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 3, 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 November 3, 2022, Denali Therapeutics Inc. (the "Company") issued a press release announcing its financial results for the third quarter ended September 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 November 3, 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: November 3, 2022

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

Denali Therapeutics Reports Third Quarter 2022 Financial Results and Business Highlights

SOUTH SAN FRANCISCO – November 3, 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 third quarter ended September 30, 2022, and provided business highlights.

“This is an exciting time in neuroscience and rare disease drug development," said Ryan Watts, Ph.D., Denali's Chief Executive Officer. "Now as a late-stage development company with a portfolio of seven therapeutic candidates designed to cross the blood-brain barrier, we remain focused on bringing treatment options to people living with neurodegenerative and lysosomal storage diseases. Our recent progress highlights the potential of our Transport Vehicle platform and portfolio, and we look forward to sharing additional program and data updates.”

Third Quarter and Recent Program Updates:

TV-ENABLED PROGRAMS

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

- In August 2022, Denali presented new, interim data from the ongoing Phase 1/2 study at the 2022 SSIEM Annual Symposium demonstrating achievement of healthy normal levels of heparan sulfate measured in cerebrospinal fluid (CSF) in all participants in the Phase 1/2 study, including those with high pre-existing anti-iduronate-2 sulfatase antibodies; improvement or stabilization in clinical symptoms and function in most participants as reported by both clinicians and caregivers; and a safety profile with up to 85 weeks of dosing, which was similar to standard of care.
- The Phase 2/3 COMPASS study continues to enroll up to 54 participants with Hunter syndrome with and without neuronopathic disease; 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.

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

- In November 2022, Denali announced interim results from Part A of the Phase 1/2 study evaluating TAK-594/DNL593 (PTV:PGRN) in healthy subjects. Single doses of DNL593 resulted in substantial increases in CSF progranulin levels suggesting brain delivery of DNL593 was achieved and has the potential to address progranulin deficiency, which drives disease progression in people living with FTD-GRN. Single doses of DNL593 were also generally well tolerated, based on blinded safety analysis.
- These data support dosing in participants with FTD-GRN in Part B of the study.

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

- Dosing is ongoing in the Phase 1 single ascending dose study in healthy volunteers in the Netherlands.

SMALL MOLECULE PROGRAMS

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

- In October 2022, Denali and Biogen announced initiation of the global Phase 3 LIGHTHOUSE study of BIIB122 in up to 400 participants with Parkinson's disease and a confirmed LRRK2 pathogenic variant.
- Dosing is ongoing in the global Phase 2b LUMA study in up to 640 participants with early-stage Parkinson’s disease.

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

- In November 2022, Sanofi presented Phase 1 healthy volunteer data on SAR443820 at the Annual Northeast Amyotrophic Lateral Sclerosis (NEALS) Meeting demonstrating a safety profile that was well-tolerated after single ascending doses and 14 days of multiple ascending doses taken orally once or twice daily, with favorable pharmacokinetic properties and excellent CNS penetrance. Maximum median inhibition of pS66-RIPK1 levels in blood cells from the study participants ranged between 93% to 99% after multiple doses, reflecting marked RIPK1-target engagement. The data further support the ongoing global Phase 2 HIMALAYA study in participants with amyotrophic lateral sclerosis (ALS). 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.

DNL343 (eIF2B activator): ALS

- Denali plans to present data from the ongoing Phase 1b study of DNL343 in participants with ALS at the International Symposium on ALS/MND being held virtually, December 6 – 9, 2022.
- Based on Phase 1 data and ongoing blinded Phase 1b data, Denali has initiated planning for a late-stage study in ALS in 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 blood-brain barrier and intended as potential treatments for patients with neurodegenerative diseases.

Recent Corporate Updates

In October 2022, Denali raised net proceeds of approximately $296.2 million through a public offering of its common stock.

Participation in Upcoming Investor Conferences

- Credit Suisse 31st Annual Healthcare Conference, November 7 - 10
- Stifel 2022 Healthcare Conference, November 15 - 16
- Jefferies London Healthcare Conference, November 15 - 17
- Evercore ISI 5th Annual HealthCONx Conference, November 29 - December 1
- Jefferies 5th Annual Denver Biopharma Summit, December 14 -15

Third Quarter 2022 Financial Results

For the three months ended September 30, 2022, Denali reported a net loss of $103.3 million compared to a net loss of $84.6 million for the three months ended September 30, 2021.

Collaboration revenue was $3.6 million for the three months ended September 30, 2022, compared to $5.3 million for the three months ended September 30, 2021. The decrease in collaboration revenue of $1.7 million for the three months ended September 30, 2022, compared to the comparative period in the prior year was primarily due to a decrease in revenue from our collaboration with Takeda as the preclinical performance obligations are now satisfied under the Takeda Collaboration Agreement, partially offset by an increase in revenue from our collaboration with Sanofi pertaining to Alzheimer's Disease service performance.

Total research and development expenses were $87.8 million for the three months ended September 30, 2022, compared to $71.6 million for the three months ended September 30, 2021. The increase of approximately $16.2 million was primarily attributable to an increase in ETV:IDS program external expenses due to progress in the clinic in 2022, LRRK2 program external expenses primarily due to the $5.0 million clinical milestone payment owed to Genentech, which was triggered upon commencement of dosing in the global phase 3 LIGHTHOUSE study of BIIB122/DNL151 by Biogen, and personnel-related expenses, including employee compensation and 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 eIF2B and PTV:PGRN programs, the advancement of the TV platform as well as Denali's continued overall investment in developing a broad pipeline. These expense increases were partially offset by decreases in ATV:TREM2 program external expenses due to timing of clinical activities and increases in cost sharing reimbursements.

General and administrative expenses were $23.3 million for the three months ended September 30, 2022, compared to $19.3 million for the three months ended September 30, 2021. The increase of approximately $4.0 million 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 other general corporate services costs including IT services and subscriptions, taxes, travel-related expenses, and consulting and legal professional services expenses.

Cash, cash equivalents, and marketable securities were approximately $1.11 billion as of September 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, 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 ongoing Phase 3 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 DNL788 of both Denali and Sanofi, including with respect to expected enrollment for a Phase 2 trial in ALS; 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; 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 September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Collaboration revenue:				
Collaboration revenue from customers[1]	$ 184	$ 5,285	$ 94,805	$ 36,143
Other collaboration revenue	3,375	—	3,375	4
Total collaboration revenue	3,559	5,285	98,180	36,147
Operating expenses:				
Research and development[2]	87,786	71,559	266,621	197,477
General and administrative	23,259	19,319	66,959	57,300
Total operating expenses	111,045	90,878	333,580	254,777
Loss from operations	(107,486)	(85,593)	(235,400)	(218,630)
Interest and other income, net	4,187	1,005	8,114	3,310
Loss before income taxes	(103,299)	(84,588)	(227,286)	(215,320)
Income tax expense	—	—	(27)	—
Net loss	$ (103,299)	$ (84,588)	$ (227,313)	$ (215,320)
Net loss per share, basic and diluted	$ (0.84)	$ (0.69)	$ (1.85)	$ (1.77)
Weighted average number of shares outstanding, basic and diluted	123,473,390	121,742,067	123,054,889	121,309,197

(1) Includes related-party collaboration revenue from a customer of $0.2 million and $2.9 million for the three and nine months ended September 30, 2022, respectively, and $0.9 million and $2.5 million for the three and nine months ended September 30, 2021, respectively.

(2) Includes expense for cost sharing payments due to a related party of $1.4 million and $3.8 million for the three and nine months ended September 30, 2022, respectively, and an offset to expense from related-party cost sharing reimbursements of $1.2 million and $5.3 million for the three and nine months ended September 30, 2021, respectively.

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

	September 30, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 118,615	$ 293,477
Short-term marketable securities	987,440	571,930
Cost sharing reimbursements due from related party	—	1,226
Prepaid expenses and other current assets	32,471	30,601
Total current assets	1,138,526	897,234
Long-term marketable securities	—	425,449
Property and equipment, net	41,692	38,865
Operating lease right-of-use assets	31,271	30,743
Other non-current assets	16,117	11,871
Total assets	$ 1,227,606	$ 1,404,162
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 7,539	$ 4,779
Cost sharing payments due to related party	1,443	—
Accrued compensation	13,253	19,013
Accrued clinical and other research & development costs	21,701	15,887
Accrued manufacturing costs	16,732	9,955
Other accrued costs and current liabilities	2,395	2,857
Operating lease liabilities, current	7,068	5,453
Related-party contract liability, current	290,516	292,386
Contract liabilities, current	23	27,915
Total current liabilities	360,670	378,245
Related-party contract liability, less current portion	276	1,295
Contract liabilities, less current portion	—	3,398
Operating lease liabilities, less current portion	54,978	58,554
Other non-current liabilities	379	379
Total liabilities	416,303	441,871
Total stockholders' equity	811,303	962,291
Total liabilities and stockholders’ equity	$ 1,227,606	$ 1,404,162

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