Denali Therapeutics Reports Third Quarter 2024 Financial Results and Business Highlights

November 6, 2024

SOUTH SAN FRANCISCO, Calif., Nov. 06, 2024 (GLOBE NEWSWIRE) -- Denali Therapeutics Inc. (Nasdaq: DNLI) today reported financial results for the third quarter ended September 30, 2024, and provided business highlights.

"As leaders in pioneering a new class of therapeutics that cross the blood-brain barrier, we are making significant progress across our Transport Vehicle (TV)-enabled portfolio," said Ryan Watts, Ph.D., Chief Executive Officer of Denali Therapeutics. "Within our Enzyme TV (ETV) franchise, we are on track to file for accelerated approval of tividenofusp alfa in MPS II in early 2025 after a successful meeting with the FDA in the third quarter. Today, we are also pleased to share that preliminary data from our Phase 1/2 study of DNL126 in MPS IIIA demonstrate a robust reduction from baseline in CSF heparan sulfate levels, including normalization. Based on these data and a positive regulatory environment, we recently expanded the study to support a potential accelerated path. In addition, our recent preclinical publication on our oligonucleotide TV (OTV) technology in *Science Translational Medicine*, which describes broad and deep brain biodistribution of oligonucleotides following systemic administration of OTV, demonstrates the power and potential of our TV platform to transform the way we treat brain diseases."

Third 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 September, announced the outcome of a successful meeting with the Center for Drug Evaluation and Research (CDER) of the U.S. Food and Drug Administration (FDA) providing a path to filing a biologics license application (BLA) for accelerated approval and subsequent conversion to full approval for tividenofusp alfa (DNL310) for the treatment of MPS II. Agreement was reached that cerebrospinal fluid heparan sulfate (CSF HS) is reasonably likely to predict clinical benefit and can be used as a surrogate endpoint to support accelerated approval for tividenofusp alfa in MPS II. Denali intends to submit the BLA under the accelerated approval pathway in early 2025.
- In September, presented new interim data from the Phase 1/2 study at the Society for the Study of Inborn Errors of Metabolism (SSIEM 2024), including data from additional study participants (N=37) and longer duration of treatment with tividenofusp alfa (up to Week 129) as well as new analyses on biomarkers and clinical outcomes.
- COMPASS, the global Phase 2/3 study, is expected to complete enrollment in 2024.

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

- DNL343 is being evaluated in Regimen G (DNL343) of the Phase 2/3 HEALEY ALS Platform Trial conducted by the Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital (MGH) in collaboration with the Northeast ALS Consortium (NEALS). Enrollment in Regimen G is complete.

SAR443820/DNL788: CNS-penetrant RIPK1 inhibitor

- In October, Denali was informed by its strategic partner Sanofi that the K2 Phase 2 study evaluating the safety and efficacy of oditrasertib (SAR443820/DNL788) on serum neurofilament light chain levels in participants with multiple sclerosis was discontinued based on not meeting the primary and key secondary endpoints.

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

- Biogen is conducting the ongoing global Phase 2b LUMA study of BIIB122 in participants with early-stage Parkinson's disease.
- Denali has initiated screening of participants for the global Phase 2a study to evaluate safety and biomarkers associated with BIIB122 in participants with Parkinson's disease and confirmed pathogenic variants of LRRK2. This study is being funded under the Collaboration and Development Funding Agreement with a third party.

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)

- Denali today announced that preliminary data from up to 25 weeks of dosing in the ongoing open-label Phase 1/2 study in MPS IIIA participants demonstrate a significant reduction in CSF HS levels from baseline, including normalization. The safety profile supports continued development. The most frequent treatment emergent adverse events were infusion related reactions of mild and moderate severity in all participants. There was one serious adverse event considered by the investigator not related to drug. Denali plans to present the data at a future medical meeting.
- Based on the preliminary Phase 1/2 results and a positive regulatory environment, Denali recently expanded the study and continues to assess the development plans including an accelerated approval path.
- DNL126 was selected in June 2024 for the FDA's Support for clinical Trials Advancing Rare disease Therapeutics (START) program to accelerate the development of rare disease therapeutics, and collaborative engagement has commenced to support progress to a pre-BLA meeting.

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

- Screening of participants for Cohort B2 in the Phase 1/2 study is ongoing.

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.
- In August, announced publication of nonclinical data in the August 14, 2024 issue of *Science Translational Medicine* (link) demonstrating the ability of the OTV platform to achieve broad biodistribution of antisense oligonucleotides (ASOs) in the central nervous system and skeletal and cardiac muscle following intravenous administration.

Antibody Transport Vehicle Amyloid beta (ATV:Abeta) program

- Denali is working to develop the next generation of anti-amyloid beta therapeutics with ATV:Abeta, which is designed to increase exposure of the therapeutic antibody and achieve broad biodistribution in the brain with the potential for improved efficacy and safety. Preclinical data demonstrated potential for a wider therapeutic window compared to a standard antibody, with superior plaque decoration and reduction and very low rates of amyloid related imaging abnormalities (ARIA). These data are included in a manuscript posted on bioRxiv (link).
- Denali plans to advance a TfR-targeting ATV:Abeta molecule as well as a CD98hc-targeting ATV:Abeta molecule into development for Alzheimer's disease.

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.

2024 Guidance on Operating Expenses

Cash, cash equivalents, and marketable securities were approximately $1.28 billion as of September 30, 2024. Denali is providing updated guidance on cash operating expenses for the full year 2024 and now anticipates an increase of approximately 5-10% compared to 2023, which is an increase from previous guidance of equal to or less than full year 2023 cash operating expenses. This updated guidance is associated with increased activities to support filing of a BLA in early 2025 and commercial readiness for tividenofusp alfa in MPS II, and to accelerate the development of additional therapeutic programs in Denali's TV platform portfolio.

Participation in Upcoming Investor Conferences

- UBS Global Healthcare Conference, November 11-14
- B. Riley Securities' Next-Gen Tissue Delivery Modalities Virtual Summit, November 14
- Stifel 2024 Healthcare Conference, November 18-19
- Jefferies London Healthcare Conference, November 19-21
- 7th Annual Evercore ISI HealthCONx Conference, December 3-5

Third Quarter 2024 Financial Results

Net losses were $107.2 million and $99.4 million for the three months ended September 30, 2024 and 2023, respectively.

There was no collaboration revenue for the quarter ended September 30, 2024, compared to $1.3 million for the quarter ended September 30, 2023. The decrease in collaboration revenue was primarily due to activities under the Biogen Collaboration Agreement.

Total research and development expenses were $98.2 million for the quarter ended September 30, 2024, compared to

$89.7 million for the quarter ended September 30, 2023. The increase of approximately $8.5 million for the quarter ended September 30, 2024 was primarily attributable to increases in costs in various clinical stage programs, including ETV:IDS, eIF2B, ETV:SGSH, and LRRK2 reflecting the continued progress of these programs in clinical trials, and increases in TV platform and other program external expenses, reflecting continued investment in TV-enabled product candidates. These increases were partially offset by a decrease in personnel and external expenses associated with the divestiture of Denali's preclinical small molecule programs.

General and administrative expenses were $24.9 million for the quarter ended September 30, 2024, and $25.3 million for the same period in 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; 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, the timing and likelihood of accelerated approval, and the timing and availability of program updates; plans and timelines regarding DNL343, including the timing and availability of data from the Phase 2/3 HEALEY ALS Platform Trial; plans, timelines, and expectations of both Denali and Sanofi regarding DNL788; 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 and the timing and likelihood of regulatory approval; plans, timelines, and expectations of both Denali and Takeda regarding DNL593 and the ongoing Phase 1/2 study; plans, timelines, and expectations regarding the advancement of OTV:MAPT and OTV:SNCA towards clinical development; plans, timelines, and expectations regarding the ATV:Abeta program, including its therapeutic potential and the clinical advancement of ATV:Abeta molecules; plans and expectations for Denali's preclinical programs; Denali's future operating expenses and anticipated cash runway; and Denali's participation in upcoming investor conferences. All drugs currently being developed by Denali are investigational and have not received regulatory approval for any indication. 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 August 1, 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 September 30,		Nine Months Ended September 30,	
	2024	**2023**	**2024**	**2023**

Collaboration revenue:				
Collaboration revenue from customers[1]	$ —	$ 1,267	$ —	$ 330,531
Other collaboration revenue	—	—	—	—
Total collaboration revenue	—	1,267	—	330,531
Operating expenses:				
Research and development[2]	98,238	89,737	296,653	316,073
General and administrative	24,949	25,325	75,379	78,585
Total operating expenses	123,187	115,062	372,032	394,658
Gain from divestiture of small molecule programs	—	—	14,537	—
Loss from operations	(123,187)	(113,795)	(357,495)	(64,127)
Interest and other income, net	15,995	14,442	49,475	38,376
Net loss	$ (107,192)	$ (99,353)	$ (308,020)	$ (25,751)
Net loss per share, basic and diluted	$ (0.63)	$ (0.72)	$ (1.89)	$ (0.19)
Weighted average number of shares outstanding, basic and diluted	169,456,988	137,644,534	162,589,325	137,076,199

(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.

(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.

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

	September 30, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	$ 90,636	$ 127,106
Short-term marketable securities	745,923	907,405
Prepaid expenses and other current assets	32,280	29,626
Total current assets	868,839	1,064,137
Long-term marketable securities	445,463	—
Property and equipment, net	50,822	45,589
Operating lease right-of-use asset	23,717	26,048
Finance lease right-of-use asset	38,685	—
Other non-current assets	26,487	18,143
Total assets	$ 1,454,013	$ 1,153,917
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 9,594	$ 9,483
Accrued clinical and other research & development costs	23,923	19,035
Accrued manufacturing costs	9,568	15,462
Accrued compensation	14,874	21,590
Operating lease liability, current	8,036	7,260
Deferred research and development funding liability, current	16,269	—
Other accrued costs and current liabilities	4,829	5,152
Total current liabilities	87,093	77,982
Operating lease liability, less current portion	38,850	44,981
Finance lease liability, less current portion	5,631	—
Deferred research funding and development liability, less current portion	3,944	—
Total liabilities	135,518	122,963
Total stockholders' equity	1,318,495	1,030,954
Total liabilities and stockholders’ equity	$ 1,454,013	$ 1,153,917

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