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):

August 4, 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 August 4, 2021, Denali Therapeutics Inc. (the "Company") issued a press release announcing its financial results for the second quarter ended June 30, 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 August 4, 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: August 4, 2021

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

Denali Therapeutics Reports Second Quarter 2021 Financial Results and Business Highlights

SOUTH SAN FRANCISCO – August 4, 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 second quarter ended June 30, 2021, and provided business highlights.

"We recently announced positive interim data from a Phase 1/2 study of DNL310 in Hunter syndrome, our lead Transport Vehicle (TV)-enabled program, showing rapid normalization of key disease-specific biomarkers in cerebrospinal fluid. This was observed even at low dose regimens, which is consistent with robust and efficient crossing of the blood-brain barrier by DNL310," said Ryan Watts, Ph.D., Denali's Chief Executive Officer. "We are also encouraged by early indications that exploratory clinical measures improved in the first cohort of five patients. In parallel with expanding the ongoing Phase 1/2 study, we are now focused on finalizing the design for and commencing a pivotal Phase 2/3 study in the first half of 2022. Furthermore, we are making significant progress in advancing additional TV-enabled programs towards clinical development as well as our broader therapeutic portfolio. We are on track to initiate late-stage clinical development with our LRRK2 inhibitor DNL151 (BIIB122) for Parkinson's disease in collaboration with Biogen by year end and to initiate a Phase 1b study with our EIF2B agonist DNL343 for amyotrophic lateral sclerosis (ALS) in the second half of this year."

Recent Business Highlights

Reported positive interim data from the Phase 1/2 study of ETV:IDS (DNL310) in patients with Hunter syndrome (MPS II): In July 2021, Denali announced longer-term safety data and 6-month biomarker data on DNL310 from Cohort A in a Phase 1/2 study in patients with Hunter syndrome. The data demonstrated durability of effect with CNS impact, improved peripheral activity after switching from standard of care, and a safety profile consistent with standard of care enzyme replacement therapy. Furthermore, initial indications of improved clinical symptoms and function, assessed as exploratory endpoints, were reported by investigators and parents in all five patients enrolled in Cohort A. Denali also shared data from Cohort B, which is designed to inform dose selection; exploratory biomarker data demonstrated activity of DNL310 across all dose regimens. Based on these data, Denali plans to begin enrolling Cohort C in the Phase 1/2 study to further investigate clinical endpoints and initiate a pivotal Phase 2/3 study of DNL310 in the first half of 2022.

Phase 2 study of DNL758 (SAR443122) for cutaneous lupus erythematosus (CLE) initiated by Sanofi: In June 2021, Denali announced that its partner Sanofi commenced dosing in a Phase 2 study of DNL758, a peripherally-restricted small molecule inhibitor of RIPK1, in patients with CLE. Denali and Sanofi entered into a broad collaboration agreement in October 2018 for the global development and commercialization of RIPK1 inhibitors. This includes peripherally restricted molecules such as DNL758 and CNS-penetrant molecules such as DNL788 (SAR443820), which is being evaluated in a Phase 1 study in healthy volunteers with potential development for neurological indications such as amyotrophic lateral sclerosis, multiple sclerosis and Alzheimer's disease. Under the collaboration agreement, Denali received a milestone payment of $15 million from Sanofi in July 2021 related to the initiation of the Phase 2 study with DNL758. Sanofi is responsible for the development and commercialization and covers all costs of DNL758. Denali is entitled to receive development, regulatory and sales milestone payments and royalties on product sales.

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), in 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. 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 Parkinson's disease by year-end 2021.

Summary Table of Upcoming 2021 Expected Key Milestones

Timing	Investigational Drug Candidate	Therapeutic Area	Expected Milestone
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:

- BTIG Virtual Biotechnology Conference 2021, August 9-10
- 2021 Wedbush PacGrow Healthcare Conference, August 10-11
- H.C. Wainwright 23rd Annual Global Investment Conference, September 13-15
- Morgan Stanley 19th Annual Global Healthcare Conference, September 9-10 & 13-15
- 2021 Cantor Virtual Global Healthcare Conference, September 27-30

Second Quarter 2021 Financial Results

For the three months ended June 30, 2021, Denali reported a net loss of $60.7 million compared with a net loss of $58.8 million for the three months ended June 30, 2020.

Collaboration revenue was $22.9 million for the three months ended June 30, 2021, compared to $5.8 million for the three months ended June 30, 2020. The increase of $17.1 million in collaboration revenue was primarily due to the achievement of a $15.0 million milestone in June 2021 under our collaboration with Sanofi related to the initiation of the Phase 2 study of DNL758, as well as an increase in revenue of $2.4 million from our collaboration with Takeda and Biogen.

Total research and development expenses were $65.7 million for the three months ended June 30, 2021, compared to $53.2 million for the three months ended June 30, 2020. The increase of approximately $12.5 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 and the development of the TV platform reflecting the increased investment in Denali's pipeline. These increases were partially offset by a decrease in external expenses related to the LRRK2 program primarily due to completion of the Phase 1 and 1b studies, as well as cost sharing reimbursements under our collaboration with Biogen.

General and administrative expenses were $19.0 million for the three months ended June 30, 2021, compared to $14.0 million for the three months ended June 30, 2020. The increase of approximately $5.0 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 and other general costs such as insurance, tax, IT and facilities related expenses. These increases were partially offset by a decrease in legal and other professional services expenses.

Cash, cash equivalents, and marketable securities were approximately $1.4 billion as of June 30, 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, including our ability to advance two additional TV-enabled programs into the clinic for FTD and Alzheimer's disease; 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 and the payment of future milestone payments and royalties on product sales; 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 June 30,		Six Months Ended June 30,	
	2021	2020	2021	2020
Collaboration revenue:				
Collaboration revenue from customers[1]	$ 22,936	$ 5,811	$ 30,858	$ 9,363
Other collaboration revenue	3	36	4	88
Total collaboration revenue	22,939	5,847	30,862	9,451
Operating expenses:				
Research and development[2]	65,711	53,152	125,918	104,168
General and administrative	19,045	13,972	37,981	26,527
Total operating expenses	84,756	67,124	163,899	130,695
Loss from operations	(61,817)	(61,277)	(133,037)	(121,244)
Interest and other income, net	1,126	2,598	2,305	5,667
Loss before income taxes	(60,691)	(58,679)	(130,732)	(115,577)
Income tax benefit (expense)	—	(79)	—	56
Net loss	$ (60,691)	$ (58,758)	$ (130,732)	$ (115,521)
Net loss per share, basic and diluted	$ (0.50)	$ (0.56)	$ (1.08)	$ (1.11)
Weighted average number of shares outstanding, basic and diluted	121,291,435	105,717,912	121,089,174	104,068,815

(1) Includes related party collaboration revenue from customer of $0.8 million and $1.7 million for the three and six months ended June 30, 2021, respectively.
(2) Includes an offset to expense from related party cost reimbursement of $1.6 million and $4.1 million for the three and six months ended June 30, 2021, respectively.

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

	June 30, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 485,680	$ 507,144
Short-term marketable securities	823,251	962,553
Cost sharing reimbursements due from related party	1,567	5,674
Accounts receivable, net	15,218	8,593
Prepaid expenses and other current assets	16,029	11,691
Total current assets	1,341,745	1,495,655
Long-term marketable securities	92,522	32,699
Property and equipment, net	40,350	40,846
Operating lease right-of-use asset	31,622	32,618
Other non-current assets	3,576	2,462
Total assets	$ 1,509,815	$ 1,604,280
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 4,235	$ 1,071
Accrued compensation	6,295	20,503
Accrued manufacturing costs	13,052	7,140
Accrued clinical and other research & development costs	11,434	11,775
Other accrued costs and current liabilities	2,148	3,037
Operating lease liability, current	5,055	4,690
Related party contract liability, current	3,438	3,569
Contract liabilities, current	5,755	19,914
Total current liabilities	51,412	71,699
Related party contract liability, less current portion	292,293	293,849
Contract liabilities, less current portion	31,308	23,325
Operating lease liability, less current portion	61,396	64,175
Other non-current liabilities	701	701
Total liabilities	437,110	453,749
Total stockholders' equity	1,072,705	1,150,531
Total liabilities and stockholders' equity	$ 1,509,815	$ 1,604,280

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