Leap Therapeutics Announces Publication of DKN-01 Mechanism of Action Data in Molecular Cancer Research

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- Results demonstrate that DKN-01 activity is both immune dependent and enhanced in combination with anti-PD-1 antibodies -

CAMBRIDGE, Mass., Dec. 22, 2020 /PRNewswire/ -- Leap Therapeutics, Inc. (Nasdaq:LPTX), a biotechnology company focused on developing targeted and immuno-oncology therapeutics, today announced the publication in *Molecular Cancer Research* of preclinical results from studies of human and murine versions of DKN-01, a humanized monoclonal antibody that binds to and blocks the activity of the Dickkopf-1 (DKK1) protein. The article, entitled "mDKN-01, a Novel Anti-DKK1 Monoclonal Antibody, Enhances Innate Immune Responses in the Tumor Microenvironment," is available online. The studies characterized a murine version of DKN-01 (mDKN-01) in order to better understand the mechanism of action (MOA) of DKK1 inhibition in two mouse cancer models.

"In the current studies, we demonstrated that the inhibition of DKK1 with a monoclonal antibody in a syngeneic melanoma model led to tumor growth inhibition (TGI) requiring host NK1.1 cells, but not T or B cells, and provided enhanced efficacy when combined with a PD-1 inhibitor. In a second model, the antibody was a potent inhibitor of breast cancer metastases to lung," said Walter Newman, Ph.D., Senior Research Fellow of Leap. "These results show the innate immune system effects of mDKN-01 and support further exploration as to how DKN-01 results in the activation of NK cells and mitigation of metastatic spread."

DKK1, a secreted modulator of Wnt/Beta-catenin and CKAP4/PI3K/AKT signaling, is overexpressed in many cancers, is associated with worse clinical outcomes, and has been shown to have immunosuppressive effects. To better understand the DKN-01 MOA, Leap engineered a murine framework for the DKN-01 CDR domains and examined the efficacy of mDKN-01 in a mouse model of melanoma. These studies show that targeting DKK1 suppresses tumor growth, reduces intra-tumoral myeloid-derived suppressor cells (MDSC) in the tumor and spleen, activates NK cells, and up-regulates PD-L1 expression on MDSC. Tumor cell signaling analysis in these studies indicates that mDKN-01 is not acting as a Wnt/B-catenin pathway agonist, but is inducing a collection of favorable immune changes in the tumor microenvironment.

In the animal model studied, mDKN-01 and an anti-PD-1 antibody demonstrated additive TGI effects. A clinical trial of DKN-01 plus pembrolizumab, an anti-PD-1 antibody, has recently been completed in esophagogastric cancer patients with promising results in patients whose tumors express high levels of DKK1. Leap has recently initiated a trial of DKN-01 in combination with BeiGene's tislelizumab, an anti-PD-1 antibody, in DKK1-high second line gastroesophageal junction and gastric cancer (GEJ/GC) patients and in combination with tislelizumab, capecitabine, and oxaliplatin in first-line GEJ/GC patients.

About DKN-01

DKN-01 is a humanized monoclonal antibody that binds to and specifically blocks the activity of the Dickkopf-1 (DKK1) protein, a modulator of Wnt/Beta-catenin and CKAP4/PI3K/AKT signaling pathways, frequently implicated in tumorigenesis. The U.S. Food and Drug Administration has granted Orphan Drug Designation for the treatment of gastric and gastroesophageal junction cancer and Fast Track Designation in combination with tislelizumab for the treatment of patients with gastric and gastroesophageal junction adenocarcinoma whose tumors express high DKK1 protein, following disease progression on or after prior fluoropyrimidine- and platinum- containing chemotherapy and if appropriate, human epidermal receptor growth factor (HER2)/neu-targeted therapy.

About Leap Therapeutics

Leap Therapeutics (Nasdaq:LPTX) is focused on developing targeted and immuno-oncology therapeutics. Leap's most advanced clinical candidate, DKN-01, is a humanized monoclonal antibody targeting the Dickkopf-1 (DKK1) protein. DKN-01 is in clinical trials in patients with esophagogastric, hepatobiliary, gynecologic, and prostate cancers. Leap has entered into a strategic partnership with BeiGene, Ltd. for the rights to develop DKN-01 in Asia (excluding Japan), Australia, and New Zealand. For more information about Leap Therapeutics, visit http://www.leaptx.com or view our public filings with the SEC that are available via EDGAR at http://www.sec.gov or via https://investors.leaptx.com/.

FORWARD-LOOKING STATEMENTS

This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, Section 21E of the Securities Exchange Act of 1934, as amended, and the Private Securities Litigation Reform Act of 1995, which involve risks and uncertainties. These statements include Leap's expectations with respect to the development and advancement of DKN-01, including the initiation, timing and design of future studies, enrollment in future studies, potential for the receipt of future option exercise, milestones or royalty payments from BeiGene, and other future expectations, plans and prospects. Although Leap believes that the expectations reflected in such forward-looking statements are reasonable as of the date made, forward-looking statements are subject to known and unknown risks, uncertainties and other factors that could cause actual results to differ materially from our expectations. Such risks and uncertainties include, but are not limited to: that the initiation, conduct, and completion of clinical trials, laboratory operations, manufacturing campaigns, and other studies may be delayed, adversely affected, or impacted by COVID-19 related issues; the accuracy of our estimates regarding expenses, future revenues, capital requirements and needs for financing; the outcome, cost, and timing of our product development activities and clinical trials; the uncertain clinical development process, including the risk that clinical trials may not have an effective design or generate positive results; our ability to obtain and maintain regulatory approval of our drug product candidates; the size and growth potential of the markets for our drug product candidates; our ability to continue obtaining and maintaining intellectual property protection for our drug product candidates; and other risks. Detailed information regarding factors that may cause actual results to differ materially will be included in Leap Therapeutics' periodic filings with the SEC, including Leap's Annual Report on Form 10-K for the fiscal year ended

December 31, 2019, as filed with the SEC on March 16, 2020 and as may be updated by Leap's Quarterly Reports on Form 10-Q and the other reports Leap files from time to time with the SEC. Any forward-looking statements contained in this release speak only as of its date. Leap undertakes no obligation to update any forward-looking statements contained in this release to reflect events or circumstances occurring after its date or to reflect the occurrence of unanticipated events.

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