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Leap Therapeutics Presents DKN-01 Clinical Data at the Society of Gynecologic Oncology 2021 Annual Meeting on Women's Cancer

March 22, 2021

- DKN-01 Monotherapy Demonstrated Clinical Activity in Patients with Endometrial Cancer
- Tumoral DKK1 Expression Biomarker Predicts Strongest Outcomes
- Conference Call to Discuss Results Today at 8:30 a.m. Eastern Time

CAMBRIDGE, Mass., March 22, 2021 /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 2 clinical trial of DKN-01 as a monotherapy and in combination with paclitaxel in patients with advanced gynecological malignancies at the Society of Gynecologic Oncology 2021 Annual Meeting on Women's Cancer, being held as a virtual meeting from March 19-25, 2021. DKN-01 is a humanized monoclonal antibody that binds to and blocks the activity of the Dickkopf-1 (DKK1) protein, leading to the activation of the innate immune system in the tumor microenvironment and anti-tumor activity.

"DKN-01 demonstrated objective responses, including a monotherapy complete response continuing now for over 2 and a half years, and durable tumor reductions as a single agent and in combination with paclitaxel in the advanced gynecologic cancer patients treated in the study," said Rebecca Arend, M.D., MSPH, Associate Professor, University of Alabama at Birmingham O'Neal Comprehensive Cancer Center. "The disease control rate and progression-free survival were strongest in patients whose tumors express high levels of DKK1 (DKK1-high), which is a group that real world evidence has shown to have poorer outcomes on other therapies."

"The activity of DKN-01 in this study was comparable to the monotherapy data from other widely-used immuno-oncology or targeted therapies," Dr. Arend continued. "As DKN-01 was extremely well tolerated, additional studies of DKN-01 as a monotherapy and in combination with anti-PD-1 antibody therapy are warranted in endometrial cancer patients with DKK1-high tumors."

The P204 Study in Advanced Gynecologic Cancers

The P204 study was a Phase 2 basket study evaluating DKN-01 as a monotherapy or in combination with paclitaxel in groups composed of epithelial endometrial cancer (EEC), epithelial ovarian cancer (EOC), or carcinosarcoma (MMMT) patients. The primary endpoint of the P204 study was overall response rate (ORR), and secondary endpoints include disease control rate (DCR) and progression-free survival (PFS). In each group, at least fifty percent (50%) of patients were required to have specified Wnt signaling pathway alterations, a subgroup of which (Wnt activating mutations) are known to drive high tumoral DKK1 expression. Tumoral DKK1 expression was determined retrospectively by RNAscope® chromogenic *in situ* hybridization and correlated with clinical outcomes.

Key Findings from the P204 Study

One hundred-eleven patients were enrolled in the study, including 29 EEC patients in a DKN-01 monotherapy group, 24 EEC patients in a DKN-01 plus paclitaxel group, 14 EOC patients in a DKN-01 monotherapy group, 19 EOC patients in a DKN-01 plus paclitaxel group, 9 MMMT patients in a DKN-01 monotherapy group, and 16 MMMT patients in a DKN-01 plus paclitaxel group. The key findings from the study were:

- ***EEC patients and patients with Wnt activating mutations express higher levels of DKK1:*** EEC patients expressed higher levels of DKK1 and had a higher frequency of Wnt activating mutations than patients with EOC. Within EEC, patients with endometrioid histology had higher DKK1 expression than those with non-endometrioid histology. Patients whose tumors had Wnt activating mutations expressed 14.4 times higher levels of DKK1.

- ***DKN-01 has enhanced activity in patients whose tumors express high levels of DKK1:*** In the group of 22 EEC patients treated with DKN-01 monotherapy for whom DKK1 expression data was available, patients with DKK1-high tumors (n=7) had greater ORR (14% vs. 0%), DCR (57% vs. 7%), and median PFS (3.0 months vs. 1.8 months [HR 0.39; 95% CI: 0.14, 1.1]) compared to patients with DKK1-low tumors (n=15). Additionally, seven patients did not have DKK1 expression results available, of whom one had a complete response (14%) and five (72%) had a best response of stable disease, including three patients with Wnt activating mutations.

  In the group of 24 EEC patients treated with DKN-01 plus paclitaxel, 72% of whom had received three or more prior systemic therapies, DKK1-high patients (n=11) 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 (n=9). Four patients did not have DKK1 expression data available.

- ***Within EEC, DKN-01 activity strongest in endometrioid histology:*** In the pooled group of 27 patients with endometrioid histology for whom DKK1 expression data was available, patients with DKK1-high tumors (n=14) had greater DCR (57% vs. 15%) and median PFS (4.1 months vs. 1.8 months [HR 0.34; 95% CI: 0.14, 0.81]) than patients with DKK1-low tumors (n=13). Additionally, seven patients with endometrioid histology did not have DKK1 expression results available, of whom one (14%) had a complete response and five (72%) had a best response of stable disease, including two patients with Wnt activating mutations.

Conference Call Details

Leap will be hosting a conference call today at 8:30 a.m. Eastern Time with Dr. Arend and members of Leap's management team to discuss the data. The call can be accessed by dialing (866) 589-0108 (U.S. and Canada) or (409) 231-2048 (international). The passcode for the conference call is 2077923. The presentation will be webcast live and may be accessed on the Investors page of the company's website at https://investors.leaptx.com/, where a replay of the event will also be available for a limited time.

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, which have 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 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 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 in clinical trials in patients with esophagogastric, hepatobiliary, gynecologic, and prostate cancers. Leap has entered into 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 view our public filings with the SEC that are available via EDGAR at http://www.sec.gov or via https://investors.leaptx.com/.

RNAscope® is a registered trademark of Advanced Cell Diagnostics, Inc., Newark, CA, USA.

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 future 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 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, 2020, as filed with the SEC on March 12, 2021 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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