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 8, 2023

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 8, 2023, Denali Therapeutics Inc. (the "Company") issued a press release announcing its financial results for the first quarter ended March 31, 2023. 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 8, 2023.
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 8, 2023

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

Denali Therapeutics Reports First Quarter 2023 Financial Results and Business Highlights

SOUTH SAN FRANCISCO – May 8, 2023 – Denali Therapeutics Inc. (Nasdaq: DNLI), a biopharmaceutical company developing a broad portfolio of product candidates engineered to cross the blood-brain barrier (BBB) for the treatment of neurodegenerative diseases and lysosomal storage diseases, today reported financial results for the first quarter ended March 31, 2023, and provided business highlights.

“In the first quarter, we continued to make significant progress across our broad therapeutic portfolio, including the advancement of multiple late-stage programs,” said Ryan Watts, Ph.D., Chief Executive Officer at Denali. “As the global Phase 2/3 COMPASS study of DNL310 (ETV:IDS) enrolls children with MPS II, we were excited to share new interim, open-label Phase 1/2 data demonstrating positive changes in behavioral and cognitive aspects of the disease that are particularly important to MPS II families and data suggesting additional peripheral activity in children who switched from standard of care. In addition, at the recent AAN meeting, we reported positive biomarker and safety data from the 28-day Phase 1b study of our eIF2B agonist, DNL343, and we are eager to learn more about the potential of DNL343 from its planned inclusion in the Phase 2/3 HEALEY Platform Trial. We look forward to continued collaboration with individuals, families, and communities impacted by neurodegenerative and lysosomal storage diseases as we strive to discover, develop, and deliver safe and effective new medicines.”

First Quarter and Recent Program Updates:

TV-ENABLED PROGRAMS

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

DNL310 is an investigational, intravenously administered, Enzyme Transport Vehicle (ETV)-enabled, brain-penetrant iduronate-2-sulfatase (IDS) replacement therapy designed to address the behavioral, cognitive and physical manifestations of MPS II (Hunter syndrome).

- In February, Denali reported new interim results at the WORLD*Symposium*™ from the ongoing open-label, single-arm Phase 1/2 study of DNL310 in children with MPS II, including data from additional participants and up to 104 weeks of treatment. Over 49 weeks of DNL310 treatment, positive changes across measures of exploratory clinical outcomes including VABS-II (adaptive behavior) and BSID-III (cognitive capabilities) scores and global impression scales were observed. In addition, the interim data also suggested that DNL310 improved hearing, as assessed by auditory brainstem response testing. Additional biomarker data out to 49 weeks continued to demonstrate that DNL310 enabled rapid and sustained normalization of CSF heparan sulfate to normal healthy levels and improvement in lysosomal function biomarkers. Reduction in urine heparan sulfate and dermatan sulfate after switch from standard of care to DNL310 suggested additional sustained peripheral activity of DNL310. The safety profile of DNL310, with up to two years of treatment, remained consistent with standard of care.
- The interim Phase 1/2 data continue to suggest robust central nervous system (CNS) and peripheral activity of DNL310 and support continued recruitment of participants with MPS II, with and without neuronopathic disease, in the global Phase 2/3 COMPASS study.

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

DNL593 is an investigational, intravenously administered, brain-penetrant progranulin (PGRN) replacement therapy enabled by Denali's Protein Transport Vehicle (PTV) technology, which is being co-developed with Takeda. Recruitment of participants with symptomatic FTD-GRN loss of function mutations in Part B (ascending multiple doses) of the Phase 1/2 study is ongoing.

- In March 2023, a $10 million milestone payment from Takeda was triggered upon achievement of a specified clinical milestone in the Phase 1/2 study, which is due in May 2023.
- Additional healthy volunteer data from Part A of the Phase 1/2 study will be presented at the Alzheimer's Association International Conference, which is taking place July 16-20, 2023.

TAK-920/DNL919 (ATV:TREM2): Alzheimer's disease

TAK-920/DNL919 is an investigational, Antibody Transport Vehicle (ATV)-enabled, brain-penetrant TREM2 agonist intended to improve microglial function as a potential treatment for Alzheimer's disease, which is being co-developed with Takeda. A Phase 1 study of DNL919 in healthy volunteers is ongoing in the Netherlands.

DNL126 (ETV:SGSH): MPS IIIA (Sanfilippo syndrome Type A)

DNL126 (ETV:SGSH) is an investigational, intravenously administered, ETV-enabled, brain-penetrant N-sulfoglucosamine sulfohydrolase (SGSH) replacement therapy designed to address the behavioral, cognitive and physical manifestations of MPS IIIA (Sanfilippo syndrome Type A).

- In February, Denali presented preclinical data at the WORLD*Symposium*, which support plans to advance DNL126 into clinical development.

Oligonucleotide Transport Vehicle (OTV) platform

Denali's OTV platform is designed to enable peripheral administration of oligonucleotide therapeutics such as antisense oligonucleotides (ASOs) to address a wide range of neurodegenerative and other neurological diseases. Denali has selected five ASO targets for further development and is focused on advancing two OTV candidates towards clinical development.

- In April, the manuscript titled, "Targeting Transferrin Receptor to Transport Antisense Oligonucleotides Across the Blood-Brain Barrier" was posted on bioRxiv here.

Antibody Transport Vehicle (ATV):Amyloid beta (ATV:Abeta) program

ATV:Abeta is designed to increase brain exposure and target engagement of antibody therapeutics directed against Abeta, which may enable improved plaque clearance and/or reduced amyloid-related imaging abnormalities (ARIA). Accumulation of Abeta plaque in the brain is a defining feature of Alzheimer's disease.

- In April, Denali announced that Biogen exercised its option to license Denali's ATV:Abeta. Biogen will assume responsibility for all development and commercial activities and associated expenses. Denali will receive a one-time option exercise payment and, if certain milestones are achieved, Denali will be eligible to receive potential development and commercial milestone payments, and royalties based on future net sales.

SMALL MOLECULE PROGRAMS

BIIB122/DNL151 (LRRK2 Inhibitor): Parkinson's disease (Idiopathic and LRKK2-Positive)

BIIB122/DNL151 is an investigational small molecule inhibitor of LRRK2, one of the most common genetic drivers of Parkinson's disease. Targeting LRRK2 has the potential to impact the underlying biology and slow the progression of Parkinson's disease. Denali and Biogen are co-developing BIIB122. Biogen is conducting two late-stage studies: the Phase 2b LUMA study in participants with early-stage Parkinson's disease and the Phase 3 LIGHTHOUSE study in participants with Parkinson's disease and a confirmed LRRK2 pathogenic variant.

SAR443820/DNL788 (CNS-Penetrant RIPK1 Inhibitor): ALS, MS
SAR443820/DNL788 is an investigational, CNS-penetrant, small molecule inhibitor of RIPK1, a critical signaling protein in a canonical inflammatory and cell death pathway. Increased RIPK1 activity in the CNS is hypothesized to drive neuroinflammation and cell necroptosis and to contribute to neurodegeneration. Denali and Sanofi are co-developing SAR443820. Sanofi is conducting the global Phase 2 HIMALAYA study for participants with amyotrophic lateral sclerosis (ALS).

- In January, Denali announced that Sanofi initiated a Phase 2 clinical trial in multiple sclerosis (MS) for which Denali received a milestone payment of $25 million.

DNL343 (eIF2B Activator): ALS

DNL343 is an investigational small molecule activator of the eukaryotic initiation factor 2B (eIF2B), is designed to inhibit the cellular integrated stress response (ISR) and prevent or slow disease progression associated with stress granule formation and TDP-43 aggregation, which is a hallmark pathology present in nearly all individuals with ALS.

- In April, Denali presented final data from the 28-day treatment period of the Phase 1b study of DNL343 in participants with ALS at the 75th Annual Meeting of the American Academy of Neurology (AAN). The results continued to demonstrate that once-daily oral dosing with DNL343 for 28 days was generally well tolerated and demonstrated extensive CSF penetration. In addition, robust inhibition of biomarkers associated with the ISR pathway was observed in blood samples from study participants. The Phase 1b data continue to support plans to initiate dosing with DNL343 in the Phase 2/3 HEALEY ALS Platform Trial.

OTHER CLINICAL PROGRAMS

SAR443122/DNL758 (Peripheral RIPK1 Inhibitor): CLE and UC

SAR443122/DNL758 (eclitasertib), is an investigational, peripherally restricted, small molecule inhibitor of RIPK1. Sanofi is solely responsible for the development and commercialization of peripherally restricted RIPK1 inhibitors. Sanofi is conducting a Phase 2 study of DNL758 in patients with cutaneous lupus erythematosus (CLE).

- In January, Denali announced that Sanofi had initiated a Phase 2 trial of SAR443122 in patients with ulcerative colitis (UC) for which a milestone payment of $10 million was received in December 2023.

DISCOVERY PROGRAMS

Denali continues to advance a broad preclinical 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 BBB and intended as potential treatments for patients with neurodegenerative diseases and lysosomal storage diseases.

Recent Corporate Updates:

- In March, a contingent consideration payment of $30 million associated with Denali's acquisition of F-star Gamma was triggered upon the achievement of a specified clinical milestone in the ETV:IDS program. This payment fully satisfies Denali's clinical contingent consideration obligations under the Purchase Agreement.

Participation in Upcoming Investor Conferences:

- Bank of America 2023 Healthcare Conference, May 9-11
- Jefferies Global Healthcare Conference, June 7-9
- Goldman Sachs 44th Annual Global Healthcare Conference, June 12-15
- BTIG Virtual Biotechnology Conference 2023, August 7-8

First Quarter 2023 Financial Results

Net losses were $109.8 million and $65.2 million for the three months ended March 31, 2023 and 2022, respectively.

Collaboration revenue was $35.1 million and $42.1 million for the three months ended March 31, 2023 and 2022, respectively. The decrease in collaboration revenue of $7.0 million for the three months ended March 31, 2023, compared to the comparative period in the prior year was primarily due to a decrease in revenue from our collaboration with Takeda primarily due to completion of the preclinical research service performance obligations, and a decrease in revenue under the Biogen Collaboration Agreement due to completion of the ATV:Abeta Option Research Services. These decreases are partially offset by an increase in revenue from our collaboration with Sanofi as a result of the $25.0 million milestone achieved in January 2023 upon first patient in a Phase 2 study of SAR443820/DNL788 in individuals with MS.

Total research and development expenses were $128.8 million and $86.1 million for the three months ended March 31, 2023 and 2022, respectively. The increase of approximately $42.7 million for the three months ended March 31, 2023 compared to the comparative period in the prior year was attributable to: an increase in ETV:IDS program external expenses primarily due to the accrued contingent consideration payment of $30.0 million related to the acquisition of F-star Gamma, which was triggered in March 2023 upon the achievement of a specified clinical milestone in the ETV:IDS program; an increase in other unallocated research and development expenses primarily due to increased facility costs as a result of accelerated depreciation on leasehold improvements associated with the termination of the previous SLC lease; and an increase in personnel-related expenses, including stock-based compensation, mainly driven by higher headcount and equity award grants. Further, net cost sharing reimbursements from collaboration partners decreased as cost sharing payments owed to Biogen increased. These net expense increases were partially offset by decreases in TV platform and other program external expenses and PTV:PGRN program external expenses due to the timing of significant external research and manufacturing related activities period over period.

General and administrative expenses were $27.1 million and $22.5 million for the three months ended March 31, 2023 and 2022, respectively. The increase of approximately $4.6 million for the three months ended March 31, 2023 compared to the comparative period in the prior year was primarily attributable to an increase in personnel-related expenses, including employee compensation and stock-based compensation expenses, driven by higher headcount and equity award grants. Additionally, there were increases in facility costs, consulting, and legal professional services expenses.

Cash, cash equivalents, and marketable securities were approximately $1.29 billion as of March 31, 2023.

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 the treatment of neurodegenerative diseases and lysosomal storage 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 expectations regarding Denali's TV technology platform, including the Enzyme Transport Vehicle (ETV), Antibody Transport Vehicle (ATV) and Oligonucleotide Transport Vehicle (OTV); plans, timelines, and expectations regarding DNL310 and the ongoing Phase 2/3 COMPASS and Phase 1/2 studies, including the continued recruitment of participants for the Phase 2/3 COMPASS study and the Phase 1/2 study interim data; plans, timelines, and expectations of both Denali and Takeda regarding DNL593 and the ongoing Phase 1/2 study, including the recruitment of patients for the Part B study; plans, timelines, and expectations of both Denali and Takeda regarding DNL919 and the ongoing Phase 1 study; plans, timelines, and expectations related to DNL126, including plans for advancement into clinical development; plans, timelines, and expectations regarding the advancement of OTV candidates towards clinical development; plans, timelines and expectations of both Denali and Biogen regarding DNL151, the ongoing Phase 2b LUMA study, and the ongoing Phase 3 LIGHTHOUSE study; plans, timelines and expectations regarding DNL788 of both Denali and Sanofi; plans, timelines and expectations regarding DNL343, including plans for the Phase 2/3 HEALEY ALS Platform Trial; plans, timelines and expectations regarding DNL758; plans, timelines and expectations of both Denali and Biogen regarding the development of Denali's ATV: Abeta for the treatment of Alzheimer's disease; plans, timelines and expectations for the new manufacturing facility lease in Utah, including the potential benefits of such manufacturing capabilities; 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 by adverse economic conditions, such as instability in the financial services sector, the impact of the COVID-19 pandemic and increased geopolitical uncertainty; 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, or 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 Annual and Quarterly Reports on Forms 10-K and 10-Q filed with the Securities and Exchange Commission (SEC) on February 27, 2023 and May 8, 2023, respectively, and Denali's future reports to be filed with the SEC. Denali does not undertake any obligation to update or revise any forward-looking statements, to conform these statements to actual results or to make changes in Denali's expectations, 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,	
	2023	**2022**
Collaboration revenue:		
Collaboration revenue from customers[(1)]	$ 35,141	$ 42,141
Total collaboration revenue	35,141	42,141
Operating expenses:		
Research and development[(2)]	128,816	86,098
General and administrative	27,140	22,541
Total operating expenses	155,956	108,639
Loss from operations	(120,815)	(66,498)
Interest and other income, net	11,034	1,278
Net loss	$ (109,781)	$ (65,220)
Net loss per share, basic and diluted	$ (0.80)	$ (0.53)
Weighted average number of shares outstanding, basic and diluted	136,524,528	122,673,935

(1) Includes related-party collaboration revenue from a customer of $0.1 million and $2.2 million for the three months ended March 31, 2023 and 2022, respectively.
(2) Includes expense for cost sharing payments due to a related party of $4.2 million and $2.7 million for the three months ended March 31, 2023 and 2022, respectively.

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

	March 31, 2023	December 31, 2022
Assets		
Current assets:		
Cash and cash equivalents	$ 68,131	$ 218,044
Short-term marketable securities	1,220,322	1,118,171
Prepaid expenses and other current assets	36,709	36,104
Total current assets	1,325,162	1,372,319
Property and equipment, net	42,117	44,087
Operating lease right-of-use assets	28,049	30,437
Other non-current assets	14,016	13,399
Total assets	$ 1,409,344	$ 1,460,242
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 2,215	$ 2,790
Cost sharing payments due to related party	8,538	4,388
Accrued clinical and other research & development costs	47,571	16,297
Accrued manufacturing costs	19,959	22,307
Other accrued costs and current liabilities	9,136	3,682
Accrued compensation	7,365	17,087
Operating lease liabilities, current	6,539	7,318
Related-party contract liability, current	289,757	290,053
Total current liabilities	391,080	363,922
Related-party contract liability, less current portion	633	479
Operating lease liabilities, less current portion	50,546	53,032
Other non-current liabilities	379	379
Total liabilities	442,638	417,812
Total stockholders' equity	966,706	1,042,430
Total liabilities and stockholders' equity	$ 1,409,344	$ 1,460,242

Investor Relations Contact:

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

Media Contact:

Angela Salerno-Robin
Senior Vice President, Media Relations, Healthcare
dna Communications
(212) 445-8219
Asalerno-robin@dna-comms.com