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 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 November 4, 2021, Denali Therapeutics Inc. (the "Company") issued a press release announcing its financial results for the third quarter ended September 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 November 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: November 4, 2021

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

Denali Therapeutics Reports Third Quarter 2021 Financial Results and Business Highlights

SOUTH SAN FRANCISCO – November 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 third quarter ended September 30, 2021, and provided business highlights.

“We continue to advance our broad therapeutic pipeline, strengthen our strategic collaborations, and build out our manufacturing and commercial capabilities,” said Ryan Watts, Ph.D., Denali's Chief Executive Officer. “In the third quarter, we began a Phase 1b study of our potential first-in-class eIF2B activator, DNL343, in individuals with amyotrophic lateral sclerosis (ALS). Also in ALS, Sanofi has advanced our RIPK1 inhibitor, SAR443820 (DNL788), into Phase 2 development. In Parkinson’s disease (PD), we presented a progress update at Biogen’s R&D Day event on our LRRK2 inhibitor collaboration, highlighting data and activities to support late-stage development of BIIB122 (DNL151). In addition, our Transport Vehicle (TV)-enabled portfolio continues to move forward. Our Phase 1/2 study of DNL310 (ETV:IDS) for Hunter syndrome is now enrolling Cohort C, which is designed to further explore clinical endpoints in participants younger than four years of age. In parallel, we have begun activities to initiate a pivotal Phase 2/3 study of DNL310 for Hunter syndrome in the first half of 2022. Furthermore, we have started building out a clinical manufacturing facility to support our development plans and expansion of our TV platform programs.”

Recent Pipeline Highlights

Expanding antisense oligonucleotides (ASOs) research collaboration with Secarna: In October 2021, Denali and Secarna expanded their strategic research collaboration for the discovery and development of ASOs to treat neurodegenerative diseases with the addition of multiple new targets and indications. As part of the research collaboration originally formed in the fall of 2020, Secarna uses its discovery and development platform, LNA-plus™ to generate ASO candidates and Denali applies its Oligonucleotide Transport Vehicle (OTV) technology designed to enhance central nervous system (CNS) delivery of ASOs. Following the discovery period, Denali is solely responsible for all development and commercialization activities. Secarna will receive a target-based technology access fee and prepaid R&D fee and is eligible to receive milestone payments and royalties for each program that Denali progresses through development and commercialization.

Commenced dosing in Phase 1b study of eIF2B activator DNL343 in ALS: In October 2021, Denali presented results from a Phase 1 healthy volunteer study demonstrating that DNL343 met safety and biomarker goals. The Phase 1 data supported initiation of a Phase 1b study in participants with ALS, which commenced dosing in August 2021 (study number NCT05006352). The Phase 1b study is a multicenter, randomized, placebo-controlled, double-blind, 28-day study followed by an 18-month open-label extension, designed to evaluate the safety, pharmacokinetics, and pharmacodynamics of DNL343 in approximately 30 participants with ALS. Further information on the Phase 1b study can be accessed on the ClinicalTrials.gov website or by clicking here.

Advancing CNS-penetrant RIPK1 inhibitor SAR443820 (DNL788) into Phase 2 study in ALS: In October 2021, Denali announced that its partner Sanofi advanced development of SAR443820 in ALS and that the U.S. FDA granted SAR443820 Fast Track designation for the potential treatment of ALS. Results from a Phase 1 study of SAR443820 in healthy volunteers demonstrated robust target engagement at doses that were generally well tolerated. Sanofi plans to initiate the Phase 2 study, named HIMALAYA, in the first quarter of 2022.

Presented BIIB122 (DNL151) program progress in PD at Biogen's R&D Day: In September, at Biogen's R&D Day event, Denali provided a progress update on its collaboration with Biogen to develop BIIB122 (DNL151) for PD. The companies highlighted data supporting the advancement to late-stage clinical development and ongoing start-up activities for BIIB122 (DNL151) in preparation to commence PD studies. As previously announced, two studies are planned: one in participants with PD who do not carry a LRRK2 mutation and another in PD participants with LRRK2 mutations. Biogen will lead operationalization and conduct of these studies.

Published preclinical proof of concept for DNL593 (PTV:PGRN) in *Cell*: In August, Denali announced publication of the company's research in *Cell* demonstrating preclinical proof of concept for using its Protein Transport Vehicle (PTV) to enhance brain uptake of peripherally administered progranulin (PTV:PGRN) by multiple cell types in the brain, including neurons and microglia. In addition, PTV:PGRN rescued both neurodegeneration and microglial dysfunction in progranulin-deficient mice. This research supports the potential utility of DNL593 in treating certain types of frontotemporal dementia (FTD), especially FTD-GRN caused by progranulin deficiency.

Recent Corporate Highlights

Expanding leadership: In September 2021, Denali announced the appointment of Katie Peng to the newly created role of Chief Commercial Officer. Ms. Peng is a proven commercial leader with broad global experience in building and running commercial organizations and successfully launching products for people with neurological and rare diseases. Ms. Peng most recently served as the Senior Vice President, Head of the OMNI Business Unit at Genentech where she was responsible for the neurology, ophthalmology, immunology, respiratory, and rare diseases portfolio representing approximately $14 billion in annual revenues and served as part of Genentech's commercial leadership team. In addition, Denali announced expansion of its Scientific Advisory Board with the appointment of Melissa Starovasnik, Ph.D., an accomplished scientific leader and executive in the fields of protein sciences, including protein/antibody therapeutics, structural biology, and small molecule drug discovery and development. Dr. Starovasnik is a 28-year veteran of Genentech who served as Vice President, Protein Sciences and leader of the large-molecule drug discovery organization from 2011-2017, and most recently as Senior Scientific Advisor, Research.

Expanding clinical manufacturing capabilities: In August 2021, Denali entered into an operating lease for approximately 50,000 square feet of laboratory, office and warehouse premises in Salt Lake City, Utah. Denali has initiated the build-out of the Utah site to expand its clinical manufacturing capabilities for biologic therapeutics (large molecules) with the goal of increasing flexibility and speed in advancing new investigational therapies into clinical trials.

Summary Table of Upcoming 2021 Expected Key Milestones

Timing	Investigational Drug Candidate	Therapeutic Area	Expected Milestone
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:

- Stifel 2021 Virtual Healthcare Conference, November 15-17
- 12th Annual Jefferies London Healthcare Conference, November 16-19
- 4th Annual Evercore ISI HealthCONx Conference, November 30 - December 2
- J.P. Morgan Healthcare Conference, January 10-13, 2022

Third Quarter 2021 Financial Results

For the three months ended September 30, 2021, Denali reported a net loss of $84.6 million compared with a net loss of $58.2 million for the three months ended September 30, 2020.

Collaboration revenue was $5.3 million for the three months ended September 30, 2021, compared to $9.4 million for the three months ended September 30, 2020. The decrease of $4.1 million in collaboration revenue was primarily due to a decrease in revenue from our collaboration with Takeda driven by decreased costs incurred in the underlying partnered programs.

Total research and development expenses were $71.6 million for the three months ended September 30, 2021, compared to $53.7 million for the three months ended September 30, 2020. The increase of approximately $17.9 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 $19.3 million for the three months ended September 30, 2021, compared to $15.8 million for the three months ended September 30, 2020. The increase of approximately $3.5 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 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 since the prior period included those expenses associated with the execution of the Biogen collaboration agreements.

Cash, cash equivalents, and marketable securities were approximately $1.36 billion as of September 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 enrollment in the Phase 1/2 study of DNL310 for Hunter Syndrome and the initiation of a Phase 2/3 study; plans and expectations relating to the build-out of a clinical manufacturing facility in Utah to expand clinical manufacturing capabilities for biologic therapeutics, including the expansion of Denali's TV platform programs; plans, timelines and expectations related to DNL151 of both Denali and Biogen, including with respect to progress updates in support of late-stage clinical development; plans, timelines and expectations related to DNL343, including with respect to the Phase 1b study commenced in August, and the initiation of any future clinical trials; plans, timelines and expectations related to SAR443820(DNL788) of both Denali and Sanofi, including with respect to the plans to initiate a Phase 2 study in the first quarter of 2022, the Fast Track designation granted to SAR443820 for the potential treatment of ALS 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 expectations regarding its expanded research collaboration with Secarna for the discovery and development of ASOs; 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, Secarna 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 attract, motivate and retain qualified managerial, scientific and medical personnel; 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 September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Collaboration revenue:				
Collaboration revenue from customers[1]	$ 5,285	$ 9,388	$ 36,143	$ 18,751
Other collaboration revenue	—	5	4	93
Total collaboration revenue	5,285	9,393	36,147	18,844
Operating expenses:				
Research and development[2]	71,559	53,704	197,477	157,872
General and administrative	19,319	15,805	57,300	42,332
Total operating expenses	90,878	69,509	254,777	200,204
Loss from operations	(85,593)	(60,116)	(218,630)	(181,360)
Interest and other income, net	1,005	1,944	3,310	7,611
Loss before income taxes	(84,588)	(58,172)	(215,320)	(173,749)
Income tax expense	—	(56)	—	—
Net loss	$ (84,588)	$ (58,228)	$ (215,320)	$ (173,749)
Net loss per share, basic and diluted	$ (0.69)	$ (0.54)	$ (1.77)	$ (1.65)
Weighted average number of shares outstanding, basic and diluted	121,742,067	107,490,702	121,309,197	105,217,770

(1) Includes related party collaboration revenue from customer of $0.9 million and $2.5 million for the three and nine months ended September 30, 2021, respectively.
(2) Includes an offset to expense from related party cost reimbursement 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, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 394,553	$ 507,144
Short-term marketable securities	644,622	962,553
Cost sharing reimbursements due from related party	1,194	5,674
Prepaid expenses and other current assets	15,140	20,284
Total current assets	1,055,509	1,495,655
Long-term marketable securities	319,472	32,699
Property and equipment, net	40,012	40,846
Operating lease right-of-use asset	31,196	32,618
Other non-current assets	3,777	2,462
Total assets	$ 1,449,966	$ 1,604,280
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 4,817	$ 1,071
Accrued compensation	10,534	20,503
Accrued manufacturing costs	13,142	7,140
Accrued clinical and other research & development costs	13,380	11,775
Other accrued costs and current liabilities	2,364	3,037
Operating lease liability, current	5,252	4,690
Related party contract liability, current	3,438	3,569
Contract liabilities, current	1,324	19,914
Total current liabilities	54,251	71,699
Related party contract liability, less current portion	291,434	293,849
Contract liabilities, less current portion	31,313	23,325
Operating lease liability, less current portion	59,990	64,175
Other non-current liabilities	701	701
Total liabilities	437,689	453,749
Total stockholders' equity	1,012,277	1,150,531
Total liabilities and stockholders' equity	$ 1,449,966	$ 1,604,280

Investor Relations Contact:

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

Media Contacts:

Lizzie Hyland
(646) 495-2706
lizzie.hyland@fgh.com

or

Morgan Warners
(202) 295-0124
morgan.warners@fgh.com