Leap Therapeutics to Present New Data from DisTinGuish Study of DKN-01 Plus Tislelizumab and WAKING Study of DKN-01 Plus Tecentriq® at the ESMO Congress

September 4, 2022

Median Progression-Free Survival of 11.3 months in first-line gastric cancer patients treated with DKN-01 plus tislelizumab and CAPOX, exceeding benchmarks in the overall population and in DKK1 and PD-L1 subgroups

Median Overall Survival is not mature with only 44% of patients deceased as of the data cut

Enrollment ongoing in the study of DKN-01 plus Tecentriq® (atezolizumab) in second- or third-line oesophagogastric cancer patients, activity in DKK1-high patients consistent with prior studies with pembrolizumab or tislelizumab

CAMBRIDGE, Mass., Sept. 4, 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 data in first-line patients with advanced gastroesophageal adenocarcinoma (GEA) from the DisTinGuish study, a Phase 2a clinical trial evaluating Leap's anti-Dickkopf-1 (DKK1) antibody, DKN-01, in combination with tislelizumab, BeiGene's anti-PD-1 antibody, and chemotherapy, at the European Society for Medical Oncology (ESMO) Congress 2022 being held on September 9-12. Safety and early efficacy data will be presented from the WAKING study, a multicenter Phase 2 non-randomized trial evaluating DKN-01 plus Tecentriq® (atezolizumab), Roche's anti-PD-L1 antibody, in patients with advanced oesophagogastric adenocarcinoma (OGA).

"Data from the DisTinGuish study continue to demonstrate promising results with the combination of DKN-01 plus tislelizumab and standard chemotherapy as a first-line treatment in patients with advanced gastroesophageal adenocarcinomas," said Samuel Klempner, MD, Associate Professor at Harvard Medical School. "The mature median progression-free survival of 11.3 months compares favorably with recent benchmarks in this patient group. The outcomes in the aggressive DKK1-high and the less checkpoint-inhibitor sensitive PD-L1-low (CPS < 5) subgroups are notable and encouraging. As the last patient enrolled in early April 2021, the overall survival results are also on track to show an increase over current standards. Gastroesophageal cancer patients and physicians want new biomarker-directed therapies to improve the standard of care in first-line treatment, and we are enthusiastic about the upcoming randomized clinical trial involving this encouraging DKN-01 combination."

"Early results from the WAKING study show the promise of boosting anti-tumor activity by targeting the Wnt signaling pathway and DKK1-driven tumor microenvironment modulation with a DKN-01 plus atezolizumab combination therapy strategy in patients with advanced OGA," said Fiona Turkes, MD, Clinical Research Fellow at The Royal Marsden Hospital. "We look forward to continuing to enroll patients and studying the biological mechanisms of this unique chemotherapy-free combination therapy, especially in those patients whose tumors express high levels of DKK1."

Key Findings DisTinGuish

- DKN-01 and tislelizumab plus CAPOX was well tolerated in first-line treatment for advanced GEA patients, with a safety profile consistent with previous reports
- Overall median progression-free-survival (PFS) of 11.3 months exceeds benchmark results in unselected patients and in all four important biomarker-directed subgroups
    - 11.3 months PFS in DKK1-high and 12.0 months in DKK1-low
    - 10.7 months PFS in PD-L1-low (CPS < 5) and 11.6 months in PD-L1-high (CPS $\geq$ 5)
- Median overall survival (OS) is not mature with only 44% of patients deceased as of the data cut (June 30, 2022), with a median duration on study of 15.7 months and last patient enrolled in early April 2021
- High and durable overall response rate (ORR) in unselected and aggressive subgroups (DKK1-high and PD-L1-low) (mITT): 68% (1 CR, 14 PR) overall
    - DKK1-high: 90% ORR (9 PR)
    - DKK1-low: 56% ORR (1 CR; 4 PR)
    - PD-L1-low expression: 79% (11 PR)
        - 100% (6/6) ORR in DKK1-high, PD-L1-low patients
    - PD-L1-high expression: 67% (1 CR; 3 PR)
        - 75% (3/4) ORR in DKK1-high, PD-L1-high patients

Key Findings WAKING

- DKN-01 up to 600mg every 2 weeks in combination with atezolizumab was considered safe
    - 3 patients with the longest time on treatment received the 600mg dose level
- At time of data cut off (August 16, 2022), 18 patients were enrolled in the study
    - 12 patients were treated in initial phase
    - 10 patients were response evaluable at the time of data cut-off
    - 1 patient had a PR and DKK1 expression of 81% tumor percentage score (TPS)

    - Disease control rate: 50% (1 PR, 4 SD, 5 PD)
- Elevated baseline DKK1 expression (TPS ≥ 20%) may be associated with clinical response
    - 4 DKK1-high patients: Best ORR 25% (1 PR, 1 SD, 1 PD, 1 NE)
- Translational analyses and assessment of PD-L1 status are ongoing
- Safety
    - No dose-limiting toxicity (DLT) was observed, and no formal maximum tolerated dose (MTD) was reached
    - No treatment-related deaths occurred, and no dose reductions were required

Leap Poster Details:

Title: DKN-01 and Tislelizumab + Chemotherapy as First-line (1L) Investigational Therapy in Advanced Gastroesophageal Adenocarcinoma (GEA): DisTinGuish Trial
First Author: Samuel J. Klempner, Harvard Medical School
Session Category: Poster Session
Session title: Oesophagogastric cancer
Date and time: Monday, September 12, 2022, at 12:00 CET
Poster Number: 1213

Title: Safety and efficacy of Wnt inhibition with a DKK1 inhibitor, DKN-01, in combination with atezolizumab in patients with advanced oesophagogastric adenocarcinoma (OGA): Phase IIa results of the WAKING trial
First Author: Fiona Turkes, The Royal Marsden NHS Foundation Trust
Session Category: Poster Session
Session title: Oesophagogastric cancer
Date and time: Monday, September 12, 2022, at 12:00 CET
Poster Number: 1253

About the DisTinGuish Study

The DisTinGuish study (NCT04363801) is a Phase 2a 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 two parts in the United States and the Republic of Korea. Enrollment of Part A has been completed with 25 first-line HER2- G/GEJ cancer patients whose tumors express either high levels of DKK1 (DKK1-high) or low levels of DKK1 (DKK1-low). Part B of the study has completed enrollment patients with second-line DKK1-high G/GEJ cancer. Part C of the study will be 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 WAKING Study

The WAKING study (NCT04166721) is a Phase IIa/b nonrandomized, open-label, multicenter study to be conducted concurrently in 2 Parts. Approximately 52 patients aged 18 years or older with inoperable, histologically confirmed locally advanced or metastatic G/GEJ adenocarcinoma with measurable disease (RECIST v1.1) requiring therapy will be enrolled in the study. Both parts are designed to evaluate safety, tolerability, and efficacy of the combination therapy of DKN-01 and atezolizumab in immunotherapy naïve, PD-L1 unselected G/GEJ adenocarcinoma patients. Treatment continues in repeating 14-day cycles until patient meets criteria for discontinuation or is no longer deriving clinical benefit. The WAKING study is being led by the Royal Marsden Hospital in the United Kingdom with financial support from Roche.

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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