Denali Therapeutics Reports Fourth Quarter and Full Year 2023 Financial Results and Business Highlights

February 27, 2024

SOUTH SAN FRANCISCO, Calif., Feb. 27, 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 fourth quarter and year ended December 31, 2023, and provided business highlights.

"2023 was a year of significant progress across our broad therapeutic portfolio and further clinical validation of our BBB-crossing Transport Vehicle (TV) platform," said Ryan Watts, Ph.D., Chief Executive Officer of Denali. "In 2024, we expect to complete enrollment of our late-stage trials in MPS II and ALS as we establish commercial readiness for our product candidates in our first peak of programs. In addition, we are well positioned to expand our TV-enabled portfolio to address large neurodegenerative diseases with TV-enabled enzymes, antibodies, and oligonucleotides. We recognize the urgent needs of patients and families living with neurodegenerative and lysosomal storage diseases and we will continue to push for the fastest path to approval of effective medicines."

Fourth Quarter 2023 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)

- Presented additional interim data from the open-label, single-arm Phase 1/2 study of DNL310 at the 2024 WORLD*Symposium*™. Data out to 104 weeks showed additional improvement and stabilization in multiple measures of clinical outcomes, including those of adaptive behavior, cognition, hearing, and growth trajectory. In addition, robust and sustained responses in biomarkers of neuronal health (e.g., CSF heparan sulfate, neurofilament light (NfL)) and peripheral activity (e.g., urine heparan sulfate and dermatan sulfate) were observed. DNL310 continued to be generally well tolerated.
- Participated in the Reagan-Udall Foundation for the Food and Drug Administration (FDA) workshop that brought together FDA representatives, patient advocates, clinical and basic science researchers, and industry to explore a case study of CSF heparan sulfate as a relevant substrate biomarker to support accelerated approval in neuronopathic mucopolysaccharidoses (MPS).
- Enrollment continues in the global Phase 2/3 COMPASS study and is expected to be completed in 2024.

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

- Enrollment continues in Regimen G (DNL343) of the Phase 2/3 HEALEY ALS Platform Trial and is expected to be completed in 2024.

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

- As previously announced, Sanofi informed Denali that the Phase 2 HIMALAYA study evaluating SAR443820/DNL788 in participants with ALS did not meet the primary endpoint of change in ALS Functional Rating Scale-Revised (ALSFRS-R). Sanofi intends to present the detailed efficacy and safety results of the ALS Phase 2 HIMALAYA study at a future scientific forum.
- Sanofi is evaluating SAR443820/DNL788 in another Phase 2 clinical trial in participants with MS, and the outcome of HIMALAYA study has no impact on the ongoing MS study.

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

- Today Denali also announced the execution of a Collaboration and Development Funding Agreement in January 2024 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. This agreement includes committed funding of $75.0 million, of which $12.5 million was received in January 2024, and the remainder will be triggered based on time and operational milestones in the study. Biogen will continue to conduct the ongoing global Phase 2b LUMA study in early-stage Parkinson’s disease. Denali and Biogen will co-commercialize BIIB122/DNL151 assuming regulatory approval. The third party will be eligible to receive low single-digit royalties from Denali on annual worldwide net sales of LRRK2 inhibitors for the treatment of Parkinson’s disease, with royalty amounts varying based on the scope of the label.

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

- Sanofi is conducting the Phase 2 trial of SAR443122/DNL758 in 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)

- Initiated dosing in the Phase 1/2 study of DNL126 in MPS IIIA; biomarker proof of concept and safety data are expected by the end of 2024.
- Presented preclinical data at WORLD*Symposium*™ demonstrating that DNL126 improves lysosomal and microglial morphology, neurodegeneration, and cognitive function in adult MPS IIIA mice.

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

- Announced Part B has been voluntarily paused in the DNL593 Phase 1/2 study in participants with FTD-GRN to implement protocol modifications, and is expected to resume this year.

Oligonucleotide Transport Vehicle (OTV) platform

- Announced two lead OTV programs in the investigational new drug (IND)-enabling stage of development: OTV:MAPT targeting tau for Alzheimer's disease and OTV:SNCA targeting alpha-synuclein for Parkinson's disease.

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.
- Presented preclinical data showing superior amyloid plaque binding and reduction with ATV:Abeta compared to a conventional Abeta antibody and the potential for ATV:Abeta to reduce the risk of amyloid-related imaging abnormalities (ARIA) associated with the treatment of Alzheimer's disease.

Discovery programs

Denali continues to use 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.

- Announced the second TV platform, which targets CD98 heavy chain (CD98hc), an amino acid transporter expressed at the BBB. The CD98hc-targeting TV platform, having distinct properties from Denali's TfR-targeting TV platform, may enable selection of the optimal platform for a given drug target.

Corporate Updates

- Announced entering into a securities purchase agreement with certain existing accredited investors to issue and sell an aggregate of 3,244,689 shares of Denali's common stock at a price of $17.07 per share and pre-funded warrants to purchase an aggregate of 26,046,065 shares of Denali's common stock at a purchase price of $17.06 per pre-funded warrant, through a private investment in public equity (PIPE) financing. Denali anticipates the gross proceeds from the PIPE to be approximately $500 million.
- Announced the intention to spin out the company's preclinical small molecule portfolio. Denali will maintain ownership of and continue to advance its current portfolio of clinical stage small molecule programs. The decision was made based on clinical validation and prioritization of Denali's TV-enabled platforms for brain delivery of large molecules.

2024 Guidance on Operating Expenses:

Cash, cash equivalents, and marketable securities were approximately $1.03 billion as of December 31, 2023. For the full year 2024, Denali anticipates its operating expenses will be less than or equal to those in 2023 based on prioritization of its portfolio. With the anticipated proceeds from the PIPE financing, Denali expects the company's cash runway to extend into 2028.

Participation in Upcoming Investor Conferences:

- Cowen 44th Annual Health Care Conference, March 4-6
- Leerink Global Biopharma Conference, March 11-13
- Jefferies Biotech on the Bay Summit, March 12-13
- Stifel 2023 CNS Days, March 19-20

Fourth Quarter 2023 Financial Results

Net losses were $119.5 million and $145.2 million for the quarter and year ended December 31, 2023, compared to net losses of $98.7 million and $326.0 million for the quarter and year ended December 31, 2022, respectively.

There was no collaboration revenue for the quarter ended December 31, 2023, compared to $10.3 million for the quarter ended

December 31, 2022. Collaboration revenue was $330.5 million for the year ended December 31, 2023, compared to $108.5 million for the year ended December 31, 2022. The decrease in collaboration revenue of $10.3 million for the quarter ended December 31, 2023, compared to the comparative period in the prior quarter was primarily due to a decrease of revenue earned under the Sanofi Collaboration of $10.0 million for a milestone triggered in December 2022 upon first patient dosed in a Phase 2 study of SAR443122/DNL758 in individuals with UC. The increase in collaboration revenue of $222.0 million for the year ended December 31, 2023 compared to the previous year was primarily due to $293.9 million in revenue recognized in April 2023 under the Biogen Collaboration Agreement as a result of Biogen exercising its option to license our ATV:Abeta program, partially offset by a decrease of $41.9 million in revenue earned under the Takeda Collaboration Agreement, as well as a decrease of $28.4 million in milestone revenue earned under the Sanofi Collaboration Agreement. The decreases in revenues from the Sanofi and Takeda Collaboration Agreements are due to the timing of underlying activities and achievement of milestones under the collaboration agreements.

Total research and development expenses were $107.8 million and $423.9 million for the quarter and year ended December 31, 2023, compared to $92.1 million and $358.7 million for the quarter and year ended December 31, 2022, respectively. The increases of approximately $15.7 million and $65.2 million for the quarter and year ended December 31, 2023 compared to the comparative period in the prior year were primarily attributable to increases in ETV:IDS and eIF2B program external expenses reflecting the continued progress of these programs in clinical trials; and an increase in personnel-related expenses mainly driven by increased salary costs as a result of higher headcount. Furthermore, net cost sharing with collaboration partners shifted from reimbursements to payments due to decreased reimbursements from Takeda and increased payments to Biogen. These expense increases were partially offset by decreases in TV platform and other program external expenses, PTV:PGRN program external expenses and other external research and development expenses due to the timing of significant external research and manufacturing related activities period over period, and LRRK2 program external expenses due to the transition of LRRK2 clinical activities to Biogen. Further, for the quarter ended December 31, 2023, there was also a decrease in other unallocated research and development expenses as a result of reduced facility costs.

General and administrative expenses were $24.8 million and $103.4 million for the quarter and year ended December 31, 2023, compared to $23.5 million and $90.5 million for the quarter and year ended December 31, 2022, respectively. The increases of approximately $1.3 million and $12.9 million for the quarter and year ended December 31, 2023, respectively, were 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 was an increase in facility and other corporate costs for the year ended December 31, 2023 associated with the new Salt Lake City manufacturing facility.

Cash, cash equivalents, and marketable securities were approximately $1.03 billion as of December 31, 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 as well as the timing of approval; plans and timelines regarding DNL343, including enrollment for 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 and the timing of data in the Phase 2 study in ALS; 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, the potential for commercialization, and the achievement of milestones under the third-party agreement; 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 implementation of protocol modifications and timing of continuation of the study; plans, timelines, and expectations regarding the advancement of OTV candidates towards clinical development; plans, timelines, and expectations of both Denali and Biogen regarding the ATV:Abeta; plans and expectations for Denali's preclinical programs and the CD98hc-targeting TV platform; Denali's future operating expenses and anticipated cash runway; Denali's PIPE financing, including the number of shares and warrants and the 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 27, 2023 and November 7, 2023, 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 December 31,		Twelve Months Ended December 31,	
	2023	**2022**	**2023**	**2022**
Collaboration revenue:				
Collaboration revenue from customers[1]	$ —	$ 10,260	$ 330,531	$ 105,065
Other collaboration revenue	—	23	—	3,398
Total collaboration revenue	—	10,283	330,531	108,463
Operating expenses:				
Research and development[2]	107,803	92,111	423,876	358,732
General and administrative	24,769	23,516	103,354	90,475
Total operating expenses	132,572	115,627	527,230	449,207
Loss from operations	(132,572)	(105,344)	(196,699)	(340,744)
Interest and other income, net	13,129	6,660	51,505	14,774
Loss before income taxes	(119,443)	(98,684)	(145,194)	(325,970)
Income tax benefit (expense)	(30)	6	(30)	(21)
Net loss	$ (119,473)	$ (98,678)	$ (145,224)	$ (325,991)
Net loss per share, basic and diluted	$ (0.86)	$ (0.75)	$ (1.06)	$ (2.60)
Weighted average number of shares outstanding, basic and diluted	138,245,382	132,877,411	137,370,897	125,530,703

(1) Includes related-party collaboration revenue from customers of $0.3 million for the quarter ended December 31, 2022, and $295.5 million and $3.2 million for the year ended December 31, 2023 and 2022, respectively. There is no related-party collaboration revenue from customers for quarter ended December 31, 2023
(2) Includes expenses for cost sharing payments due to a related party of $3.2 million and $17.7 million for the quarter end year ended December 31, 2023, respectively, and $4.4 million and $8.2 million for the quarter and year ended December 31, 2022.

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

	December 31, 2023	December 31, 2022
Assets		
Current assets:		
Cash and cash equivalents	$ 127,106	$ 218,044
Short-term marketable securities	907,405	1,118,171
Prepaid expenses and other current assets	29,626	36,104
Total current assets	1,064,137	1,372,319
Property and equipment, net	45,589	44,087

Operating lease right-of-use asset	26,048	30,437
Other non-current assets	18,143	13,399
Total assets	$ 1,153,917	$ 1,460,242
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 9,483	$ 2,790
Cost sharing payments due to related party	—	4,388
Accrued expenses and other current liabilities	68,499	66,691
Related-party contract liability, current	—	290,053
Total current liabilities	77,982	363,922
Related-party contract liability, less current portion	—	479
Operating lease liability, less current portion	44,981	53,032
Other non-current liabilities	—	379
Total liabilities	122,963	417,812
Total stockholders' equity	1,030,954	1,042,430
Total liabilities and stockholders’ equity	$ 1,153,917	$ 1,460,242

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