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):

November 7, 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 November 7, 2023, Denali Therapeutics Inc. (the "Company") issued a press release announcing its financial results for the third quarter ended September 30, 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 November 7, 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: November 7, 2023

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

Denali Therapeutics Reports Third Quarter 2023 Financial Results and Business Highlights

SOUTH SAN FRANCISCO, Calif., – November 7, 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 third quarter ended September 30, 2023, and provided business highlights.

“Exciting progress in the field related to treating neurodegenerative diseases highlights the significant potential for our broad therapeutic portfolio and differentiated Transport Vehicle (TV) platform technology to effectively deliver therapeutic enzymes, antibodies, and antisense oligonucleotides (ASOs) to the brain,” said Ryan Watts Ph.D., Chief Executive Officer at Denali. “We continue to focus on clinical execution, expansion of our TV platform and commercial readiness as we advance our therapeutic pipeline and act with urgency to bring new treatments to people living with neurodegenerative and lysosomal storage diseases.”

Third 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, iduronate-2-sulfatase (IDS) replacement therapy designed to cross the BBB and address the behavioral, cognitive, and physical manifestations of MPS II (Hunter syndrome). Recruitment is ongoing in the global Phase 2/3 COMPASS study of DNL310 in neuronopathic and non-neuronopathic MPS II.

- In August, Denali presented new interim data from the Phase 1/2 study of DNL310 in MPS II in an oral presentation at the Society for the Study of Inborn Errors of Metabolism (SSIEM) Annual Symposium 2023. Additional biomarker data up to two years of treatment continued to demonstrate rapid and sustained normalization of cerebral spinal fluid (CSF) heparan sulfate to normal healthy levels and improvement in lysosomal function biomarkers. Additional safety data up to two years of treatment continued to demonstrate that DNL310 was generally well tolerated. Previously reported data showed robust and statistically significant reduction of neurofilament light (NfL), a marker of neuronal damage, and positive clinical outcome changes in adaptive behavior, cognition, and auditory function. The interim clinical outcomes data, safety profile, and biomarker effects, including normalization of CSF heparan sulfate and reduction in NfL, continue to support development of DNL310 in MPS II.

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

DNL593 is an investigational, intravenously administered, Protein Transport Vehicle (PTV)-enabled progranulin (PGRN) replacement therapy designed to restore normal levels of PGRN in the brain without interfering with normal PGRN transport and processing. DNL593 is being co-developed with Takeda. Recruitment is ongoing in Part B (ascending multiple doses) of the Phase 1/2 study of DNL593 in symptomatic patients with a loss of function FTD-GRN mutation.

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

DNL126 (ETV:SGSH) is an investigational, intravenously administered, ETV-enabled N-sulfoglucosamine sulfohydrolase (SGSH) replacement therapy designed to cross the BBB and address the behavioral, cognitive, and physical manifestations of MPS IIIA (Sanfilippo syndrome Type A). Start-up activities are ongoing for the Phase 1/2 study of DNL126 in MPS IIIA.

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 submitted a manuscript for publication, which can be found on bioRxiv here. Denali has selected five ASO targets for further development and is focused on advancing two OTV candidates towards clinical development.

Antibody Transport Vehicle Amyloid beta (ATV-amyloid-beta) program

ATV-amyloid-beta is an investigational, ATV-enabled anti-amyloid-beta therapy designed to increase brain exposure and target engagement of antibody therapeutics directed against amyloid-beta, which may enable improved plaque clearance and/or reduced amyloid-related imaging abnormalities (ARIA). Accumulation of amyloid-beta plaque in the brain is a defining feature of Alzheimer's disease. Biogen exercised its option to license Denali's ATV-amyloid-beta program and is responsible for all development and commercial activities and associated expenses.

SMALL MOLECULE PROGRAMS

BIIB122/DNL151 (LRRK2 Inhibitor): Parkinson's disease

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 the global Phase 2b LUMA study of BIIB122 in early-stage Parkinson's disease with and without LRRK2 mutations.

- In August, Denali and Biogen executed an amendment to the Definitive LRRK2 Collaboration and License Agreement and Waiver of and Amendment to Right of First Negotiation (ROFN), Option, and License Agreement. As part of the amendment, certain milestone criteria were changed while the total amount of development, regulatory, and commercial milestones across all indications remains the same. In addition, Biogen agreed to waive the remaining option and rights of first negotiation under the ROFN and Option Agreement.

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 has completed enrollment of both the global Phase 2 HIMALAYA study in amyotrophic lateral sclerosis (ALS) and the Phase 2 study in multiple sclerosis (MS).

DNL343 (eIF2B Activator): ALS

DNL343 is an investigational small molecule activator of the eukaryotic initiation factor 2B (eIF2B) designed to inhibit the cellular integrated stress response (ISR) and prevent or slow disease progression by interfering with stress granule formation and TDP-43 aggregation, which is a hallmark pathology present in virtually all individuals with ALS. Previously announced results of a Phase 1b study in participants with ALS demonstrated that once-daily oral dosing with DNL343 for 28 days was generally well-tolerated and was associated with extensive distribution in the cerebrospinal fluid as well as robust inhibition of ISR biomarkers. Recruitment is ongoing in Regimen G (DNL343) of the Phase 2/3 HEALEY ALS Platform Trial.

OTHER CLINICAL PROGRAMS

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

Eclitasertib (SAR443122/DNL758), is an investigational, peripherally restricted, small molecule inhibitor of RIPK1. Sanofi is solely responsible for the development and commercialization of peripherally restricted RIPK1 inhibitors.

- In October, Sanofi announced that the development of eclitasertib in cutaneous lupus erythematosus (CLE) is being discontinued because the Phase 2 proof-of-concept study did not meet its primary endpoint (percent change from baseline in CLASI-A at week 12). Eclitasertib was found to be generally well-tolerated. Sanofi continues to recruit the Phase 2 study of eclitasertib in ulcerative colitis (UC).

DISCOVERY PROGRAMS

Denali continues to selectively advance a broad preclinical portfolio including programs enabled by the Enzyme Transport Vehicle, the Antibody Transport Vehicle, 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.

2023 Guidance on Operating Expenses:

Cash, cash equivalents, and marketable securities were approximately $1.12 billion as of September 30, 2023. Denali is providing updated guidance on cash operating expenses for the full year 2023 and now anticipates an increase of approximately 15-20% compared to 2022, which is a decrease from previous guidance of 25-30%. The expected decrease is a result of portfolio prioritization and measures to contain costs.

Participation in Upcoming Investor Conferences:

- Jefferies London Healthcare Conference, November 14-16

Third Quarter 2023 Financial Results

Net losses were $99.4 million and $103.3 million for the three months ended September 30, 2023 and 2022, respectively.

Collaboration revenue was $1.3 million and $3.6 million for the three months ended September 30, 2023 and 2022, respectively. The decrease in collaboration revenue of $2.3 million for the three months ended September 30, 2023, compared to the comparative period in the prior year was primarily due to a decrease of revenue earned under the Sanofi Collaboration of $3.4 million, partially offset by an increase of $1.1 million in revenue earned under the Biogen Collaboration Agreement due to the August 2023 amendment which resulted in the satisfaction of the research services performance obligation for the second option program.

Total research and development expenses were $89.7 million and $87.8 million for the three months ended September 30, 2023 and 2022, respectively. The increase of approximately $1.9 million for the three months ended September 30, 2023 compared to the comparative period in the prior year was primarily attributable to increases in ETV:IDS and eIF2B program external expenses reflecting the continued progress of these programs in clinical trials during 2023; 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 LRRK2 program external expenses due to the transition of LRRK2 clinical activities to Biogen, 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 $25.3 million and $23.3 million for the three months ended September 30, 2023 and 2022, respectively. The increase of approximately $2.0 million for the three months ended September 30, 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. These increases were partially offset by decreases in professional services and other corporate costs.

Cash, cash equivalents, and marketable securities were approximately $1.12 billion as of September 30, 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); statements made by Denali's Chief Executive Officer; plans, timelines, and expectations regarding DNL310 and the ongoing Phase 2/3 COMPASS and Phase 1/2 studies; 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 related to DNL126, including the Phase 1/2 study; plans, timelines, and expectations regarding the advancement of OTV candidates towards clinical development and the potential publication of related manuscripts; 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 of both Denali and Biogen regarding DNL151 and the ongoing Phase 2b LUMA study, as well as any milestones available under Denali's agreement with Biogen; plans, timelines, and expectations of both Denali and Sanofi regarding DNL788 and the ongoing Phase 2 HIMALAYA study in ALS and Phase 2 study in MS; plans, timelines, and expectations regarding DNL343, including plans and enrollment for Regimen G of the Phase 2/3 HEALEY ALS Platform Trial; plans, timelines, and expectations regarding DNL758, including the ongoing Phase 2 study in patients with UC; and plans and expectations for Denali's preclinical programs. 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; 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; 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; 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 August 7, 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 September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Collaboration revenue:				
Collaboration revenue from customers[1]	$ 1,267	$ 184	$ 330,531	$ 94,805
Other collaboration revenue	—	3,375	—	3,375
Total collaboration revenue	1,267	3,559	330,531	98,180
Operating expenses:				
Research and development[2]	89,737	87,786	316,073	266,621
General and administrative	25,325	23,259	78,585	66,959
Total operating expenses	115,062	111,045	394,658	333,580
Loss from operations	(113,795)	(107,486)	(64,127)	(235,400)
Interest and other income, net	14,442	4,187	38,376	8,114
Loss before income taxes	(99,353)	(103,299)	(25,751)	(227,286)
Income tax expense	—	—	—	(27)
Net loss	$ (99,353)	$ (103,299)	$ (25,751)	$ (227,313)
Net loss per share, basic and diluted	$ (0.72)	$ (0.84)	$ (0.19)	$ (1.85)
Weighted average number of shares outstanding, basic and diluted	137,644,534	123,473,390	137,076,199	123,054,889

(1) Includes related-party collaboration revenue from customers of $1.3 million and $295.5 million for the three and nine months ended September 30, 2023, respectively, and $0.2 million and $2.9 million for the three and nine months ended September 30, 2022, respectively.

(2) Includes expenses for cost sharing payments due to a related party of $3.4 million and $14.5 million for the three and nine months ended September 30, 2023, respectively, and $1.4 million and $3.8 million for the three and nine months ended September 30, 2022.

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

	September 30, 2023	December 31, 2022
Assets		
Current assets:		
Cash and cash equivalents	$ 148,011	$ 218,044
Short-term marketable securities	961,245	1,118,171
Prepaid expenses and other current assets	33,628	36,104
Total current assets	1,142,884	1,372,319
Long-term marketable securities	7,905	—
Property and equipment, net	48,101	44,087
Operating lease right-of-use assets	26,750	30,437
Other non-current assets	11,137	13,399
Total assets	$ 1,236,777	$ 1,460,242
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 1,182	$ 2,790
Cost sharing payments due to related party	10,354	4,388
Accrued clinical and other research & development costs	14,534	16,297
Accrued manufacturing costs	12,421	22,307
Other accrued costs and current liabilities	9,331	3,682
Accrued compensation	16,344	17,087
Operating lease liabilities, current	7,014	7,318
Related-party contract liability, current	—	290,053
Total current liabilities	71,180	363,922
Related-party contract liability, less current portion	—	479
Operating lease liabilities, less current portion	46,887	53,032
Other non-current liabilities	379	379
Total liabilities	118,446	417,812
Total stockholders' equity	1,118,331	1,042,430
Total liabilities and stockholders' equity	$ 1,236,777	$ 1,460,242

Investor and Media Contact:

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