain. Denali is conducting a Phase 1 clinical study of DNL952 in participants with late-onset Pompe disease. More information about the study can be found here.

**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 the lives of people living with neurodegenerative, lysosomal storage 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, statements regarding Denali Therapeutics Inc.'s ("Denali" or the "Company") business strategy and business plans, including expected key milestones for Denali's therapeutic portfolio in 2026 and beyond and Denali's ability to execute on its commercial strategies; plans, timelines and expectations related to Denali's ETV franchise and its therapeutic and commercial potential; plans, timelines and expectations relating to tividenofusp alfa (DNL310), including the timing, likelihood and scope of regulatory approvals and commercial launch, the therapeutic potential of tividenofusp alfa, and the likelihood of the Phase 2/3 COMPASS data to support confirmatory evidence for global regulatory submissions and approval; plans, timelines and expectations related to DNL126, including the timing and availability of data from the Phase 1/2 study, the therapeutic potential of DNL126, the likelihood of regulatory approval, and the plans to initiate a Phase 3 study; plans and expectations regarding DNL952, the design of the Phase 1 study and the program's therapeutic potential; expectations regarding Denali's leadership in developing transferrin receptor (TfR)-enabled and BBB-crossing therapeutics; and statements by Drs. Chin and Jalazo. 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: uncertainties related to the FDA's policies and accelerated approval program, including risks that the PDUFA action date may be extended and the FDA may not approve tividenofusp alfa; the possibility of events or changes that could lead to the termination of Denali's collaboration agreements; Denali's dependence on successful development and commercialization 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 and commercial products; 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 27, 2025, and November 6, 2025, 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.

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