
**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

**Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934**

Date of Report (Date of earliest event reported):

January 14, 2020

Denali Therapeutics Inc.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation)

001-38311
(Commission
File Number)

46-3872213
(I.R.S. Employer
Identification No.)

**161 Oyster Point Blvd.
South San Francisco, California 94080**
(Address of principal executive offices, including zip code)

(650) 866-8548
(Registrant's telephone number, including area code)

Not Applicable
(Former name or former address, if changed since last reports)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Stock, par value \$0.01 per share	DNLI	NASDAQ Global Select Market

Item 8.01 Other Events.

On January 14, 2020, Denali Therapeutics Inc. (the "**Company**") issued a press release announcing positive clinical results from its LRRK2 program for Parkinson's disease in addition to IND and CTA submissions for two additional programs. A copy of the press release is attached hereto as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release dated January 14, 2020.

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

DENALI THERAPEUTICS INC.

Date: January 14, 2020

By: /s/ Steve E. Krognes
Steve E. Krognes
Chief Financial Officer



DENALI THERAPEUTICS ANNOUNCES BROAD PIPELINE PROGRESS INCLUDING POSITIVE RESULTS FROM ITS LRRK2 PROGRAM FOR PARKINSON'S DISEASE

- *LRRK2 inhibitor DNL201 Phase 1b demonstrated high levels of target and pathway engagement and improvement of lysosomal biomarkers in patients with Parkinson's disease*
- *LRRK2 inhibitor DNL151 Phase 1 demonstrated high levels of target and pathway engagement and modulation of lysosomal biomarkers in healthy volunteers and continues in an expanded Phase 1b study in patients with Parkinson's disease*
- *IND submitted for DNL310 (ETV:IDS) for Hunter syndrome, Denali's first clinical submission for a large molecule therapeutic enabled by its Transport Vehicle platform technology*
- *CTA approved for DNL343, a small molecule activator of EIF2B for ALS and other neurodegenerative diseases*
- *RIPK1 inhibitor DNL747 Phase 1b trials in Alzheimer's and ALS fully enrolled and open label extension in ALS ongoing with data readouts on track for mid-2020*

SOUTH SAN FRANCISCO — January 14, 2020 — 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 the results of its Phase 1b clinical trial of LRRK2 inhibitor DNL201 in patients with Parkinson's disease and its Phase 1 clinical trial of LRRK2 inhibitor DNL151 in healthy volunteers.

Denali also announced that it submitted an IND for DNL310 for Hunter syndrome, which is the company's first submission with a biotherapeutic product candidate engineered to cross the BBB enabled by the Transport Vehicle technology. Furthermore, a CTA for a Phase 1 first-in-human healthy volunteer study of EIF2B activator DNL343, intended for the treatment of ALS and other neurodegenerative diseases, has been approved. This is Denali's third small molecule program engineered to cross the BBB to advance to clinical testing.

"We are pleased with the continued progress across our pipeline, including a significant step forward for our LRRK2 program with encouraging clinical data in patients and healthy subjects for two molecules," said Ryan Watts, Ph.D., CEO. "We are also enthusiastic about advancing two new molecules toward the clinic, DNL343 for ALS and other neurodegenerative diseases and DNL310 for Hunter syndrome, which is also expected to generate proof-of-concept in humans for our Transport Vehicle blood-brain barrier delivery platform."

DNL201 and DNL151 (LRRK2 inhibitors) for Parkinson's disease

Phase 1b results with DNL201 in patients with Parkinson's disease met all biomarker goals by demonstrating greater than 50 percent inhibition of pS935 LRRK2 and pRAB10 in blood for both doses tested and improvement of the lysosomal biomarker BMP (22:6-bis-monoacylglycerophosphate) by 20 percent and 60 percent in urine at the low and high dose, respectively.

DNL201 was generally well tolerated at the low dose and the majority of subjects experienced either no or mild adverse events ("AEs"). There was one SAE considered unrelated to drug. At the high dose, the majority of subjects experienced either mild or moderate AEs and there was one severe AE (headache) leading to dose reduction and one study withdrawal (headache and nausea). All treatment-related AEs were manageable and reversible.

Phase 1 results with DNL151 in more than 150 healthy volunteers also met all safety and biomarker goals. DNL151 was generally safe and well tolerated at all doses tested, and the majority of subjects experienced either no or mild AEs. Target and pathway engagement of greater than 50 percent and a dose-dependent reduction of BMP in urine of up to 50 percent were observed at clinically relevant doses. Given these positive data, the DNL151 Phase 1 and Phase 1b clinical trials have been expanded to study higher doses.

Denali intends to select either DNL201 or DNL151 in mid-2020 to advance into Phase 2/3 clinical trials in patients with Parkinson's disease.

“We are excited about the results from both the DNL201 and DNL151 clinical trials which show that LRRK2 inhibition is a promising and potentially disease-modifying approach to treat Parkinson’s disease,” said Carole Ho, M.D., CMO. “We look forward to further exploring the full therapeutic potential of LRRK2 inhibitors in future clinical studies.”

DNL310 (ETV:IDS) for Hunter syndrome

Denali submitted an IND in late December 2019 for DNL310, or ETV:IDS, a recombinant form of the iduronate 2-sulfatase (“IDS”) enzyme engineered to cross the BBB using Denali’s proprietary Enzyme Transport Vehicle technology. DNL310 is intravenously administered and intended to improve overall clinical manifestations of Hunter syndrome, including both peripheral and neurological symptoms, which are not adequately addressed by currently approved therapies. If Denali receives clearance of the IND, it intends to initiate a Phase 1/2 clinical trial of DNL310 in patients with Hunter syndrome.

DNL343 (EIF2B Activator) for ALS and other neurodegenerative diseases

Denali submitted a CTA in early December 2019 for DNL343, a small molecule brain-penetrant activator of EIF2B. Mutations in EIF2B are genetically linked to neurodegenerative diseases. Activation of EIF2B with DNL343 is expected to restore protein synthesis and reduce formation of stress granules, which are commonly associated with disease pathology in ALS and Alzheimer’s disease. The CTA cleared in January 2020, and Denali plans to initiate a Phase 1 clinical trial for DNL343 in healthy volunteers.

Further data from the clinical trials with DNL201 and DNL151, and data from preclinical studies with DNL310 and DNL343 will be shared at the J.P. Morgan 38th Annual Healthcare Conference on January 14, 2020 at 8.30am PT in San Francisco. The presentation will also be accessible by webcast through Denali’s website at

<https://www.denalitherapeutics.com/investors/events>

About the DNL151 Phase 1b clinical trial

This study ([NCT04056689](https://clinicaltrials.gov/ct2/show/study/NCT04056689)) is a 28-day, multicenter, randomized, placebo controlled, double-blind Phase 1b clinical trial in patients with mild-to-moderate Parkinson’s disease. Its purpose is to evaluate safety, tolerability, pharmacokinetics, pharmacodynamics, including target and pathway engagement biomarkers as well as certain exploratory clinical endpoints, after multiple oral doses of DNL151. To date, 25 patients have been enrolled in the study, and the protocol has been amended to expand the study with up to 10 additional patients. Final data readout from this trial is expected to be presented in mid-2020. Further details are available at [ClinicalTrials.gov](https://clinicaltrials.gov)

About Denali

Denali is a biopharmaceutical company developing a broad portfolio of product candidates engineered to cross the 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.

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, Denali's plans and expectations to select either DNL151 or DNL201 in mid-2020 to advance into Phase 2/3 clinical trials in Parkinson's disease patients; Denali's expectations regarding what the results of the DNL151 Phase 1b clinical trial will inform; Denali's expectations regarding patient enrollment in, and the timing, objectives and results of, the DNL151 Phase 1b clinical trial; Denali's plans to conduct further clinical testing in connection with its LRRK2 program; Denali's expectations regarding what the results of the DNL747 Phase 1b clinical trials will inform; Denali's expectations regarding anticipated regulatory and development timelines and plans to initiate clinical trials for DNL310 and DNL343, including timing and objectives; Denali's expectations that DNL310 will generate proof-of-concept in humans of its Transport Vehicle BBB delivery platform; Denali's expectations with respect to anticipated benefits from the activation of EIF2B with DNL343; and statements made by Denali's CMO and CEO.

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 early stages of clinical drug development; Denali's ability to complete the development and, if approved, commercialization of its product candidates; Denali's dependence on successful development of its BBB technology; Denali's ability to conduct or complete clinical trials on expected timelines; Denali's ability to obtain the requisite regulatory approvals for its product candidates; the uncertainty that any of Denali's 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, and other risks, including those described in Denali's Annual Report on Form 10-K filed with the SEC on March 12, 2019, Denali's Quarterly Report on Form 10-Q filed with the SEC on November 6, 2019 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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