Denali Therapeutics Announces Completion of Enrollment for Regimen G Evaluating eIF2B Agonist DNL343 in the Phase 2/3 HEALEY ALS Platform Trial

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SOUTH SAN FRANCISCO, Calif., May 01, 2024 (GLOBE NEWSWIRE) -- Denali Therapeutics Inc. (Nasdaq: DNLI), a biopharmaceutical company developing a broad portfolio of product candidates engineered to cross the blood-brain barrier (BBB) for the treatment of neurodegenerative and lysosomal storage diseases, today announced that the Sean M. Healey & AMG Center in collaboration with the Northeast ALS Consortium (NEALS) completed enrollment for Regimen G of the Phase 2/3 HEALEY ALS Platform Trial, which evaluates Denali's eIF2B agonist DNL343.

"We are excited to move to the next phase of Regimen G and evaluate the effects of DNL343," said Merit Cudkowicz, MD, MSc, principal investigator and sponsor of the HEALEY ALS Platform Trial, director of the Sean M. Healey & AMG Center for ALS, chair of the Department of Neurology at MGH, and the Julieanne Dorn Professor of Neurology at Harvard Medical School. "We are grateful for the continued support of the ALS community and look forward to sharing the results."

Regimen G is co-led by Suma Babu, MBBS, MPH, and Sabrina Paganoni, MD, PhD, physician investigators at the Healey & AMG Center for ALS at MGH.

"The conclusion of enrollment for Regimen G marks a critical step forward for the HEALEY ALS platform Trial," said Drs. Paganoni and Babu. "We extend our thanks to Denali, academic collaborators, and benefactors of the trial as we move to the next stage."

"We are thrilled with the achievement of this important clinical milestone in the DNL343 development program and thank the HEALEY ALS Platform Trial investigators and their sites for making this possible and the participants and families for their participation," said Carole Ho, MD, Chief Medical Officer of Denali. "We look forward to continued collaboration with the ALS community to advance the science and ultimately to deliver effective treatment options for people living with ALS."

About DNL343

DNL343 is a novel investigational ALS therapy that targets eIF2B, a central regulator of the integrated stress response (ISR). The ISR appears to be overactive in ALS, leading to the formation of stress granules containing TDP-43. Buildup of TDP-43 is harmful and leads to neuronal degeneration. In the lab, inhibition of the ISR by DNL343 dissolves TDP-43 containing stress granules and decreases ISR biomarkers. The safety, pharmacokinetics, and pharmacodynamics of DNL343 have been characterized in both healthy participants and people with ALS, in a Phase 1 (N=47) and a Phase 1b (N=29) study, respectively, with dosing for up to 28 days. Results from both studies demonstrated that once-daily oral dosing with DNL343 was generally well tolerated and exhibited extensive cerebrospinal fluid (CSF) penetration. In addition, robust inhibition of biomarkers associated with the ISR pathway was observed in blood samples from study participants. DNL343 is an investigational therapeutic and has not been approved by any regulatory authority for any commercial use.

About the HEALEY ALS Platform Trial

The HEALEY ALS Platform Trial is a large-scale collaborative effort made possible by contributions from patients and families, clinical trial sites, industry partners and research collaborators to evaluate multiple investigational therapies simultaneously with the goal of accelerating the development of potential new treatments for ALS. The platform trial is led by the Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital (MGH) in collaboration with the Northeast ALS Consortium (NEALS). Therapeutic candidates that enter the platform trial are chosen by a group of expert ALS scientists and members of the Healey & AMG Center.

About Denali Therapeutics

Denali Therapeutics is a biopharmaceutical company developing a broad portfolio of product candidates engineered to cross the blood-brain barrier (BBB) for the treatment of neurodegenerative and lysosomal storage diseases. Denali pursues new treatments by rigorously assessing genetically validated targets, engineering delivery across the BBB 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 DNL343, including the ongoing Regimen G of the Phase 2/3 study and the timing and availability of data; the therapeutic potential of DNL343; and statements made by the Healey ALS Platform Trial's principal investigator and 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, risks related 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 with the Securities and Exchange Commission (SEC) on February 28, 2024, 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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