Denali Therapeutics Announces U.S. FDA Breakthrough Therapy Designation Granted to Tividenofusp Alfa for the Treatment of Hunter Syndrome (MPS II)

January 8, 2025

Denali expects to submit a Biologics License Application for tividenofusp alfa in early 2025 for regulatory review under the accelerated approval pathway

SOUTH SAN FRANCISCO, Calif., Jan. 08, 2025 (GLOBE NEWSWIRE) -- Denali Therapeutics Inc. (NASDAQ: DNLI), today announced that the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation for tividenofusp alfa (DNL310) for the treatment of individuals with Hunter syndrome (MPS II). This designation is in addition to Fast Track Designation, Orphan Drug Designation, and Rare Pediatric Disease Designation, all previously granted by the FDA for tividenofusp alfa in Hunter syndrome. Denali expects to submit a Biologics License Application (BLA) for tividenofusp alfa in early 2025 for regulatory review under the accelerated approval pathway.

“FDA Breakthrough Therapy Designation is another significant achievement in the development of tividenofusp alfa, our first Enzyme TransportVehicle™ program, uniquely designed to optimize enzyme delivery to both brain and body, addressing the full spectrum of Hunter syndrome, a progressive and devastating disease,” said Carole Ho, M.D., Chief Medical Officer of Denali Therapeutics. “Data from the open-label Phase 1/2 study have shown promising results, with positive effects on evidence-based surrogate endpoints and early signs of improved clinical outcomes in participants with Hunter syndrome. We are grateful to the FDA for recognizing the potential of tividenofusp alfa as a meaningful treatment option for individuals with Hunter syndrome. We look forward to continued collaboration with the FDA to bring an effective therapy to the Hunter syndrome community as soon as possible.”

Breakthrough Therapy Designation is intended to expedite the development and review of therapeutic candidates that are under investigation for the treatment of serious or life-threatening conditions. Breakthrough Therapy Designation requires preliminary clinical evidence suggesting a candidate may provide substantial improvement over available therapy on at least one clinically significant endpoint. This designation provides Denali with more intensive FDA guidance, including involvement of senior reviewers, and eligibility for rolling review and priority review of the marketing application.

About Hunter Syndrome (MPS II)

Hunter syndrome (MPS II) is a rare genetic disease that affects over 2,000 individuals in commercially accessible geographies, primarily males, and leads to physical, cognitive, and behavioral symptoms. Hunter syndrome is caused by mutations in the iduronate-2-sulfatase (IDS) gene, which leads to a deficiency of the IDS enzyme. Symptoms often begin emerging around age two and include physical complications, including organ dysfunction, joint stiffness, hearing loss and impaired growth, and neurocognitive symptoms with impaired development. The disease is characterized by a buildup of glycosaminoglycans (GAGs) in lysosomes — the part of the cell that breaks down materials including GAGs. The current standard of care, enzyme replacement therapy, partially treats physical symptoms but does not cross the blood-brain barrier, and as a result, cognitive and behavioral symptoms experienced by the majority of individuals with Hunter syndrome are not addressed. Therapies that address the range of behavioral, cognitive, and physical manifestations of the disease are recognized as an unmet need for the Hunter syndrome community.[1]

About Tividenofusp Alfa

Tividenofusp alfa (or DNL310) is composed of iduronate 2-sulfatase (IDS) fused to Denali’s proprietary Enzyme TransportVehicle™ (ETV), which is engineered for active transport into the brain and broad delivery throughout the body with the goal of addressing behavioral, cognitive, and physical symptoms of Hunter syndrome (MPS II). In 2021, the U.S. Food and Drug Administration granted Fast Track designation to tividenofusp alfa for the treatment of patients with Hunter syndrome (MPS II). In 2022, the European Medicines Agency granted tividenofusp alfa Priority Medicines designation. Denali has announced the outcome of a meeting with the FDA providing a path to filing a biologics license application (BLA) for accelerated approval and subsequent conversion to full approval for the treatment of Hunter syndrome (MPS II). Tividenofusp alfa is an investigational drug and its safety and efficacy profile has not yet been established. Tividenofusp alfa has not been approved by any Health Authority for any use.

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 Denali's plans, timelines, and expectations related to tividenofusp alfa (DNL310), including interactions with the FDA, the timing of planned regulatory filings, and the timing, pathway, and likelihood of regulatory approval; Denali's overall development plans; and statements made by Denali's Chief Medical 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. 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.

References

1. Muenzer, J., *et al.* Community consensus for Heparan sulfate as a biomarker to support accelerated approval in Neuronopathic Mucopolysaccharidoses. *Mol Genet Metab*. 2024 Aug;142(4):108535

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

DENALI
THERAPEUTICS

Source: Denali Therapeutics Inc.