# Leap Therapeutics to Present Updated Data for DKN-01 Monotherapy and Paclitaxel Combination In Gynecologic Cancers

April 23, 2020

**- Enhanced Survival Outcomes Achieved in Patients with Wnt Activating Mutations and DKK1-high Tumors**
**- DKN-01 Monotherapy Treated Endometrial Cancer Patient Maintains a Complete Response**
**- Responses Observed in Carcinosarcoma Patients Treated with DKN-01 Plus Paclitaxel Combination**
**- Conference Call and Webcast to be Held April 23, 2020 at 8:30 A.M. EDT**

CAMBRIDGE, Mass., April 23, 2020 /PRNewswire/ -- Leap Therapeutics, Inc. (Nasdaq: LPTX), a biotechnology company focused on developing targeted and immuno-oncology therapeutics, today announced updated clinical data from its ongoing Phase 2 clinical trial of DKN-01, its anti-Dickkopf-1 (DKK1) antibody, as both a monotherapy and in combination with paclitaxel chemotherapy in patients with advanced gynecological malignancies. Leap will host a conference call with Rebecca Arend, M.D., Assistant Professor and Associate Scientist, Gynecologic Oncology Clinic, The University of Alabama at Birmingham School of Medicine Comprehensive Cancer Center Experimental Therapeutics Program, today, April 23, 2020, at 8:30 A.M. EDT to discuss the data.

"We are seeing clinically meaningful monotherapy activity of DKN-01 in heavily pre-treated endometrial cancer and carcinosarcoma populations, including a complete response, a partial response, and durable tumor reductions in many patients. In combination with paclitaxel, DKN-01 is generating durable responses and disease control in paclitaxel-experienced patients," said Dr. Arend.

"This study also demonstrates the importance of mechanism of action based biomarkers for DKN-01 therapy, as patients with high tumor DKK1 expression or Wnt activating mutations had enhanced progression-free survival and overall survival. These biomarkers should be the foundation for additional DKN-01 studies in endometrial and carcinosarcoma patients, as monotherapy and in combination with other active agents," continued Dr. Arend.

**The P204 Study in Gynecologic Cancers**

The P204 study is a Phase 2 basket study evaluating DKN-01 as a monotherapy and in combination with paclitaxel in patients with relapsed/refractory epithelial endometrial cancer (EEC), epithelial ovarian cancer (EOC), or carcinosarcoma (also known as Malignant Mixed Mullerian Tumor (MMMT)). As of the cut-off date of December 30, 2019, 105 heavily pretreated patients had been enrolled across the six groups of the study. Approximately 67% of all patients had tumors with identified Wnt pathway alterations, which included approximately 20% with Wnt activating mutations. Patients with EEC and carcinosarcoma had higher tumor DKK1 expression and a higher percentage of Wnt activating mutations than the ovarian cancer patients. Patients whose tumors had Wnt activating mutations expressed 15 times higher levels of tumoral DKK1.

**Key Findings from the P204 Study**

- ***DKN-01 single agent activity***
    - ***Endometrial Cancer***: Twenty-nine EEC patients were enrolled in the DKN-01 monotherapy arm, over 75% of whom had experienced three or more prior lines of therapy. Of those patients, 26 were evaluable for response. In the 20 patients with a Wnt signaling alteration, one patient (5%) has an ongoing complete response, one patient (5%) had a partial response, eight patients (40%) had a best response of stable disease, and 10 patients (50%) had progressive disease, representing an overall response rate (ORR) of 10% and a disease control rate (DCR) of 50%. In the group of six patients without any Wnt signaling alterations, one patient (16.6%) had a best response of stable disease and five patients (83.3%) had progressive disease.
    - ***Carcinosarcoma***: Ten patients with carcinosarcoma have been enrolled in the DKN-01 monotherapy arm, five of whom were evaluable for response as of the data-cut off date. Two patients (40%) had a best response of stable disease, one of which has continued on monotherapy for nearly two years, and three patients (60%) had progressive disease. Five patients had not reached their first tumor assessment.
- ***DKN-01 plus paclitaxel combination activity***
    - ***Carcinosarcoma***: Fifteen patients with carcinosarcoma were enrolled in the DKN-01 plus paclitaxel arm, six of whom were evaluable for response as of the data-cut off date. Two patients (33%) have had a partial response, one patient (17%) has had a best response of stable disease, and three patients (50%) had progressive disease, representing an ORR of 33% and a DCR of 50%. Nine patients had not reached their first tumor assessment.
    - ***Endometrial Cancer***: Twenty-five patients with heavily pretreated EEC were enrolled in the DKN-01 plus paclitaxel arm. All of these patients had previously received paclitaxel, 44% had received hormonal therapies, 32% had

received bevacizumab, 20% had received immunotherapy, and 12% had received a PARP inhibitor. Of those patients, 22 were evaluable for response. A total of 12 patients (55%) have had a best response of stable disease, and ten patients (45%) had progressive disease.

- ***Monotherapy Patients with Wnt activating mutations have longer Progression-Free Survival (PFS) and Overall Survival (OS)*:** In a pooled analysis of all DKN-01 monotherapy patients, patients with Wnt activating mutations have demonstrated a longer median PFS of 168 days as compared to patients without Wnt activating mutations with median PFS of 56 days. Median OS has not been reached in the Wnt activating mutation group in the pooled analysis as compared to median OS of 328 days in the non-Wnt activating mutation group.

- ***Monotherapy Patients with DKK1-high tumors have longer PFS and OS:*** DKK1 expression as measured by *in situ* hybridization RNAscope assay is currently available for 68 of the patients on the study, 32 of whom were treated with DKN-01 monotherapy. Seven patients (22%) were identified as having DKK1-high tumoral expression. Consistent with the results from Leap's study in patients with esophagogastric cancer, patients whose tumors are DKK1-high have prolonged median PFS of 168 days as compared to patients with tumors that are DKK1-low with median PFS of 56 days. Median OS was 450 days in the DKK1-high group in the pooled analysis as compared 276 days in the DKK1-low group.

**Conference Call Details:**
**U.S. Dial-in Number:** (866) 589-0108
**International Dial-in Number:** (409) 231-2048
**Conference ID:** 1190677

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 the presentation slides and a replay of the event will also be available for a limited time.

**About Gynecological Cancers**
There are numerous forms of gynecologic cancers, but two of the most prevalent types are cancers of the uterus or ovaries. According to the National Cancer Institute, there are more than 61,000 patients diagnosed with uterine cancer. There are currently very few post-surgical treatment options for these patients, typically consisting of chemotherapy, local radiation therapy, and hormonal agents, and poor treatment outcomes. Patients with endometrial cancers have a high frequency of mutations in a protein known as beta-catenin, with alterations estimated at approximiately 30% of cases by The Cancer Genome Atlas. These beta-catenin mutations are often driver mutations leading to rapid disease progression and poor outcomes. Carcinosarcoma, or Malignant Mixed Mullerian Tumor, is a uterine cancer comprised of carcinoma and sarcoma cells and accounts for less than five percent of all uterine cancer. Carcinosarcoma is an aggressive tumor with poor patient prognosis and poor response to chemotherapy.

**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.

**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 formed a 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 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, 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 regarding 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. 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.

**CONTACT:**

Douglas E. Onsi

President and CEO
Leap Therapeutics, Inc.
617-714-0360
donsi@leaptx.com

Heather Savelle
Investor Relations
Argot Partners
212-600-1902
heather@argotpartners.com

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