# Denali Therapeutics Reports Second Quarter 2024 Financial Results and Business Highlights

August 1, 2024

SOUTH SAN FRANCISCO, Calif., Aug. 01, 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 second quarter ended June 30, 2024, and provided business highlights.

"In the second quarter, our Enzyme Transport Vehicle franchise gained additional momentum with continued engagement with the FDA on an accelerated approval pathway for tividenofusp alfa (DNL310, ETV:IDS) in MPS II and the FDA's selection of DNL126 (ETV:SGSH) in MPS IIIA for the START program," said Ryan Watts, Ph.D., Chief Executive Officer of Denali Therapeutics. “Today, we are also pleased to share that we have regained the rights to our TfR-based ATV:Abeta program from Biogen, thereby expanding our opportunities for addressing Alzheimer's disease with a potential best-in-class approach. We look forward to continuing to make significant progress as leaders in the promising and growing field of BBB-crossing therapeutics."

**Second 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 April, completed enrollment of 47 participants with MPS II in the Phase 1/2 open-label study.
- COMPASS, the global Phase 2/3 study, is expected to complete enrollment in 2024.
- In July, *Molecular Genetics and Metabolism* published a review co-authored by Denali's Chief Medical Officer, Carole Ho, M.D., titled, "Community consensus for heparan sulfate as a biomarker to support accelerated approval in neuronopathic mucopolysaccharidoses", which summarizes many of the presentations at the Reagan-Udall Foundation workshop held in February 2024 and provides a perspective on the path forward for neuronopathic MPS disorders.
- Following the Reagan-Udall Foundation workshop, Denali received written communication from the Center for Drug Evaluation and Research (CDER) division of the FDA indicating openness to discussing an accelerated approval pathway for tividenofusp alfa in MPS II with cerebrospinal fluid heparan sulfate (CSF HS) as a surrogate biomarker. Denali looks forward to continued engagement with CDER regarding Denali’s intention to file for approval of tividenofusp alfa using the accelerated approval pathway. Denali will provide an update in 2H 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.

**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 plans to initiate a global Phase 2a study in 2024 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)

- In June, Denali announced that the CDER selected DNL126 for participation in the FDA's Support for clinical Trials Advancing Rare disease Therapeutics (START) Pilot Program to further accelerate the development of novel drug and

biological products for rare diseases. Participation in START is expected to facilitate and accelerate development of DNL126.
- 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)

- Denali has finalized the protocol amendment for the Phase 1/2 study and prescreening of participants for Cohort B2 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.

**Antibody Transport Vehicle Amyloid beta (ATV:Abeta) program**

- Today, Denali also announced that Biogen terminated its license to the ATV:Abeta program enabled by Denali's TfR-targeting technology against amyloid beta for the potential treatment of Alzheimer's disease and granted Denali rights to data generated during the collaboration. As a result of the termination, all rights to develop, manufacture, perform medical affairs activities, and commercialize new TfR-targeting ATV:Abeta therapeutics reverted to Denali. Biogen licensed Denali's TfR-targeting ATV:Abeta program in April 2023 having exercised an option that was part of the 2020 collaboration agreement between the two companies. Biogen's decision was not related to any efficacy or safety concerns with the Transport Vehicle platform.
- 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 recent manuscript posted on bioRxiv.
- 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.

- In July, Denali posted the manuscript titled, "Fc-engineered large molecules targeting the blood-brain barrier transferrin receptor and CD98hc have distinct central nervous system and peripheral biodistribution compared to standard antibodies" on bioRxiv. Using comprehensive and unbiased approaches, Denali scientists reveal distinct biodistribution of the TfR and CD98hc transport vehicle delivery platforms from the brain single-cell level all the way to the whole body.

**Participation in Upcoming Investor Conferences**

- BTIG Virtual Biotechnology Conference, August 5-6
- 2024 Wedbush PacGrow Healthcare Conference, August 13-14
- Morgan Stanley 22nd Annual Global Healthcare Conference, September 4-6
- H.C. Wainwright 26th Annual Global Investment Conference, September 9-11
- 2024 Cantor Global Healthcare Conference, September 17-19

**Second Quarter 2024 Financial Results**

Net loss was $99.0 million for the quarter ended June 30, 2024, compared to net income of $183.4 million for the quarter ended June 30, 2023.

There was no collaboration revenue for the quarter ended June 30, 2024, compared to $294.1 million for the quarter ended June 30, 2023. The decrease in collaboration revenue was primarily due to $293.9 million of revenue recognized in the quarter ended June 30, 2023 as a result of Biogen exercising their option to license our ATV:Abeta program.

Total research and development expenses were $91.4 million for the quarter ended June 30, 2024, compared to $97.5 million for the quarter ended June 30, 2023. The decrease of approximately $6.1 million for the quarter ended June 30, 2024 was primarily attributable to a decrease in personnel and external expenses associated with the divestiture of the Company's preclinical small molecule programs. 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, the Company commenced recognition of research funding for the LRRK2 program from the Collaboration and Development Funding Agreement executed in January 2024. These decreases were partially offset by increases in costs in various clinical stage programs, including eIF2B, ETV:SGSH and ETV:IDS reflecting the continued progress of these programs in clinical trials.

General and administrative expenses were $25.2 million for the quarter ended June 30, 2024, compared to $26.1 million for the quarter ended June 30, 2023. The decrease of $0.9 million for the quarter ended June 30, 2024 was primarily attributable to a decrease in personnel-related expenses consisting of employee compensation and stock-based compensation expense, partially offset by combined increases of $0.2 million in professional services, facilities and other corporate costs.

Cash, cash equivalents, and marketable securities were approximately $1.35 billion as of June 30, 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, the timing and likelihood of accelerated approval, and the timing and availability of program updates; 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 and the impact on development of participation in START; 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; 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 June 30, | | Six Months Ended June 30, | |
|---|---|---|---|---|
| | 2024 | 2023 | 2024 | 2023 |
| Collaboration revenue: | | | | |
| Collaboration revenue from customers[1] | $ — | $ 294,123 | $ — | $ 329,264 |
| Total collaboration revenue | — | 294,123 | — | 329,264 |
| Operating expenses: | | | | |
| Research and development[2] | 91,399 | 97,520 | 198,415 | 226,336 |
| General and administrative | 25,194 | 26,120 | 50,430 | 53,260 |
| Total operating expenses | 116,593 | 123,640 | 248,845 | 279,596 |
| Gain from divestiture of small molecule programs | — | — | 14,537 | — |
| Income (loss) from operations | (116,593) | 170,483 | (234,308) | 49,668 |
| Interest and other income, net | 17,567 | 12,900 | 33,480 | 23,934 |
| Net income (loss) | $ (99,026) | $ 183,383 | $ (200,828) | $ 73,602 |
| Net income (loss) per share: | | | | |
| Net income (loss) per share, basic | $ (0.59) | $ 1.34 | $ (1.26) | $ 0.54 |
| Net income (loss) per share, diluted | $ (0.59) | $ 1.30 | $ (1.26) | $ 0.52 |
| Weighted-average shares used in calculating: | | | | |
| Net income (loss) per share, diluted | 168,831,329 | 137,047,227 | 159,117,759 | 136,787,321 |
| Weighted average number of shares outstanding, basic and diluted | 168,831,329 | 140,930,625 | 159,117,759 | 140,550,226 |

(1) Includes related-party collaboration revenue from customers of $294.1 million and $294.3 million for the three and six months ended June 30, 2023, respectively.

(2) Includes expenses for cost sharing payments due to a related party of $7.0 million and $11.1 million for the three and six months ended June 30, 2023, respectively.

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

| | June 30, 2024 | December 31, 2023 |
|---|---|---|
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 74,679 | $ 127,106 |
| Short-term marketable securities | 821,365 | 907,405 |
| Prepaid expenses and other current assets | 32,339 | 29,626 |
| Total current assets | 928,383 | 1,064,137 |
| Long-term marketable securities | 450,994 | — |
| Property and equipment, net | 48,077 | 45,589 |
| Operating lease right-of-use asset | 24,533 | 26,048 |
| Other non-current assets | 50,578 | 18,143 |
| Total assets | $ 1,502,565 | $ 1,153,917 |
| **Liabilities and stockholders' equity** | | |
| Current liabilities: | | |
| Accounts payable | $ 13,936 | $ 9,483 |
| Accrued clinical and other research & development costs | 19,915 | 19,035 |
| Accrued manufacturing costs | 7,111 | 15,462 |
| Other accrued costs and current liabilities | 6,013 | 5,152 |
| Accrued compensation | 9,555 | 21,590 |
| Operating lease liability, current | 7,771 | 7,260 |

| | | |
|---|---|---|
| Deferred research funding liability | 10,232 | — |
| Total current liabilities | 74,533 | 77,982 |
| Operating lease liability, less current portion | 40,981 | 44,981 |
| Total liabilities | 115,514 | 122,963 |
| Total stockholders' equity | 1,387,051 | 1,030,954 |
| Total liabilities and stockholders’ equity | $ 1,502,565 | $ 1,153,917 |

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