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):
February 25, 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 February 25, 2021, Denali Therapeutics Inc. (the "Company") issued a press release announcing its financial results for the fourth quarter and year ended December 31, 2020. 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 February 25, 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: February 25, 2021

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

Denali Therapeutics Reports Full Year 2020 Financial Results and Business Highlights

SOUTH SAN FRANCISCO – February 25, 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 full year ended December 31, 2020 and provided business highlights.

"We kicked off 2021 with more encouraging data from our ETV:IDS (DNL310) Phase 1/2 study in Hunter syndrome, further suggesting that we may be able to treat a wide array of diseases with CNS and bodily manifestations via intravenous infusion by leveraging our blood-brain barrier Transport Vehicle technology," said Ryan Watts, Ph.D., Denali's Chief Executive Officer. "In 2021 we plan to advance our lead LRRK2 inhibitor, DNL151 (BIIB122), with Biogen into late-stage development for Parkinson's disease and initiate our first patient study with our lead EIF2B activator, DNL343, in amyotrophic lateral sclerosis (ALS). In our RIPK1 inhibitor program partnered with Sanofi, we expect DNL758 (SAR443122), our lead peripherally-restricted molecule, to enter a Phase 2 study for cutaneous lupus erythematosus (CLE) and DNL788 (SAR443820), our lead brain-penetrant molecule, to complete a Phase 1 study in healthy volunteers. In parallel, we continue to advance additional therapeutic modalities, including PTV:PGRN (DNL593) for frontotemporal dementia and ATV:TREM2 (DNL919) for Alzheimer's disease, towards the clinic. We believe that we are well positioned to deliver on our ambitious goals this year on our path to becoming a fully integrated global organization to serve patients with neurodegenerative diseases."

Recent Business Highlights

Reported positive 3-month data from Phase 1/2 study of DNL310 in patients with Hunter syndrome (MPS II): In February 2021, Denali reported additional interim data from Cohort A (n=5) in its Phase 1/2 study of DNL310 in patients with Hunter syndrome. The data showed that at dose levels resulting in robust and durable glycosaminoglycan (GAG) response in the central nervous system (CNS) and periphery, DNL310 was generally well tolerated with a safety profile consistent with standard of care enzyme replacement therapy (ERT). In addition, early effects on GAGs initially seen after four weeks of treatment with DNL310 (as announced in November 2020) were sustained after three months of dosing, and reductions in levels of exploratory lipid biomarkers in the CSF indicated an improvement in lysosomal function. Enrollment in Cohort B (approximately 12 patients) is ongoing and, as announced in January 2021, Denali plans to add a third Cohort C (approximately 12 patients) to the ongoing Phase 1/2 study to enable further exploration of clinical endpoints in younger neuronopathic patients.

Added five new Enzyme Transport Vehicle (ETV) programs for LSDs: In January 2021, following achievement of human biomarker proof of concept for its Transport Vehicle (TV) technology, Denali announced five new brain-penetrant ERT programs in its ETV portfolio including: (1) ETV:GBA for Gaucher disease and Parkinson's disease; (2) ETV:GAA for Pompe disease; (3) ETV:IDUA for MPS I; (4) ETV:NAGLU for MPS IIIB; and (5) ETV:ARSA for MLD.

Expanding manufacturing capabilities and continuing to build out commercial capabilities: In January 2021, in conjunction with broadening of its ETV development portfolio, Denali announced that activities are underway to expand clinical manufacturing capabilities and to continue to build out commercial capabilities. More than 30,000 patients suffer from lysosomal storage diseases (LSDs) world-wide, with approximately two-thirds having CNS manifestations that are not addressed by currently available ERTs. Denali believes that DNL310 has the potential to be its first approved medicine and that certain efficiencies of scale can be leveraged in the LSD field to support further development and potential commercialization of additional therapeutics for LSDs.

Completed Phase 1b study of DNL151 (BIIB122), supporting late-stage development: In January 2021, Denali announced that its Phase 1b study of LRRK2 inhibitor, DNL151, in Parkinson's disease was completed and met target engagement and pathway engagement goals. Denali and Biogen expect to initiate late-stage clinical development of DNL151 in Parkinson's patients by year-end 2021. Two clinical studies are planned: one in Parkinson's patients who carry LRRK2 mutations and the other in Parkinson's patients independent of mutation status.

Reported completion of single ascending dose portion of DNL343 Phase 1 study in healthy volunteers: Mutations in genes associated with ALS and frontotemporal dementia (FTD) alter RNA homeostasis, which contributes to the aggregation of TDP-43 or other RNA binding proteins observed in a large proportion of patients. Activators of EIF2B have demonstrated benefits in resolving TDP-43 aggregation, restoring protein translation and attenuating neurodegeneration via inhibition of the cellular integrated stress response (ISR) in numerous *in vitro* and *in vivo* models. Denali's lead EIF2B activator, DNL343, is a brain-penetrant small molecule designed to rescue EIF2B function and restore normal RNA metabolism. In January 2021, Denali reported completion of dosing in the single ascending dose portion of its Phase 1 study of DNL343 with safety, tolerability, pharmacokinetic and pharmacodynamic data supporting pathway engagement and continued development. Denali plans to initiate a Phase 1b study of DNL343 in patients with ALS in 2H 2021.

RIPK1 program updates: In October 2020, Denali announced that its partner Sanofi submitted an investigational new drug (IND) application for DNL788 (SAR443820), a potent, selective and brain-penetrant small molecule inhibitor of RIPK1 intended to treat patients with Alzheimer's disease, ALS, multiple sclerosis (MS) and potentially other indications. First-in-human dosing in a healthy volunteer study commenced in December 2020. In October 2020, Denali reported that Sanofi completed enrollment in a Phase 1b clinical trial of DNL758 (SAR443122), a peripherally-restricted small molecule inhibitor of RIPK1, in hospitalized adult patients with severe COVID-19 lung disease. DNL758 was found to be generally well tolerated and resulted in changes in disease relevant biomarkers and clinical outcome trends consistent with the proof of mechanism. Based on the rapidly evolving landscape of treatment and prevention options for COVID-19, Sanofi has made a sponsor decision to hold further development in COVID-19 at this time. Separately, Sanofi plans to initiate a Phase 2 clinical trial of DNL758 in CLE in early 2021.

Milestones with Takeda met for progress in PTV:PGRN and ATV:TREM2 programs: DNL593 (PTV:PGRN) and DNL919 (ATV:TREM2), intravenously administered recombinant biotherapeutics enabled by Denali's TV technology and intended for the potential treatment of frontotemporal dementia and Alzheimer's disease, respectively, have advanced into IND-enabling stage. For the achievement of this milestone, Denali received an $8 million milestone payment from Takeda in January 2021 for DNL593, and expects to receive another $8 million milestone payment for DNL919 later in Q1 2021.

Strong financial position: Cash, cash equivalents, and marketable securities were $1.5 billion as of December 31, 2020. For 2021, Denali anticipates an increase of approximately 20-25% in cash operating expenses compared to 2020.

Summary Table of Upcoming 2021 Expected Key Milestones

Timing	Investigational Drug Candidate	Therapeutic Area	Expected Milestone
Q1	ATV:TREM2 (DNL919)	Alzheimer's disease	Receive milestone payment from Takeda for initiation of IND-enabling studies
1H	RIPK1 inhibitor (DNL758)	CLE	Initiate Phase 2 study in CLE patients (Sanofi)
1H	EIF2B activator (DNL343)	ALS, FTD	Phase 1 data in healthy volunteers
Mid 2021	ETV:IDS (DNL310)	Hunter syndrome (MPS II)	24-week data from Cohort A of Phase 1/2 study
2H	EIF2B activator (DNL343)	ALS, FTD	Initiate Phase 1b study in ALS patients
2H	RIPK1 inhibitor (DNL788)	ALS, Alzheimer's disease, MS	Phase 1 data in healthy volunteers (Sanofi)
Late 2021	LRRK2 inhibitor (DNL151)	Parkinson's disease	Initiate late-stage clinical development
Late 2021	PTV:PRGN (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:

- H.C. Wainwright Global Life Sciences Conference, March 9-10
- Stifel CNS Day, March 31
- UBS Global Healthcare Virtual Conference, May 24-26
- Jefferies Healthcare Conference, June 1-3
- Goldman Sachs 42nd Annual Global Healthcare Conference, June 8-10

Fourth Quarter and Full Year 2020 Financial Results

Net income was $244.9 million and $71.1 million for the quarter and year ended December 31, 2020, compared to net losses of $54.0 million and $197.6 million for the quarter and year ended December 31, 2019, respectively.

Collaboration revenue was $316.8 million and $335.7 million for the quarter and year ended December 31, 2020, compared to $4.7 million and $26.7 million for the quarter and year ended December 31, 2019, respectively. The increases of $312.1 million and $309.0 million for the quarter and year ended December 31, 2020, respectively, compared to the same periods ended December 31, 2019 were primarily due to $307.4 million of revenue recognized under the Biogen Collaboration Agreement in 2020.

Total research and development expenses were $54.7 million and $212.6 million for the quarter and year ended December 31, 2020, compared to $51.6 million and $193.4 million for the quarter and year ended December 31, 2019, respectively. The increases of approximately $3.1 million and $19.2 million for the quarter and year ended December 31, 2020, respectively, were primarily attributable to an increase in personnel-related expenses, including stock-based compensation, driven primarily by higher headcount and additional equity award grants. 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 2020. Other increases include TV platform and other program external expenses reflecting the increased investment in Denali's pipeline. These increases were partially offset by a decrease in the LRRK2 program external expenses primarily due to cost sharing reimbursements from Biogen under the Biogen Collaboration Agreement as well as a decrease in other external research and development expenses.

General and administrative expenses were $18.0 million and $60.3 million for the quarter and year ended December 31, 2020, compared to $10.9 million and $46.5 million for the quarter and year ended December 31, 2019, respectively. The increases of approximately $7.1 million and $13.8 million for the quarter and year ended December 31, 2020, respectively, were primarily attributable to an increase in personnel-related expenses, including stock-based compensation, driven primarily by higher headcount and additional equity award grants. Additionally, there were increases in legal and other professional services expenses, including those associated with the execution of the Biogen Collaboration Agreement, and other general costs such as insurance, tax and IT related expenses.

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; the potential benefits, expectations and results of the collaboration with Biogen; plans to conduct clinical development activities and commercialize products; LRRK2 inhibitors as modifying therapy for Parkinson's disease; plans, timelines and expectations related to DNL310 and Denali's TV technology; plans, timelines and expectations related to DNL151, including with respect to initiation of late-stage clinical development; plans, timelines and expectations related to DNL343, including with respect to the initiation of future clinical trials; plans, timelines and expectations related to DNL788 and DNL758 of both Denali and Sanofi, including with respect to the availability of data and the initiation of future clinical trials; Denali's expectations regarding DNL593 and DNL919 and plans and expectations regarding planned regulatory filings and milestone payments with respect to such programs; Denali's priorities, regulatory approvals, timing and likelihood of success and expectations regarding collaborations; Denali's plans to expand clinical manufacturing and commercial capabilities; Denali's expectations regarding cash operating expenses for 2021; 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 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 product candidates currently in its core program; Denali's and it's 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 or clinical trials of any other product candidates to differ from preclinical, preliminary or expected results; 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 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 December 31,		Twelve Months Ended December 31,	
	2020	2019	2020	2019
Collaboration revenue:				
Collaboration revenue from customers[1]	$ 316,810	$ 4,603	$ 335,561	$ 26,320
Other collaboration revenue	5	69	98	358
Total collaboration revenue	316,815	4,672	335,659	26,678
Operating expenses:				
Research and development[2]	54,743	51,551	212,615	193,382
General and administrative	17,994	10,879	60,326	46,480
Total operating expenses	72,737	62,430	272,941	239,862
Income (loss) from operations	244,078	(57,758)	62,718	(213,184)
Interest and other income, net	1,630	3,808	9,241	15,219
Income (loss) before income taxes	245,708	(53,950)	71,959	(197,965)
Income tax (expense) benefit	(823)	(75)	(823)	351
Net income (loss)	$ 244,885	$ (54,025)	$ 71,136	$ (197,614)
Net income (loss) per share:				
Basic net income (loss) per share	2.04	(0.56)	0.65	(2.07)
Diluted net income (loss) per share	1.91	(0.56)	0.63	(2.07)
Weighted-average shares used in calculating:				
Basic net income (loss) per share	120,161,578	96,078,950	108,974,137	95,608,208
Diluted net income (loss) per share	128,297,841	96,078,950	112,703,108	95,608,208

(1) Includes related party collaboration revenue from customer of $307,437 for the quarter and year ended December 31, 2020.
(2) Includes an offset to expense from related party cost reimbursement of $9,260 for the quarter and year ended December 31, 2020.

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

	December 31, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 507,144	$ 79,449
Short-term marketable securities	962,553	335,907
Cost sharing reimbursements due from related party	5,674	—
Prepaid expenses and other current assets	20,284	14,675
Total current assets	1,495,655	430,031
Long-term marketable securities	32,699	39,886
Property and equipment, net	40,846	46,732
Operating lease right-of-use asset	32,618	33,923
Other non-current assets	2,462	2,659
Total assets	$ 1,604,280	$ 553,231
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 1,071	$ 2,590
Accrued expenses and other current liabilities	47,145	24,015
Related party contract liability, less current portion	3,569	—
Contract liabilities, current	19,914	18,739
Total current liabilities	71,699	45,344
Contract liabilities, less current portion	23,325	43,753
Related party contract liabilities, less current portion	293,849	—
Operating lease liability, less current portion	64,175	68,865
Other non-current liabilities	701	379
Total liabilities	453,749	158,341
Total stockholders' equity	1,150,531	394,890
Total liabilities and stockholders' equity	$ 1,604,280	$ 553,231

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