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 8, 2022

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 8, 2022, Denali Therapeutics Inc. (the "Company") issued a press release announcing its financial results for the second quarter ended June 30, 2022. 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 8, 2022.
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 8, 2022

By: /s/ Alexander O. Schuth
Alexander O. Schuth, M.D.
Chief Operating and Financial Officer

Denali Therapeutics Reports Second Quarter 2022 Financial Results and Business Highlights

SOUTH SAN FRANCISCO – August 8, 2022 – 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, 2022, and provided business highlights.

“The Phase 1 study of DNL919 (ATV:TREM2) is now underway, making this our third BBB Transport Vehicle (TV)-enabled program, and seventh program overall, in clinical development,” said Ryan Watts, Ph.D., Denali's Chief Executive Officer. “Furthermore, advancement of our portfolio to late-stage development was highlighted in the quarter with initiation of late-stage studies for BIIB122 (LRRK2 inhibitor) and SAR443820 (RIPK1 inhibitor) in Parkinson’s disease and ALS, respectively. We also look forward to presenting data from ongoing studies of DNL310 (ETV:IDS) in Hunter syndrome and DNL343 (eIF2B activator) in ALS in the second half of the year.”

Second Quarter and Recent Program Updates:

Denali-Led Programs

DNL310 (ETV:IDS): MPS II (Hunter syndrome)

- New longer-term interim data from the ongoing Phase 1/2 study will be presented at the 2022 Society for the Study of Inborn Errors of Metabolism (SSIEM) Annual Symposium being held in Freiburg, Germany, August 30 – September 2, 2022.
- Interim data continue to show sustained normalization to healthy levels of CSF heparan sulfate and improvements in markers of lysosomal function consistent with durable CNS activity; safety profile with up to 85 weeks of dosing remains comparable with standard of care therapy.
- In addition, 49-week open label data on global impression of change continues to suggest stabilization and/or improvement in MPS II symptoms.
- Denali has initiated recruitment of the Phase 2/3 COMPASS study which will enroll approximately 54 MPS II patients. Upon completion of the ongoing Phase 1/2 study, and together with data from the global COMPASS study, this combined data package will potentially support registration.

DNL343 (eIF2B activator): Amyotrophic Lateral Sclerosis (ALS)

- Denali plans to present data from the ongoing Phase 1b study in ALS in the second half of 2022.
- Based on Phase 1 data and ongoing blinded Phase 1b data, Denali has initiated planning for late-stage development of DNL343 in ALS.

TAK-594/DNL593 (PTV:PGRN): Frontotemporal Dementia-Granulin (FTD-GRN)

- Denali is conducting a Phase 1/2 study, which continues to enroll healthy volunteers in Part A.
- Pending initial clinical data, Denali expects to begin dosing participants with FTD-GRN in the second half of 2022.

TAK-920/DNL919 (ATV:TREM2): Alzheimer’s Disease (AD)

- Dosing has commenced in the Phase 1 single ascending dose study in healthy volunteers in the Netherlands, following clearance of the Clinical Trial Application as previously reported in July 2022.

Partner-Led Programs

BIIB122/DNL151 (LRRK2 inhibitor): Parkinson's disease (idiopathic and LRKK2-positive)

- In May 2022, Denali and Biogen announced that dosing had commenced in the global Phase 2b LUMA study to evaluate the efficacy and safety of BIIB122 as compared to placebo in 640 participants with early-stage Parkinson's disease.
- The Phase 3 LIGHTHOUSE study in approximately 400 participants with Parkinson's disease with a confirmed LRRK2 pathogenic variant is expected to begin in the second half of 2022.
- In June 2022, *Science Translational Medicine* published Denali's research supporting the potential of LRRK2 inhibition as a novel mechanism for the treatment of Parkinson's disease.

SAR443820/DNL788 and SAR443122/DNL758 (RIPK1 inhibitors): Neurodegenerative and peripheral inflammatory diseases

- In May 2022, Denali announced that Sanofi began dosing with SAR443820 in the Phase 2 HIMALAYA study, which is expected to enroll approximately 260 participants with ALS.
- Denali received a $40 million milestone payment from Sanofi in the second quarter related to initiation of the Phase 2 HIMALAYA study.
- A Phase 2 study of SAR443820 in multiple sclerosis is also planned.
- Sanofi continues to conduct a Phase 2 study of the peripherally restricted RIPK1 inhibitor SAR443122 (eclitasertib) in cutaneous lupus erythematosus; a Phase 2 study in ulcerative colitis is also planned.

Discovery Programs

Denali continues to advance a broad pre-clinical portfolio including programs enabled by the Enzyme Transport Vehicle, the Antibody Transport Vehicle, and the Oligonucleotide Transport Vehicle, and several small molecules engineered to cross the blood-brain barrier and intended as potential treatments for patients with neurodegenerative diseases.

Participation in Upcoming Investor Conferences

- 2022 Wedbush PacGrow Healthcare Virtual Conference, August 9 – 10
- Citi's 17th Annual BioPharma Conference, September 7 – 8
- Morgan Stanley 20th Annual Global Healthcare Conference, September 12 – 14
- H.C. Wainwright 24th Annual Global Investment Conference, September 12 – 14
- Berenberg US CEO Conference 2022, Nov 2

Second Quarter 2022 Financial Results

For the three months ended June 30, 2022, Denali reported a net loss of $58.8 million compared to a net loss of $60.7 million for the three months ended June 30, 2021.

Collaboration revenue was $52.5 million for the three months ended June 30, 2022, compared to $22.9 million for the three months ended June 30, 2021. The increase in collaboration revenue of $29.6 million for the three months ended June 30, 2022 compared to the three months ended June 30, 2021 was primarily due to a $12.0 million preclinical milestone earned for approval of the CTA for TAK-920/DNL919 (ATV:TREM2) in the second quarter of 2022 and $40.0 million for milestone revenue earned in April 2022 upon dosing the first patient in a Phase 2 study of SAR443820/DNL788 in individuals with ALS, compared with a $15.0 million milestone recognized in the comparable period related to the initiation of a Phase 2 study of SAR443122/DNL758.

Total research and development expenses were $92.7 million for the three months ended June 30, 2022, compared to $65.7 million for the three months ended June 30, 2021. The increase of approximately $27.0 million was primarily attributable to an increase in ETV:IDS and LRRK2 program external expenses due to progress in the clinic in 2022, and personnel-related expenses, including stock-based compensation, driven primarily by higher headcount and equity award grants. Additionally, there were increases in external expenses related to the progression of other programs in Denali's portfolio, including the advancement of the TV platform reflected by the progress in the PTV:PGRN and ATV:TREM2 programs, as well as Denali's continued overall investment in developing a broad pipeline. These expense increases were partially offset by decreases in other external and unallocated research and development expenses and increases in cost sharing reimbursements.

General and administrative expenses were $21.2 million for the three months ended June 30, 2022, compared to $19.0 million for the three months ended June 30, 2021. The increase of approximately $2.2 million was primarily attributable to an increase in personnel-related expenses, including stock-based compensation, driven by higher headcount and equity award grants. Additionally, there were increases in other general corporate services costs including IT services and subscriptions, taxes, insurance and travel related expenses. These increases were partially offset by a decrease in consulting and legal and other professional services expenses.

Cash, cash equivalents, and marketable securities were approximately $1.16 billion as of June 30, 2022.

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 Denali's TV platform, including its Enzyme Transport Vehicle (ETV), Antibody Transport Vehicle (ATV), and Protein Transport Vehicle (PTV) technologies, as well as preclinical programs enabled by the ETV, ATV and Oligonucleotide Transport Vehicle technologies; plans, timelines and expectations regarding DNL151 for the treatment of Parkinson's disease in collaboration with Biogen, including the ongoing Phase 2b LUMA study and the planned LIGHTHOUSE study; plans, timelines and expectations regarding DNL310, including the presentation of data from the ongoing Phase 1/2 study and the potential for the DNL310 combined data package to support registration of DNL310; plans timelines and expectations regarding DNL919 for the treatment of Alzheimer's disease; plans, timelines and expectations regarding DNL788 of both Denali and Sanofi, including with respect to expected enrollment for a Phase 2 trial in ALS and a planned Phase 2 study in multiple sclerosis; plans, timelines and expectations regarding DNL758 of both Denali and Sanofi, including with respect to the planned Phase 2 study in ulcerative colitis; plans, timelines and expectations regarding DNL593, including Phase 1/2 trial dosing and initial clinical data from the Phase 1 portion of such trial; plans, timelines and expectations regarding DNL343, including the presentation of initial data from the ongoing Phase 1b study of DNL343 in ALS; 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 ongoing 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 transition to a late stage clinical drug development company; Denali's and its collaborators' ability to complete the development and, if approved, commercialization of its product candidates; Denali's and its collaborators' 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 programs and product candidates; Denali's and its collaborators' 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 attract, motivate and retain qualified managerial, scientific and medical personnel; 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 related to its product candidates; implementation of Denali's strategic plans for its business, product candidates and blood-brain barrier platform technology; Denali's ability to obtain additional capital to finance its operations, as needed; Denali's ability to accurately forecast future financial results in the current environment; general economic and market conditions; and other risks and uncertainties, including those described in Denali's most recent Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on August 8, 2022 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,	
	2022	2021	2022	2021
Collaboration revenue:				
Collaboration revenue from customers[1]	$ 52,480	$ 22,936	$ 94,621	$ 30,858
Other collaboration revenue	—	3	—	4
Total collaboration revenue	52,480	22,939	94,621	30,862
Operating expenses:				
Research and development[2]	92,737	65,711	178,835	125,918
General and administrative	21,159	19,045	43,700	37,981
Total operating expenses	113,896	84,756	222,535	163,899
Loss from operations	(61,416)	(61,817)	(127,914)	(133,037)
Interest and other income, net	2,649	1,126	3,927	2,305
Loss before income taxes	(58,767)	(60,691)	(123,987)	(130,732)
Income tax expense	(27)	—	(27)	—
Net loss	$ (58,794)	$ (60,691)	$ (124,014)	$ (130,732)
Net loss per share, basic and diluted	$ (0.48)	$ (0.50)	$ (1.01)	$ (1.08)
Weighted average number of shares outstanding, basic and diluted	123,008,558	121,291,435	122,842,171	121,089,174

(1) Includes related-party collaboration revenue from a customer of $0.5 million and $2.7 million for the three and six months ended June 30, 2022, respectively, and $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 sharing reimbursements of $0.4 million and expense for cost sharing payments to a related party of $2.4 million for the three and six months ended June 30, 2022, respectively, and an offset to expense from related-party cost sharing reimbursements 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, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 155,088	$ 293,477
Short-term marketable securities	913,580	571,930
Cost sharing reimbursements due from related party	357	1,226
Prepaid expenses and other current assets	45,575	30,601
Total current assets	1,114,600	897,234
Long-term marketable securities	94,220	425,449
Property and equipment, net	38,703	38,865
Operating lease right-of-use asset	29,755	30,743
Other non-current assets	15,184	11,871
Total assets	$ 1,292,462	$ 1,404,162
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 7,116	$ 4,779
Accrued compensation	8,315	19,013
Accrued clinical and other research & development costs	16,429	15,887
Accrued manufacturing costs	17,929	9,955
Other accrued costs and current liabilities	2,076	2,857
Operating lease liability, current	5,871	5,453
Related-party contract liability, current	290,424	292,386
Contract liabilities, current	—	27,915
Total current liabilities	348,160	378,245
Related-party contract liability, less current portion	552	1,295
Contract liabilities, less current portion	3,398	3,398
Operating lease liability, less current portion	55,525	58,554
Other non-current liabilities	379	379
Total liabilities	408,014	441,871
Total stockholders' equity	884,448	962,291
Total liabilities and stockholders' equity	$ 1,292,462	$ 1,404,162

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