Denali Therapeutics Reports First Quarter 2024 Financial Results and Business Highlights

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SOUTH SAN FRANCISCO, Calif., May 07, 2024 (GLOBE NEWSWIRE) -- 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, 2024, and provided business highlights.

"It has been an impactful first quarter, and we are excited about multiple opportunities to accelerate and expand our portfolio. We presented new positive two-year clinical data on tividenofusp alfa in MPS II at WORLD*Symposium*™*,* and we are encouraged by recent interactions with the FDA about the potential path to patients," said Ryan Watts, Ph.D., Chief Executive Officer of Denali Therapeutics. “We also initiated the first clinical trial with our second enzyme replacement therapy, DNL126, for children with MPS IIIA, and we achieved an important milestone with our eIF2B agonist program, DNL343, completing enrollment in the Phase 2/3 HEALEY ALS Platform Trial. With a focus on our Transport Vehicle platform and additional capital raised, we are well positioned to lead in the promising field of BBB-crossing therapeutics for people living with neurodegenerative and lysosomal storage diseases."

First Quarter 2024 and Recent Program Updates

Late-stage and mid-stage clinical programs

Tividenofusp alfa (DNL310): Enzyme Transport Vehicle (ETV)-enabled, iduronate-2-sulfatase (IDS) replacement therapy in development for MPS II (Hunter syndrome)

- In February, new positive data from the ongoing Phase 1/2 study of tividenofusp alfa in MPS II were presented at the 20th Annual WORLD*Symposium*™ demonstrating sustained normalization of heparan sulfate in cerebrospinal fluid (CSF HS), robust and sustained reductions in biomarkers of lysosomal dysfunction and neuronal damage (NfL; neurofilament light), and improvements and stabilization of multiple clinical outcomes measures over two years of treatment.
- Also in February, Denali participated in the Reagan-Udall Foundation for the Food and Drug Administration (FDA) workshop on CSF HS as a potential surrogate biomarker to support accelerated approval in MPS.
- Based on continued dialogue with the Center for Drug Evaluation and Research (CDER) division of the FDA, Denali believes the division may be open to discussing an accelerated path for tividenofusp alfa. Denali looks forward to continuing the productive dialogue with CDER and, in parallel, conducting the global Phase 2/3 COMPASS study, which is expected to complete enrollment in 2024.

DNL343: eIF2B activator in development for the treatment of amyotrophic lateral sclerosis (ALS)

- In May, the Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital (MGH) in collaboration with the Northeast ALS Consortium (NEALS) announced that enrollment is complete in Regimen G (DNL343) of the Phase 2/3 HEALEY ALS Platform Trial.

SAR443820/DNL788: CNS-penetrant RIPK1 inhibitor in development for the treatment of multiple sclerosis (MS)

- Sanofi is evaluating SAR443820/DNL788 in a Phase 2 study in participants with MS, which is fully enrolled.
- In February, Sanofi discontinued development of SAR443820/DNL788 in ALS based on the results of the Phase 2 HIMALAYA study, which did not meet the primary endpoint.

BIIB122/DNL151: LRRK2 inhibitor in development for the treatment of Parkinson’s disease (PD)

- In February, Denali announced the execution of a Collaboration and Development Funding Agreement with a third party related to a global Phase 2a study of BIIB122/DNL151, which Denali plans to solely operationalize to evaluate safety and biomarkers associated with BIIB122 in participants with Parkinson’s disease and confirmed pathogenic variants of LRRK2. Denali plans to initiate the Phase 2a study in 2024.
- Biogen is conducting the ongoing global Phase 2b LUMA study of BIIB122 in participants with early-stage Parkinson’s disease.

Eclitasertib (SAR443122/DNL758): Peripheral RIPK1 inhibitor in development for the treatment of ulcerative colitis (UC)

- Sanofi is conducting the ongoing Phase 2 study of SAR443122/DNL758 in participants with UC.

Early-stage clinical and preclinical programs

DNL126: ETV-enabled N-sulfoglucosamine sulfohydrolase (SGSH) replacement therapy in development for the treatment of MPS

IIIA (Sanfilippo syndrome Type A)

- In February, Denali announced initiation of dosing in the Phase 1/2 study of DNL126 in participants with MPS IIIA and presented supportive preclinical data at WORLD*Symposium* ™ .
- Phase 1/2 biomarker and safety data are expected by the end of 2024.

TAK-594/DNL593: Protein Transport Vehicle (PTV)-enabled progranulin (PGRN) replacement therapy in development for the treatment of frontotemporal dementia-granulin (FTD-GRN)

- In January, Denali announced a voluntary pause in the DNL593 Phase 1/2 study in participants with FTD-GRN to implement protocol modifications and expects the study to resume this year.

Oligonucleotide Transport Vehicle (OTV) platform

- Denali is advancing OTV:MAPT, targeting tau for Alzheimer's disease, and OTV:SNCA, targeting alpha-synuclein for Parkinson's disease, in the investigational new drug (IND)-enabling stage of development.

Antibody Transport Vehicle Amyloid beta (ATV:Abeta) program

- ATV:Abeta using Denali's TfR-targeting TV technology is licensed by Biogen and is in the IND-enabling stage of development.

Discovery programs

Denali applies its deep scientific expertise in neurodegeneration biology and the BBB to discover and develop medicines and platforms with the focus on programs enabled by the TV technology and targeting neurodegenerative disease, including Alzheimer's and Parkinson's, and lysosomal storage diseases.

Corporate Updates

- In February, Denali announced completion of a private investment in public equity (PIPE) financing with gross proceeds of $500 million.
- In January, Denali announced the intention to divest the company's preclinical small molecule portfolio, which was completed on March 1, 2024.

Participation in Upcoming Investor Conferences

- BofA Securities Healthcare Conference 2024, May 14-16
- Jefferies Global Healthcare Conference, June 5-6
- Goldman Sachs 45th Annual Global Healthcare Conference, June 10-13

First Quarter 2024 Financial Results

Net loss was $101.8 million for the quarter ended March 31, 2024, compared to net loss of $109.8 million for the quarter ended March 31, 2023.

There was no collaboration revenue for the quarter ended March 31, 2024, compared to $35.1 million for the quarter ended March 31, 2023. The decrease in collaboration revenue was primarily due to decreases in revenue earned under the Sanofi Collaboration and Takeda Collaboration of $25.0 million and $10.0 million, respectively.

Total research and development expenses were $107.0 million for the quarter ended March 31, 2024, compared to $128.8 million for the quarter ended March 31, 2023. The decrease of approximately $21.8 million for the quarter ended March 31, 2024 compared to the comparative period in the prior year was primarily attributable to a decrease in ETV:IDS program external expenses because the first quarter of 2023 included expense for a 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. Further, there were also decreases in external expenses associated with the ATV:TREM2 and PTV:PGRN programs due to the discontinuation of clinical development of TAK-920/DNL919 (ATV:TREM2) in Alzheimer's disease and voluntary pause of Part B in the TAK-594/DNL593 (PTV:PGRN) Phase 1/2 study, respectively. Additionally, there was a decrease in LRRK2 program external expenses due to the transition of LRRK2 clinical activities to Biogen. These decreases were partially offset by increases in the ETV:SGSH and eIF2B program external expenses reflecting the continued progress of these programs in clinical trials, and an increase in net cost sharing payments due to increased payments due to Biogen as a result of increased LRRK2 clinical trial costs incurred by Biogen.

General and administrative expenses were $25.2 million for the quarter ended March 31, 2024, compared to $27.1 million for the quarter ended March 31, 2023. The decrease of $1.9 million for the quarter ended March 31, 2024 was primarily attributable to $2.4 million of combined decreases in professional services, facilities and other corporate costs, partially offset by $0.5 million of increased personnel-related expenses consisting of employee compensation and stock-based compensation expense.

The loss from operations also includes a non-cash gain from divestiture of small molecule programs of $14.5 million, reflecting the

gain associated with the divestiture of assets associated with select preclinical small molecule programs in exchange for equity consideration.

Cash, cash equivalents, and marketable securities were approximately $1.43 billion as of March 31, 2024.

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; 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 as well as the likelihood of receiving accelerated approval; plans and timelines regarding DNL343, including in Regimen G of the Phase 2/3 HEALEY ALS Platform Trial; plans, timelines, and expectations of both Denali and Sanofi regarding DNL788, including the Phase 2 study in MS; plans, timelines, and expectations regarding DNL151, including with respect to the ongoing LUMA study as well as enrollment and timing of the proposed Phase 2a study in PD patients with LRRK2 mutations; expectations regarding DNL758, including the ongoing Phase 2 study in patients with UC; plans, timelines, and expectations related to DNL126, including the timing and availability of data in the ongoing Phase 1/2 study; plans, timelines, and expectations of both Denali and Takeda regarding DNL593 and the ongoing Phase 1/2 study, including the timing of continuation of the study; plans, timelines, and expectations regarding the advancement of OTV:MAPT towards clinical development; plans, timelines, and expectations of both Denali and Biogen regarding the ATV:Abeta; plans and expectations for Denali's preclinical programs; Denali's future operating expenses and anticipated cash runway; Denali's PIPE financing and its anticipated proceeds; and Denali's participation in upcoming investor conferences. 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 28, 2024 and May 7, 2024, 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,	
	2024	**2023**
Collaboration revenue:		
Collaboration revenue from customers[1]	$ —	$ 35,141
Total collaboration revenue	—	35,141
Operating expenses:		
Research and development[2]	107,016	128,816
General and administrative	25,236	27,140

Total operating expenses	132,252	155,956
Gain from divestiture of small molecule programs	14,537	—
Loss from operations	(117,715)	(120,815)
Interest and other income, net	15,913	11,034
Net loss	$ (101,802)	$ (109,781)
Net loss per share, basic and diluted	$ (0.68)	$ (0.80)
Weighted average number of shares outstanding, basic and diluted	149,404,188	136,524,528

(1) Includes related-party collaboration revenue from customers of $0.1 million for the three months ended March 31, 2023.
(2) Includes expenses for cost sharing payments due to a related party of $4.2 million for the three months ended March 31, 2023.

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

	March 31, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	$ 60,574	$ 127,106
Short-term marketable securities	876,295	907,405
Prepaid expenses and other current assets	36,706	29,626
Total current assets	973,575	1,064,137
Long-term marketable securities	490,723	—
Property and equipment, net	46,863	45,589
Operating lease right-of-use asset	25,309	26,048
Other non-current assets	44,621	18,143
Total assets	$ 1,581,091	$ 1,153,917
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 11,855	$ 9,483
Accrued clinical and other research & development costs	19,956	19,035
Accrued manufacturing costs	16,720	15,462
Other accrued costs and current liabilities	5,986	5,152
Accrued compensation	8,053	21,590
Operating lease liability, current	7,512	7,260
Deferred research funding liability, current	12,500	—
Total current liabilities	82,582	77,982
Operating lease liability, less current portion	43,034	44,981
Total liabilities	125,616	122,963
Total stockholders' equity	1,455,475	1,030,954
Total liabilities and stockholders' equity	$ 1,581,091	$ 1,153,917

Investor and Media Contact:

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

DENALI THERAPEUTICS

Source: Denali Therapeutics Inc.