Leap Therapeutics and BeiGene Announce First Patient Dosed in Study of DKN-01 in Combination with Tislelizumab for the Treatment of Metastatic Gastric or Gastroesophageal Junction Cancer

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CAMBRIDGE, Mass. and BEIJING, Sept. 21, 2020 /PRNewswire/ -- Leap Therapeutics, Inc. (Nasdaq:LPTX), a biotechnology company focused on developing targeted and immuno-oncology therapeutics, and BeiGene, Ltd., (Nasdaq:BGNE; HKEX: 06160), a commercial-stage biotechnology company focused on developing and commercializing innovative medicines worldwide, today announced that the first patient has been dosed in the DisTinGuish study, a Phase 2a clinical trial evaluating Leap's investigational anti-Dickkopf-1 antibody (DKK1), DKN-01, in combination with tislelizumab, BeiGene's anti-PD-1 antibody, with or without chemotherapy, in patients with gastric or gastroesophageal junction cancer (G/GEJ).

"Dosing of the first patient in the DisTinGuish study is a key milestone for the DKN-01 development program," said Cynthia Sirard, M.D., Chief Medical Officer of Leap Therapeutics. "We are excited to have the opportunity to combine DKN-01 with tislelizumab due to the promising signals in a DKK1 biomarker-defined population of esophagogastric cancer patients. We look forward to working closely alongside BeiGene to evaluate this potential new combination therapy for a patient population with a high global unmet medical need."

The DisTinGuish trial (NCT04363801) is a Phase 2a, nonrandomized, open-label, multicenter study of DKN-01 in combination with tislelizumab with or without chemotherapy as first-line or second-line therapy in adult patients with inoperable, locally advanced G/GEJ adenocarcinoma. The study, which will be conducted in two parts, is expected to enroll up to 72 patients.

Part A will enroll up to 24 patients with G/GEJ adenocarcinoma who have received no prior systemic treatment in the locally advanced/metastatic setting (first-line treatment), and Part B will enroll up to 48 patients with previously treated, inoperable, locally advanced or metastatic DKK1-high G/GEJ adenocarcinoma (second-line treatment). The study is designed to evaluate safety, tolerability, and efficacy of the combination therapy of intravenous DKN-01 and tislelizumab ± CAPOX (capecitabine + oxaliplatin) in G/GEJ adenocarcinoma patients. Treatment will be conducted in repeating 21-day cycles until the patient meets pre-established criteria for discontinuation or is no longer deriving clinical benefit. Part A and Part B of the study will be conducted concurrently.

Leap is conducting this combination study in the United States 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 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. DKN-01 has received Orphan Drug Designation for the treatment of gastric and gastroesophageal junction cancer from the U.S. Food and Drug Administration.

About Tislelizumab

Tislelizumab is a humanized IgG4 anti-PD-1 monoclonal antibody specifically designed to minimize binding to FcγR on macrophages. In pre-clinical studies, binding to FcγR on macrophages has been shown to compromise the anti-tumor activity of PD-1 antibodies through activation of antibody-dependent macrophage-mediated killing of T effector cells. Tislelizumab is approved by the China National Medical Products Administration (NMPA) as a treatment for patients with classical Hodgkin's lymphoma who received at least two prior therapies and for patients with locally advanced or metastatic urothelial carcinoma (UC) with PD-L1 high expression whose disease progressed during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

In addition, three supplemental new drug applications (sNDAs) for tislelizumab have been accepted by the Center for Drug Evaluation (CDE) of the NMPA and are under review – for first-line treatment of patients with advanced squamous non-small cell lung cancer (NSCLC) in combination with chemotherapy, for first-line treatment of patients with advanced non-squamous NSCLC in combination with chemotherapy, and for previously treated unresectable hepatocellular carcinoma.

Tislelizumab is not approved for use outside of China.

About gastric / gastroesophageal junction cancer

Gastric adenocarcinoma (gastric cancer) remains one of the most common and deadly cancers worldwide, especially among older males[i]. Based on GLOBOCAN 2018 data, stomach cancer is the 5th most common neoplasm and the 3rd most deadly cancer, with an estimated 783,000 deaths globally in 2018[i]. Ninety-five percent of cancers of the stomach are adenocarcinomas [i]. Gastric cancer incidence and mortality are highly variable by region and highly dependent on diet and Helicobacter pylori infection[i]. The gastroesophageal junction (GEJ) is the area where the esophagus and stomach join together. Given its anatomic location, GEJ adenocarcinomas have often been grouped together with either esophageal or gastric cancers in clinical trials.

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 entered into a 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/.

About BeiGene

BeiGene is a global, commercial-stage biotechnology company focused on discovering, developing, manufacturing, and commercializing innovative medicines to improve treatment outcomes and access for patients worldwide. Our 4,200+ employees in China, the United States, Australia, Europe, and elsewhere are committed to expediting the development of a diverse pipeline of novel therapeutics. We currently market two internally discovered oncology products: BTK inhibitor BRUKINSA® (zanubrutinib) in the United States and China, and anti-PD-1 antibody tislelizumab in China. We also market or plan to market in China additional oncology products licensed from Amgen Inc., Celgene Logistics Sàrl, a Bristol Myers Squibb (BMS) company, and EUSA Pharma. To learn more about BeiGene, please visit www.beigene.com and follow us on Twitter at @BeiGeneUSA.

LEAP 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 relating to 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 we file from time to time with the SEC. 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.

BEIGENE FORWARD-LOOKING STATEMENTS

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and other federal securities laws, including statements regarding plans for the advancement of, anticipated clinical development and regulatory milestones, and the potential opportunity of DKN-01 and tislelizumab as a combination therapy. Actual results may differ materially from those indicated in the forward-looking statements as a result of various important factors, including BeiGene's ability to demonstrate the efficacy and safety of its drug candidates; the clinical results for its drug candidates, which may not support further development or marketing approval; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials and marketing approval; BeiGene's ability to achieve commercial success for its marketed products and drug candidates, if approved; BeiGene's ability to obtain and maintain protection of intellectual property for its technology and drugs; BeiGene's reliance on third parties to conduct drug development, manufacturing and other services; BeiGene's limited operating history and BeiGene's ability to obtain additional funding for operations and to complete the development and commercialization of its drug candidates; the impact of the COVID-19 pandemic on the Company's clinical development, commercial and other operations, as well as those risks more fully discussed in the section entitled "Risk Factors" in BeiGene's most recent quarterly report on Form 10-Q, as well as discussions of potential risks, uncertainties, and other important factors in BeiGene's subsequent filings with the U.S. Securities and Exchange Commission. All information in this press release is as of the date of this press release, and BeiGene undertakes no duty to update such information unless required by law.

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[i] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6444111/

View original content to download multimedia:http://www.prnewswire.com/news-releases/leap-therapeutics-and-beigene-announce-first-patient-dosed-in-study-of-dkn-01-in-combination-with-tislelizumab-for-the-treatment-of-metastatic-gastric-or-gastroesophageal-junction-cancer-301134397.html

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