



## Denali Therapeutics Announces Upcoming Presentations on EIF2B Activator DNL343 and RIPK1 Inhibitor SAR443820/DNL788 at the 2021 Annual Northeast Amyotrophic Lateral Sclerosis (NEALS) Meeting

September 29, 2021

- Denali to present results from Phase 1 healthy volunteer study of EIF2B activator DNL343
- Sanofi to present Phase 2 study plans in ALS for RIPK1 inhibitor SAR443820
- Denali to host analyst and investor webinar on October 6, at 4:30 p.m. Eastern Time

SOUTH SAN FRANCISCO, Calif., Sept. 29, 2021 (GLOBE NEWSWIRE) -- [Denali Therapeutics Inc.](#) (NASDAQ: DNL), a biopharmaceutical company developing a broad portfolio of product candidates engineered to cross the blood-brain barrier (BBB) for neurodegenerative diseases, today announced upcoming presentations at the 2021 Annual Northeast Amyotrophic Lateral Sclerosis (NEALS) Meeting being held virtually, October 6-7.

Denali will present preclinical and clinical data including results from a Phase 1 healthy volunteer study of its CNS-penetrant EIF2B activator DNL343, which is currently under investigation in a Phase 1b study in participants with ALS. Denali's partner Sanofi will present plans for a Phase 2 study in participants with ALS, with the CNS-penetrant RIPK1 inhibitor SAR443820, which completed investigation in a Phase 1 study in healthy volunteers.

### Presentations at NEALS

**Title:** The EIF2B Agonist DNL343 Modulates the Integrated Stress Response: Results from the EIF2B R191H Mouse Model and a Phase 1 Study in Healthy Volunteers

**Date:** Wednesday, October 6, 2021

**Time:** 4:00-5:00 p.m. Eastern Time

**Title:** A Phase 2, Multi-Center, Randomized, Double-Blind, Placebo-Controlled Study, Followed by an Open-Label Long-Term Extension, to Evaluate the Efficacy and Safety of SAR443820 in Adult Participants with Amyotrophic Lateral Sclerosis

**Date:** Thursday, October 7, 2021

**Time:** 4:00-5:00 p.m. Eastern Time

### About DNL343

Modulation of EIF2B activity with DNL343 is a novel and targeted investigational approach with first-in-class potential for the treatment of ALS. EIF2B is an intracellular protein complex that regulates protein synthesis and is required for neuronal health and function. When neurons experience stress, as occurs in ALS, EIF2B activity is suppressed. This leads to impaired protein synthesis and results in the formation of "stress granules," which are thought to be a precursor of TDP-43 aggregation, a hallmark pathology in ALS. DNL343 is designed to activate EIF2B and thereby restore protein synthesis, disperse TDP-43 aggregates, and improve neuronal survival.

Denali is conducting a multicenter, randomized, placebo-controlled, double-blind, 28-day study followed by an 18-month open-label extension, designed to evaluate the safety, pharmacokinetics, and pharmacodynamics of DNL343 in participants with ALS. Further information on the Phase 1b study (study number NCT05006352) can be accessed on the [ClinicalTrials.gov](#) website or by clicking [here](#).

### About SAR443820/DNL788

SAR443820/DNL788 is a novel, CNS-penetrant, small molecule inhibitor of RIPK1, a critical signaling mediator of necroptotic cell death, cytokine release, and inflammatory pathways. Denali and Sanofi entered into a broad collaboration in October 2018 for the global development and commercialization of RIPK1 inhibitors. This includes CNS-penetrant molecules such as SAR443820/DNL788, which was evaluated in a Phase 1 study in healthy volunteers, with potential development for neurological indications such as ALS, multiple sclerosis (MS) and Alzheimer's disease (AD).

### Denali Webinar for Analysts and Investors on October 6, 2021

Denali plans to host a webinar for analysts and investors to highlight development programs in ALS and frontotemporal dementia (FTD) on October 6, starting at approximately 4:30 p.m. Eastern Time. During the webinar, Denali will review the NEALS presentations related to its investigational small molecule therapeutics DNL343 and SAR443820. Denali will also review preclinical data on PTV-PGRN, its Transport Vehicle (TV)-enabled biotherapeutic in development for FTD-GRN, which was recently [published](#) in *Cell*. The webinar will be available on Denali's corporate website on the Events page under the Investor section at <https://www.denalitherapeutics.com/investors/events>. An archived replay of the webinar will be available for at least 30 days following the event. Preregistration for the webinar can be accessed [here](#).

## 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 neurodegenerative 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](http://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 progress, business plans, business strategy, product candidates, expected milestones, planned preclinical studies and clinical trials and presentations of data from such trials, timelines and expectations related to DNL343, including the potential for the treatment of amyotrophic lateral sclerosis (ALS), and timelines and expectations related to DNL788 and its potential for the treatment of ALS and other neurological conditions. 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: any and all risks to Denali's business and operations caused directly or indirectly by the evolving COVID-19 pandemic; risk of the occurrence of any event, change or other circumstance that could give rise to the termination of Denali's collaboration agreements; Denali's early stages of clinical drug development; Denali's and its partners' ability to complete the development and, if approved, commercialization of its product candidates; Denali's reliance on third parties for the manufacture and supply of its product candidates for clinical trials; Denali's and its partners' ability to conduct or complete clinical trials on expected timelines; the uncertainty that product candidates will receive regulatory approval necessary to be commercialized; Denali's ability to continue to create a pipeline of product candidates or develop commercially successful products; Denali's ability to obtain, maintain, or protect intellectual property rights related to its product candidates; implementation of Denali's strategic plans for its business, product candidates and blood-brain barrier platform technology; and other risks, including those described in Denali's most recent Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on August 4, 2021, Denali's Annual Report on Form 10-K filed with the SEC on February 26, 2021, and Denali's future reports to be filed with the SEC. The forward-looking statements in this press release are based on information available to Denali as of the date hereof. Denali disclaims any obligation to update any forward-looking statements, except as required by law.

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