./cypherpunk

Leap Therapeutics Announces Initiation of New DKN-01 Clinical Trials in Gastric Cancer, Colorectal Cancer and Endometrial Cancer

July 12, 2022

Randomized Controlled First-Line Gastric Cancer Trial of DKN-01 plus tislelizumab and chemotherapy in collaboration with BeiGene

Leap to host R&D Day today at 12:00 p.m. ET

CAMBRIDGE, Mass., July 12, 2022 /PRNewswire/ -- Leap Therapeutics, Inc. (NASDAQ: LPTX), a biotechnology company focused on developing targeted and immuno-oncology therapeutics, and BeiGene, Ltd. (NASDAQ: BGNE; HKEX: 06160; SSE: 688235), a global, science-driven biotechnology company focused on developing innovative and affordable medicines to improve treatment outcomes and acc688235ess for patients worldwide, today announced the initiation of Part C of the ongoing DisTinGuish study to evaluate DKN-01, Leap's anti-SSEDickkopf 1 (DKK1) antibody, in combination with tislelizumab, BeiGene's anti-PD-1 antibody, and chemotherapy compared to a tislelizumab and chemotherapy control arm, in patients with gastric or gastroesophageal junction cancer (G/GEJ).

Additionally, Leap is initiating a new company-sponsored trial of DKN-01 in combination with standard of care bevacizumab and chemotherapy in second-line patients with colorectal cancer that is designed to expand into a randomized study. Leap is also supporting an investigator-initiated trial of DKN-01 plus pembrolizumab in patients with endometrial cancer to be conducted at The University of Texas M.D. Anderson Cancer Center and at the University of Alabama at Birmingham.

Leap's management team, together with key opinion leaders, will host an R&D Day today to provide updates on the Company's DKN-01 program including G/GEJ, colorectal cancer, endometrial cancer, and prostate cancer.

"Since the presentation of the data for DKN-01 plus tislelizumab and chemotherapy in first-line G/GEJ patients demonstrating compelling overall response rates and progression-free survival, Leap and BeiGene have been working together to create an optimal global strategy for this unique combination therapy. We are excited to enhance the development program and our collaboration with BeiGene through a randomized controlled trial in first-line patients, with a focus on those patients whose tumors express high levels of DKK1," said Douglas E. Onsi, President and Chief Executive Officer of Leap.

"Based on our clinical and preclinical data, Leap is committed to developing DKN-01 aggressively in multiple indications," said Cynthia Sirard, MD, Chief Medical Officer of Leap. "Through a strategic review and prioritization process, we have decided to initiate a company-sponsored study in second-line colorectal cancer patients of DKN-01 in combination with standard of care bevacizumab and chemotherapy. We will also support an investigator-initiated study in endometrial cancer patients of DKN-01 in combination with pembrolizumab, building on previous data showing single-agent activity of DKN-01."

R&D Day:

Leap's management team will host an R&D Day today at 12:00 p.m. Eastern Time and will be joined by key opinion leaders:

Samuel Klempner, MD, Associate Professor at Harvard and Massachusetts General Hospital;
Zev Wainberg, MD, Co-Director of the GI Oncology Program at University of California Los Angeles;
Rebecca Arend, MD, Assistant Professor at University of Alabama at Birmingham Comprehensive Cancer Center; and
David Wise, MD, PhD, Assistant Professor at NYU Langone Health.

The live webcast presentation of the R&D Day can be accessed by registering at https://edge.media-server.com/mmc/p/4zp7m6pw. A replay of the event will be available for a limited time and may be accessed on the Investors page of the Company's website at https://investors.leaptx.com/

Gastric Cancer

The DisTinGuish study (NCT04363801) is a Phase 2 study of DKN-01 in combination with tislelizumab and standard of care (SOC) chemotherapy in patients with inoperable, locally advanced, G/GEJ adenocarcinoma. Part C of the DisTinGuish study will enroll approximately 160 first-line, HER2-negative patients who have had no prior therapy for unresectable locally advanced or metastatic G/GEJ adenocarcinoma. Patients will be randomized 1:1 to study DKN-01 in combination with tislelizumab and SOC chemotherapy, compared to tislelizumab and SOC chemotherapy. The primary objective of Part C is progression-free survival (PFS) in patients whose tumors express high levels of DKK1 (DKK1-high). Secondary objectives of Part C include PFS in all patients regardless of DKK1 expression, as well as overall survival (OS) and objective response rate (ORR) as measured by RECIST v1.1 in DKK1-high and all patients.

Part A and Part B of the DisTinGuish study are currently being conducted in the United States and the Republic of Korea. Part A enrolled 25 first-line HER2- G/GEJ cancer patients. As of December 10, 2021, the median PFS for all patients in Part A was 10.7 months, with 11.9 months PFS for DKK1-high patients, and the ORR for all patients who had completed a full cycle of therapy was 68%, with 90% ORR for DKK1-high patients. Part B of the study has enrolled 51 patients with second-line DKK1-high G/GEJ cancer. Additional follow-up data from Part A is expected to be presented in the third quarter 2022 and from Part B in the fourth quarter 2022.

Colorectal Cancer

The DeFianCe study is a Phase 2 study of DKN-01 in combination with bevacizumab and SOC chemotherapy in patients with advanced colorectal cancer 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 SOC chemotherapy. The primary objective is PFS. Secondary objectives include ORR, duration

of response (DOR), and OS. The study is expected to enroll its first patient in the third quarter 2022.

Endometrial Cancer

The investigator-initiated trial of DKN-01 in combination with pembrolizumab is an open-label, Bayesian design, Phase 2 trial and will initially enroll 15 patients each into DKK1-high and DKK1-low cohorts. If the efficacy criteria is met in either or both of the 15 patient cohort(s), then the cohort(s) will be expanded by an additional 15 patients. The primary objective of the study is ORR. Secondary objectives include clinical benefit rate (CBR), PFS, OS, and DOR. The study is expected to enroll its first patient in the fourth quarter 2022.

Leap has previously studied DKN-01 as a monotherapy and in combination with paclitaxel in patients with endometrial cancer. In the group of 23 patients treated with DKN-01 monotherapy for whom DKK1 expression data was available, patients with DKK1-high tumors achieved 1 complete response and 1 partial response, along with greater ORR (25% vs. 0%), CBR (63% vs. 7%), and median PFS (4.3 months vs. 1.8 months [HR 0.26; 95 CI: 0.09, 0.75]) compared to patients with DKK1-low tumors. In the group of 24 patients treated with DKN-01 plus paclitaxel, 72% of whom had received three or more prior systemic therapies, DKK1-high patients had improved median PFS (5.4 months vs. 1.8 months [HR 0.34; 95% CI: 0.12, 0.97]) compared to DKK1-low patients.

About DKN-01

DKN-01 is a humanized monoclonal antibody that binds to and blocks the activity of the Dickkopf-1 (DKK1) protein. DKK1 modulates the Wnt/Beta-catenin and PI3kinase/AKT signaling pathways and has an important role in promoting tumor proliferation, metastasis, angiogenesis, and in mediating an immune suppressive tumor microenvironment through enhancing the activity of myeloid-derived suppressor cells and downregulating NK cell ligands on tumor cells. The U.S. Food and Drug Administration has granted DKN-01 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 the Leap/BeiGene Collaboration

Leap is conducting the DisTinGuish study as part of an exclusive option and license agreement with BeiGene for the development of DKN-01 in Asia (excluding Japan), Australia, and New Zealand. Leap retains exclusive rights for the development, manufacturing, and commercialization of DKN-01 for the rest of the world.

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, colorectal, and prostate 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 forward-looking statements include statements regarding Leap's business strategies, collaborations and partnerships, and expectations with respect to the development and advancement of DKN-01 in clinical trials, including the outcomes, status and timing of current or future studies. 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: the uncertain clinical development process, including the risk that clinical trials may not have an effective design or generate positive results; 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; unstable global market and economic conditions; the accuracy of our estimates regarding expenses, future revenues, capital requirements and needs for financing; the benefits to be derived from our agreement with BeiGene, Ltd. ("BeiGene") or any other collaborations, license agreements, or other acquisition efforts; the rate and degree of market acceptance of DKN-01; the success of other competing therapies that may become available; the manufacturing capacity for DKN-01; our ability to maintain and protect our intellectual property rights; and other risks and uncertainties. Detailed information regarding factors that may cause actual results to differ materially from expectations 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.

CONTACT:
Douglas E. Onsi
President & Chief Executive Officer
Leap Therapeutics, Inc.
617-714-0360
donsi@leaptx.com

Matthew DeYoung
Investor Relations
Argot Partners
212-600-1902
leap@argotpartners.com

View original content to download multimedia:https://www.prnewswire.com/news-releases/leap-therapeutics-announces-initiation-of-new-dkn-01-clinical-trials-in-gastric-cancer-colorectal-cancer-and-endometrial-cancer-301584158.html

SOURCE Leap Therapeutics, Inc.