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):

May 3, 2021

Denali Therapeutics Inc.

(Exact name of registrant as specified in its charter)

Delaware	001-38311	46-3872213
(State or other jurisdiction of incorporation)	(Commission File Number)	(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 2.02 Results of Operations and Financial Condition.

On May 3, 2021, Denali Therapeutics Inc. (the "Company") issued a press release announcing its financial results for the first quarter ended March 31, 2021. The full text of the press release is attached hereto as Exhibit 99.1 and is incorporated herein by reference.

All of the information furnished in this Item 2.02 and Item 9.01 (including Exhibit 99.1) shall not be deemed to be “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and shall not be incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, except as shall be expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release dated May 3, 2021.
104	Cover Page Interactive Data File (formatted as Inline XBRL)

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: May 3, 2021

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

Denali Therapeutics Reports First Quarter 2021 Financial Results and Business Highlights

SOUTH SAN FRANCISCO – May 3, 2021 – Denali Therapeutics Inc. (NASDAQ: DNLI), a biopharmaceutical company developing a broad portfolio of product candidates engineered to cross the blood-brain barrier (BBB) for neurodegenerative diseases, today reported financial results for the first quarter ended March 31, 2021, and provided business highlights.

“Our programs have reached a number of exciting milestones so far this year across our broad portfolio of targeted therapeutics for neurodegenerative diseases,” said Ryan Watts, Ph.D., Denali’s Chief Executive Officer. “We remain focused on advancing our lead clinical programs including DNL310 for Hunter syndrome, DNL151 (BIIB122) in collaboration with Biogen for Parkinson's disease, and DNL343 for amyotrophic lateral sclerosis (ALS). In addition, based on human biomarker proof of concept achieved with DNL310, we see significant potential in using our Transport Vehicle (TV) technology to create new, effective biologic therapeutics previously not possible due to limitations posed by the blood-brain barrier, and we continue to rigorously advance additional TV-enabled programs towards the clinic."

Recent Business Highlights

Achieved clinical and regulatory milestones with DNL310: In February 2021, Denali reported three-month data from Cohort A (n=5) in a Phase 1/2 study of DNL310, Denali’s lead TV-enabled brain-penetrant enzyme replacement therapy, in patients with Hunter syndrome (MPS II). The data showed that DNL310 treatment resulted in normalization of glycosaminoglycan (GAG) levels in cerebrospinal fluid and a safety and tolerability profile consistent with standard of care enzyme replacement therapy. In March 2021, Denali announced that the U.S. Food and Drug Administration (FDA) granted Fast Track designation to DNL310 for the treatment of patients with Hunter syndrome. Denali plans to report six-month data from Cohort A in mid-2021 at a medical conference.

Met safety and biomarker goals in DNL151 (BIIB122) Phase 1/1b studies: In May 2021, Denali presented results from two studies of its small molecule LRRK2 inhibitor, DNL151 (BIIB122), a Phase 1 study in healthy volunteers and a Phase 1b study in patients with Parkinson's disease, at the International Association of Parkinsonism and Related Disorders Virtual Congress held on May 1-4. DNL151 (BIIB122) was generally well tolerated, and target engagement and pathway engagement biomarker goals were met. Denali and Biogen plan to initiate late-stage clinical development of DNL151 (BIIB122) in patients with Parkinson's disease by year-end 2021.

Met safety and pathway engagement biomarker goals in DNL343 Phase 1 healthy volunteer study: Based on interim data from the ongoing Phase 1 single- and multiple-ascending-dose study of Denali’s small molecule EIF2B activator, DNL343, in healthy volunteers, safety and pathway engagement biomarker goals of the study were met. A maximum tolerated dose was not reached, and an additional multiple dose cohort has been added to the study to further explore the therapeutic window. Based on these data, Denali plans to initiate a Phase 1b study in patients with ALS in the second half of 2021.

DNL758 (SAR443122) advancing into Phase 2 study for cutaneous lupus erythematosus (CLE): In February 2021, Denali announced its partner Sanofi's decision, upon completion of a Phase 1b study in hospitalized adult patients with severe COVID-19 lung disease, to cease further development of DNL758 (SAR443122), a peripherally-restricted small molecule inhibitor of RIPK1, in COVID-19 based on the rapidly evolving landscape of treatment and prevention options for COVID-19. Although the Phase 1b study did not meet its primary endpoint, DNL758 (SAR443122) was generally well tolerated and did generate positive signals of relevant biological effect. Sanofi plans to commence dosing in a Phase 2 study of DNL758 (SAR443122) in CLE patients in the first half of 2021.

Summary Table of Upcoming 2021 Expected Key Milestones

Timing	Investigational Drug Candidate	Therapeutic Area	Expected Milestone
1H 2021	RIPK1 inhibitor (DNL758/SAR443122)	CLE	Commence dosing in Phase 2 study in CLE patients (Sanofi)
Mid 2021	ETV:IDS (DNL310)	Hunter syndrome (MPS II)	6-month data from Cohort A of Phase 1/2 study
2H 2021	EIF2B activator (DNL343)	ALS, FTD	Initiate Phase 1b study in ALS patients
2H 2021	RIPK1 inhibitor (DNL788/SAR443820)	ALS, Alzheimer’s disease, MS	Phase 1 data in healthy volunteers (Sanofi)
Late 2021	LRRK2 inhibitor (DNL151/BIIB122)	Parkinson’s disease	Initiate late-stage clinical development in Parkinson's patients
Late 2021	PTV:PGRN (DNL593)	FTD	File IND application or CTA
Late 2021/Early 2022	ATV:TREM2 (DNL919)	Alzheimer’s disease	File IND application or CTA

Participation in Upcoming Investor Conferences

Members of Denali’s management will participate in the following upcoming investor conferences:

- UBS Global Healthcare Virtual Conference, May 24-26
- Jefferies Healthcare Conference, June 1-3
- Goldman Sachs 42nd Annual Global Healthcare Conference, June 8-10
- 2021 Wedbush PacGrow Healthcare Conference, August 10-11

First Quarter 2021 Financial Results

For the three months ended March 31, 2021, Denali reported a net loss of $70.0 million compared with a net loss of $56.8 million for the three months ended March 31, 2020.

Collaboration revenue was $7.9 million for the three months ended March 31, 2021, compared to $3.6 million for the three months ended March 31, 2020. The increase of $4.3 million in collaboration revenue was primarily due to an increase in revenue from our collaboration with Takeda driven by increased costs incurred in the underlying partnered programs.

Total research and development expenses were $60.2 million for the three months ended March 31, 2021, compared to $51.0 million for the three months ended March 31, 2020. The increase of approximately $9.2 million was primarily attributable to an increase in personnel-related expenses, including stock-based compensation, driven primarily by higher headcount and additional equity award grants at a higher market price. Additionally, there were increases in external expenses related to progression of Denali's portfolio, including costs related to the progress of the EIF2B and ETV:IDS programs in the clinic in 2021. Other increases included TV platform and other program external expenses reflecting the increased investment in Denali's pipeline. These increases were partially offset by a decrease in the LRRK2 program external expenses primarily due to completion of the Phase 1 and 1b studies, as well as cost sharing reimbursements from Biogen under the Biogen collaboration agreement, and a decrease in other external research and development expenses.

General and administrative expenses were $18.9 million for the three months ended March 31, 2021, compared to $12.6 million for the three months ended March 31, 2020. The increase of approximately $6.3 million was primarily attributable to an increase in personnel-related expenses, including stock-based compensation, driven primarily by higher headcount and additional equity award grants at a higher market price. Additionally, there were increases in legal and other professional services expenses, including accounting and tax expenses associated with assessing the Biogen collaboration agreement, and other general costs such as insurance, tax and IT related expenses.

Cash, cash equivalents, and marketable securities were $1.45 billion as of March 31, 2021.

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.

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, planned preclinical studies and clinical trials and expected milestones; plans to conduct clinical development activities across various programs; plans, timelines and expectations related to DNL310 and Denali's TV technology; plans, timelines and expectations related to DNL151 of both Denali and Biogen, including with respect to initiation of late-stage clinical development; plans, timelines and expectations related to DNL343, including with respect to the initiation of future clinical trials; plans, timelines and expectations related to DNL788 and DNL758 of both Denali and Sanofi, including with respect to the availability of data and the initiation of future clinical trials; Denali's expectations regarding DNL593 and DNL919 and plans and expectations regarding planned regulatory filings; Denali's priorities, regulatory approvals, timing and likelihood of success and expectations regarding collaborations; and statements made by Denali's Chief Executive 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: 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 agreements with Sanofi, Takeda, Biogen or any of Denali's other 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 and its partners' ability to enroll patients in its ongoing and future clinical trials; Denali's reliance on third parties for the manufacture and supply of its product candidates for clinical trials; Denali's dependence on successful development of its blood-brain barrier platform technology and its current programs and product candidates; Denali's and its partners' ability to conduct or complete clinical trials on expected timelines; the risk that preclinical profiles of Denali's product candidates may not translate in clinical trials; the potential for clinical trials to differ from preclinical, early clinical, preliminary or expected results; the risk of significant adverse events, toxicities or other undesirable side effects; 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 Annual Report on Form 10-K filed with the Securities and Exchange Commission (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.

Denali Therapeutics Inc.
Condensed Consolidated Statements of Operations
(Unaudited)
(In thousands, except share and per share amounts)

	Three Months Ended March 31,	
	2021	**2020**
Collaboration revenue:		
Collaboration revenue from customers[1]	$ 7,922	$ 3,552
Other collaboration revenue	1	52
Total collaboration revenue	7,923	3,604
Operating expenses:		
Research and development[2]	60,207	51,016
General and administrative	18,936	12,555
Total operating expenses	79,143	63,571
Loss from operations	(71,220)	(59,967)
Interest and other income, net	1,179	3,069
Loss before income taxes	(70,041)	(56,898)
Income tax benefit	—	135
Net loss	$ (70,041)	$ (56,763)
Net loss per share, basic and diluted	$ (0.58)	$ (0.55)
Weighted average number of shares outstanding, basic and diluted	120,884,665	102,419,718

(1) Includes related party collaboration revenue from customer of $0.9 million for the three months ended March 31, 2021.
(2) Includes an offset to expense from related party cost reimbursement of $2.5 million for the three months ended March 31, 2021.

Denali Therapeutics Inc.
Condensed Consolidated Balance Sheets
(Unaudited)
(In thousands)

	March 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 435,321	$ 507,144
Short-term marketable securities	977,827	962,553
Cost sharing reimbursements due from related party	2,511	5,674
Prepaid expenses and other current assets	15,963	20,284
Total current assets	1,431,622	1,495,655
Long-term marketable securities	38,885	32,699
Property and equipment, net	41,376	40,846
Operating lease right-of-use asset	32,236	32,618
Other non-current assets	3,739	2,462
Total assets	$ 1,547,858	$ 1,604,280
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 1,626	$ 1,071
Accrued compensation	4,963	20,503
Accrued clinical costs	5,049	6,497
Accrued manufacturing costs	13,342	7,140
Other accruals and other current liabilities	8,299	8,315
Operating lease liability, current	4,876	4,690
Related party contract liability, current	3,569	3,569
Contract liabilities, current	12,886	19,914
Total current liabilities	54,610	71,699
Related party contract liability, less current portion	292,956	293,849
Contract liabilities, less current portion	31,322	23,325
Operating lease liability, less current portion	62,916	64,175
Other non-current liabilities	701	701
Total liabilities	442,505	453,749
Total stockholders' equity	1,105,353	1,150,531
Total liabilities and stockholders' equity	$ 1,547,858	$ 1,604,280

Investor Relations Contact:

Laura Hansen, Ph.D.
Vice President, Investor Relations
(650) 452-2747
hansen@dnli.com

Media Contacts:

Lizzie Hyland
(646) 495-2706
lizzie.hyland@fgh.com

or

Morgan Warners
(202) 295-0124
morgan.warners@fgh.com