Denali Therapeutics Announces Broad Collaboration with Sanofi to Develop RIPK1 Inhibitors for the Treatment of Neurological and Inflammatory Diseases

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- *Candidate RIPK1 inhibitor molecules have the potential to treat Alzheimer's disease, amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), and systemic inflammatory diseases*
- *Denali to receive $125 million upfront payment and future milestone payments that could exceed $1 billion*
- *Denali and Sanofi plan to jointly develop and commercialize programs for neurological indications, and Sanofi will develop and commercialize programs for systemic inflammatory indications*

SOUTH SAN FRANCISCO, Calif., Nov. 01, 2018 (GLOBE NEWSWIRE) -- Denali Therapeutics Inc. (NASDAQ: DNLI), a biopharmaceutical company developing a broad portfolio of therapeutic candidates for neurodegenerative diseases, today announced that it will collaborate with Sanofi on the development of multiple RIPK1 inhibitor molecules with the potential to treat a range of neurological and systemic inflammatory diseases.

The two lead molecules DNL747 and DNL758 target a critical signaling protein known as the receptor-interacting serine/threonine-protein kinase 1 (RIPK1) in the TNF receptor pathway, which regulates inflammation and cell death in tissues throughout the body. The companies plan to study DNL747 in Alzheimer's disease, amyotrophic lateral sclerosis and multiple sclerosis, and DNL758 in systemic inflammatory diseases such as rheumatoid arthritis and psoriasis.

Under the terms of the agreement, Sanofi will make an upfront cash payment to Denali of $125 million, with future development and commercial milestone payments that could exceed $1 billion. Sanofi and Denali will share commercial profits and losses from DNL747 in the U.S. and China equally, while Denali will receive a royalty from Sanofi for other territories for DNL747 and worldwide for DNL758.

Phase 1b and 2 clinical development costs for DNL747 will be fully funded by Sanofi for MS, ALS, and other neurological indications, except in Alzheimer's disease, which will be funded by Denali. Phase 3 trials for all neurological indications will be jointly funded by Sanofi (70%) and Denali (30%). Sanofi will fully fund the clinical development costs for DNL758 in systemic inflammatory diseases.

"This collaboration with Denali is yet another example of Sanofi's commitment to accelerate the development of transformative and best-in-class treatments for patients living with serious illnesses," said Rita Balice-Gordon, Ph.D., Global Head of Rare and Neurologic Diseases Research at Sanofi. "We look forward to working with Denali on the RIPK1 program as we explore the potential of this mechanism in neurologic and inflammatory diseases."

"RIPK1 is a promising target with the potential to bring disease modifying medicines to patients suffering from neurodegenerative diseases as well as systemic inflammatory diseases. We are very excited to partner with Sanofi and expand our RIPK1 program into new indications," said Ryan Watts, Ph.D., CEO of Denali. "With its considerable infrastructure and experience in both clinical development and commercial functions, Sanofi is an ideal partner for Denali to maximize the clinical and commercial success of our RIPK1 program."

RIPK1 Inhibitor Molecules

- DNL747 is a brain-penetrant small molecule inhibitor of RIPK1. It is currently being evaluated in early clinical stage trials, known as Phase 1. Phase 1b studies in Alzheimer's disease and ALS patients are expected to commence in the near-term. Denali will lead Phase 2 clinical trials in Alzheimer's disease while Sanofi will lead Phase 2 clinical trials in MS and ALS, as well as future Phase 3 trials in all neurological indications.

- DNL758 is a small molecule inhibitor of RIPK1 that does not penetrate the brain. Sanofi will lead clinical development activities for all systemic inflammatory diseases. The clinical trials are expected to begin in 2019.

The collaboration also includes additional pre-clinical RIPK1 inhibitor molecules.

The transaction is expected to close in the coming months in accordance with customary regulatory approvals.

About Denali Therapeutics

Denali is a biopharmaceutical company developing a broad portfolio of product candidates for neurodegenerative diseases. Denali pursues new treatments by rigorously assessing genetically validated targets, engineering delivery across the blood-brain barrier and guiding development with biomarker monitoring to demonstrate target engagement and select patients. 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, the potential benefits of the collaboration; plans to commence Phase 1b clinical studies of DNL747 in Alzheimer's disease and ALS patients in the near-term; the expectation as to when the transaction will close; expectations for future clinical development activities and the timing of future clinical trials; plans for Sanofi and Denali to collaborate on development of RIPK1 inhibitor molecules; 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: the risk that the transaction may not close in a timely manner or at all; risks related to obtaining the requisite regulatory approvals; the risk of the occurrence of any event, change or other circumstance that could give rise to the termination of the agreement (including without limitation the failure to timely obtain requisite regulatory approvals); risks related to the effect of the announcement of the transaction on Denali's business relationships, operating results and business generally; Denali's early stages of clinical drug development; Denali's ability to complete the development and, if approved, commercialization of its product candidates; Denali's ability to conduct or complete clinical trials on expected timelines; implementation of Denali's strategic plans for its business, product candidates and BBB platform technology; and other risks, including those described in Denali's Annual Report on Form 10-K filed with the SEC on March 19, 2018, Denali's Quarterly Report on Form 10-Q filed with the SEC on August 9, 2018 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.

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