Leap Therapeutics to Present Updated Data from the DisTinGuish Study of DKN-01 Plus Tislelizumab and Preclinical Data in Colorectal Cancer Models at the SITC Annual Meeting

November 7, 2022

55% ORR, 73% DCR, and 7.7 month PFS in DKK1-high/PD-L1-high second-line gastric cancer patients

DKN-01 also demonstrated preclinical tumor regression data in CRC models supporting ongoing clinical trial

CAMBRIDGE, Mass., Nov. 7, 2022 /PRNewswire/ -- Leap Therapeutics, Inc. (Nasdaq:LPTX), a biotechnology company focused on developing targeted and immuno-oncology therapeutics, today announced the Company will be presenting updated data from Part B of the DisTinGuish study evaluating DKN-01 in combination with tislelizumab, BeiGene's anti-PD-1 antibody, in second-line gastroesophageal adenocarcinoma (GEA) cancer patients whose tumors express high levels of DKK1 (DKK1-high) at the Society of Immunotherapy for Cancer (SITC) 37th Annual Meeting being held in Boston, MA on November 8-12, 2022.

Leap is also presenting preclinical DKN-01 data supporting the DeFianCe study, a Phase 2 study of DKN-01 in combination with bevacizumab and standard of care chemotherapy in patients with advanced colorectal cancer (CRC) who have received one prior systemic therapy.

"The combination of DKN-01 plus tislelizumab continues to demonstrate a well-tolerated and active combination in previously treated, DKK1-high, anti-PD-1/PD-L1 naïve GEA cancer patients," said Samuel Klempner, MD, Associate Professor at Harvard Medical School who leads the gastric and esophageal cancer program at Massachusetts General Hospital Cancer Center and is a principal investigator on the DisTinGuish study. "In Keynote-061, anti-PD-1 monotherapy generated a 2% ORR in second-line GEA patients with PD-L1 expression combined positive score (CPS) < 1 and a 24.5% ORR in patients with CPS $\geq$ 10. As DKK1-high patients appear to have more aggressive disease, the updated second-line DKN-01 plus tislelizumab Part B data provides further evidence of activity in this difficult-to-treat patient population, particularly among the DKK1-high/PD-L1-high patients. These results continue to support the decision to start Part C, the randomized controlled clinical trial in first-line patients."

"The preclinical results in CRC models showed impressive monotherapy and chemotherapy combination activity in multiple xenograft models, including those that are resistant to 5-FU treatment, which is commonly used to treat metastatic disease," said Cynthia Sirard, MD, Chief Medical Officer of Leap Therapeutics. "Colorectal cancer is the third most frequent cancer globally and the second leading cause of death. We enrolled our first patient in the Phase 2 DeFianCe study in October evaluating DKN-01 in combination with standard of care bevacizumab and chemotherapy as a second-line treatment for patients with CRC and look forward reporting initial data in mid-2023."

Key Findings DisTinGuish

- DKN-01 and tislelizumab administered in DKK1-high (H-score $\geq$ 35), PD-1 naïve patients were well tolerated at both 300mg and 600mg DKN-01 doses
  - Higher DKN-01 dose at 600mg was not associated with higher frequency of adverse events (AEs)
  - There were no Grade 5 treatment-emergent AEs (TEAE) and no TEAEs leading to study drug discontinuation or dose reduction
- High and durable 27% overall response rate (ORR) in evaluable anti-PD-1/PD-L1 naïve mITT population (n=43)
  - 55% ORR, 73% disease control rate, and 7.7 months median progression-free survival in DKK1-high/PD-L1-high vCPS ≥ 10 patients (n=12: 6 PR, 2 SD, 3 PD, 1 NE)
  - 27% ORR in DKK1-high/PD-L1-negative vCPS < 1 patients (n=11: 3 PR, 1 SD, 7 PD)
- Overall, 7 of 10 responders remain on therapy

Key Findings Preclinical CRC

- DKN-01 showed additive activity with 5-fluorouracil (5-FU) and can overcome 5-FU-resistance in two CRC xenograft models, resulting in tumor regressions
  - 5-FU-resistant models are reflective of a second-line CRC population currently being recruited in the DeFianCe study (NCT05480306)
- DKN-01 as monotherapy or in combination with anti-PD-1 resulted in tumor regression in a CT26 syngeneic CRC model
  - Treatment increased PD-L1 immunoreactivity
  - Promoted substantial tumor necrosis which was associated with a robust immune cell infiltrate
  - Tumor immune infiltrate contained a substantial number of CD3+ and CD8+ cells, implying the presence of an adaptive immune response to tumor antigen

Leap Poster Details:

Title: DKN-01 and Tislelizumab as a Second-line (2L) Investigational Therapy in Advanced DKK1-high Gastroesophageal Adenocarcinoma (GEA): DisTinGuish Trial
First Author: Samuel J. Klempner, Harvard Medical School
Session Category: Poster Session
Session title: Immune-stimulants and immune modulators

Date and time: Thursday, November 10, 2022, at 9:00 a.m. ET
Poster Number: 553

Title: DKN-01 Demonstrates Immune Modulatory Activity and Robust Efficacy in Colorectal Cancer Models
First Author: Michael Haas, Leap Therapeutics
Session Category: Poster Session
Session title: Immune-stimulants and immune modulators
Date and time: Thursday, November 10, 2022, at 9:00 a.m. ET
Poster Number: 1141

About the DisTinGuish Study

The DisTinGuish study (NCT04363801) is a Phase 2 study of DKN-01 in combination with tislelizumab, an anti-PD-1 antibody, with or without chemotherapy as first-line or second-line therapy in patients with inoperable, locally advanced, G/GEJ adenocarcinoma. The study is being conducted in three parts in the United States and the Republic of Korea. Part A has been completed with 25 first-line HER2- GEA cancer patients whose tumors express either high levels of DKK1 (DKK1-high) or low levels of DKK1 (DKK1-low). Part B has completed enrolling patients with second-line DKK1-high GEA cancer. Part C of the study is enrolling approximately 160 first-line patients in a randomized controlled trial of DKN-01 in combination with tislelizumab and chemotherapy compared to tislelizumab and chemotherapy. Leap is conducting this combination study as part of an exclusive option and license agreement with BeiGene.

About the DeFianCe Study

The DeFianCe study (NCT05480306) is a Phase 2, randomized, open-label, multicenter study of DKN-01 in combination with standard of care bevacizumab and chemotherapy in patients with advanced CRC who have received one prior systemic therapy. The study is designed with an initial 20 patient cohort and to then expand into a 130-patient randomized controlled trial against bevacizumab and standard of care chemotherapy.

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 being developed in patients with esophagogastric, gynecologic, and colorectal cancers. Leap has entered into a strategic collaboration 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 clinical studies, potential for the receipt of future option exercise, milestone, 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, global conflict or supply chain related issues; unstable global market and economic conditions; 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 is 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, 2021, as filed with the SEC on March 11, 2022 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 statement contained in this release speaks only as of its date. Leap undertakes no obligation to update any forward-looking statement 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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