Leap Therapeutics Presents Updated Data for DKN-01 in Esophagogastric Cancer Patients at SITC 2020 35th Annual Meeting

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- High Levels of Tumoral DKK1 Expression Correlated with Improved Clinical Outcomes in Heterogenous Esophagogastric Cancer Patients Treated with DKN-01 as a Monotherapy or in Combination

- DKK1-high Anti-PD-1/PD-L1 Refractory Patients Treated with DKN-01 Plus Pembrolizumab Had Longer PFS and OS as compared to DKK1-low Patients

CAMBRIDGE, Mass., Nov. 9, 2020 /PRNewswire/ -- Leap Therapeutics, Inc. (Nasdaq: LPTX), a biotechnology company focused on developing targeted and immuno-oncology therapeutics, today announced the presentation of clinical data from its Phase 1b/2a clinical trial of DKN-01 in patients with advanced esophagogastric cancer (EGC) at the Society for Immunotherapy of Cancer's 35th Anniversary Annual Meeting. DKN-01 is a humanized monoclonal antibody that binds to and blocks the activity of the Dickkopf-1 (DKK1) protein.

In the study, high levels of tumoral DKK1 expression correlated with improved clinical outcomes in heterogeneous EGC patients treated with DKN-01 as monotherapy or in combination with pembrolizumab or paclitaxel. Pooled data for the 69 patients in the study for whom tumoral DKK1 expression data is available demonstrated that DKK1-high patients experienced higher overall response rates (ORR), a doubling of median progression-free survival (PFS), and longer median overall survival (OS) as compared to DKK1-low patients. Additionally, DKK1-high anti-PD-1/PD-L1 refractory patients treated with DKN-01 plus pembrolizumab experienced longer PFS and OS compared to DKK1-low patients, suggesting that DKK1 tumoral expression may serve as a predictive biomarker to identify patients for treatment with DKN-01 in combination with anti-PD-1 antibodies. No notable differences were found in baseline MSS, TMB, or PD-L1 expression between DKK1-high versus DKK1-low groups.

"We continue to observe clinically meaningful activity of DKN-01 in patients with advanced previously treated esophagogastric cancer that reinforces our belief that elevated tumoral DKK1 expression is a predictive biomarker for improved outcomes, particularly for those patients treated with DKN-01 in combination with an anti-PD-1 antibody," said Samuel J. Klempner, MD, Assistant Professor, Massachusetts General Hospital Cancer Center and Harvard Medical School.

"We believe that the totality of the results from this study provides strong support for the ongoing study of DKN-01 in combination with 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," continued Dr. Klempner.

The P102 Study in Relapsed or Refractory Esophagogastric Cancer

The P102 study (KEYNOTE-731) is a multi-part Phase 1/2 study of DKN-01 as a monotherapy and in combination with paclitaxel or KEYTRUDA® (pembrolizumab) in advanced EGC patients, with a median of two previous treatments with standard therapies, representing a difficult to treat population. The study is intended to establish the safety and activity of DKN-01 as a monotherapy and in combination with paclitaxel or pembrolizumab, with efficacy endpoints of ORR, PFS, and OS. Tumoral DKK1 expression was determined retrospectively by RNAscope® chromogenic *in situ* hybridization and correlated with clinical outcomes. Pembrolizumab was provided for the study through a clinical trial collaboration agreement with Merck (known as MSD outside the United States and Canada).

Key DKN-01/Pembrolizumab Findings from the P102 Study

- ***Anti-PD-1/PD-L1 refractory patients (all)***: The four DKK1-high patients had a significantly longer PFS of 12.8 weeks and OS of 46 weeks as compared to the five DKK1-low patients who experienced PFS of 6 weeks and OS of 16 weeks.
- ***Anti-PD1/PD-L1 refractory GEJ/GC patients***: The three DKK1-high patients had a best response of stable disease (SD) and a longer PFS of 13.4 weeks and OS of 37.4 weeks, as compared to the two DKK1-low patients who both had progressive disease (PD) with a PFS of 3.6 weeks and OS of 11.7 weeks.
- ***Anti-PD-1/PD-L1 naïve GEJ/GC patients***: As previously reported, DKK1-high patients experienced over 22 weeks PFS and nearly 32 weeks OS, with a 50% overall response rate and 80% disease control rate (DCR) in ten evaluable patients. DKK1-low patients experienced nearly 6 weeks PFS and over 17 weeks OS, with a 20% DCR in fifteen evaluable patients. PD-L1 Combined Positive Scores (CPS) did not predict efficacy on the combination of DKN-01 plus pembrolizumab. In multi-variate analysis, DKK1-high status correlated with longer PFS independent of PD-L1 CPS scores.

About DKN-01
DKN-01 is a humanized monoclonal antibody that binds to and blocks the activity of the Dickkopf-1 (DKK1) protein, a modulator of Wnt/Beta-catenin signaling, a signaling pathway frequently implicated in tumorigenesis and suppressing the immune system. DKK1 has an important role in tumor cell signaling and in mediating an immuno-suppressive tumor microenvironment through enhancing the activity of myeloid-derived suppressor cells and downregulating NK ligands on tumor cells. 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, a Wnt pathway modulator. DKN-01 is in clinical trials in patients with esophagogastric, hepatobiliary, gynecologic, and prostate cancers. Leap has formed 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 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, Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act of 1995, which involve risks and uncertainties. These statements include statements regarding 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. Any forward-looking statements contained in this release speak only as of its date. We undertake 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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