Leap Therapeutics to Present New Clinical Data from Part A of DeFianCe Study at the 2024 ASCO Gastrointestinal Cancers Symposium

January 16, 2024

30% ORR and 93% DCR across heterogenous second-line CRC patients treated with DKN-01 plus bevacizumab and chemotherapy

Subgroup analysis reveals greatest benefit in left-sided tumors, particularly rectal and rectosigmoid patients with 46% ORR, 100% DCR, and preliminary median PFS of 9.4 months.

Leap to host conference call to report additional clinical data including further subgroup analyses on Tuesday, January 23, 2024 at 8:30 a.m. ET

CAMBRIDGE, Mass., Jan. 16, 2024 /PRNewswire/ -- Leap Therapeutics, Inc. (Nasdaq:LPTX), a biotechnology company focused on developing targeted and immuno-oncology therapeutics, today announced new data from Part A of the DeFianCe study, a Phase 2 study evaluating DKN-01, Leap's anti-Dickkopf-1 (DKK1) antibody, in combination with standard of care bevacizumab and chemotherapy in second-line patients with advanced colorectal cancer (CRC), to be presented at the upcoming 2024 American Society of Clinical Oncology (ASCO) Gastrointestinal Cancers Symposium taking place in San Francisco, CA and virtually on January 18-20, 2024.

"Data from Part A of the DeFianCe study demonstrates that the addition of DKN-01 to bevacizumab and chemotherapy can generate clinically meaningful response rates and durable tumor reductions with a favorable safety profile in second-line CRC patients, particularly those with rectal or rectosigmoid tumors," said Meredith Pelster, MD, Assistant Director of Gastrointestinal Research at Sarah Cannon Research Institute and a study investigator. "We are very interested in utilizing DKN-01 to modulate the Wnt pathway, which is active in a high percentage of CRC patients, particularly left-sided tumors, to overcome resistance to chemotherapy, and to decrease angiogenesis in order to enhance the activity of the standard of care bevacizumab plus chemotherapy regimens. These results provide a strong foundation for the randomized controlled Part B of this study, which is enrolling extremely well and expected to complete enrollment mid-year."

"In this heterogenous second-line population with several unfavorable characteristics, the DKN-01 plus bevacizumab and chemotherapy Part A ORR of 30%, with a disease control rate of over 90%, and enhanced activity in left-sided tumors and rectal tumors, with a 46% ORR and 9.4 month preliminary PFS, represent an encouraging efficacy signal," said Zev Wainberg, MD, Professor of Medicine and Co-Director of the GI Oncology Program at UCLA. "CRC is a heterogenous disease where the selection of therapy and expected outcomes vary based on whether the tumor is on the left or right side, the presence or absence of genetic mutations, microsatellite instability, and prior therapy. Physicians want to be able to select a second-line therapy combination based on the patient's personalized tumor characteristics, which is what we hope to achieve by adding DKN-01 and understanding the subgroups with the greatest clinical benefit."

Leap will host a conference call on January 23, 2024 at 8:30 a.m. Eastern Time in which Dr. Pelster and Dr. Wainberg will further discuss the new data from the DeFianCe study.

Key Findings:

- As of the December 6, 2023 data cutoff, 33 patients enrolled in Part A of the DeFianCe study
- Across all evaluable patients with second-line microsatellite stable CRC (n=27):
  - Objective response rate (ORR) was 30% and disease control rate (DCR) was 93%, including 8 partial responses (PR) and 17 patients with a best response of stable disease (SD)
  - Median progression-free survival (PFS) was 6.3 months
  - 9 patients remain on therapy beyond 8.5 months
- Analysis revealed a breadth of clinical activity across additional subgroups, including patients with left-sided tumors (n=25)
  - 33% ORR and 100% DCR in response-evaluable population (7 PRs, 14 SDs)
  - Preliminary median PFS of 8.6 months (9 patients continuing on therapy within subgroup)
- Patients with rectal/rectosigmoid carcinomas (n=15) represent an important subpopulation:
  - 46% ORR and 100% DCR in response-evaluable population (6 PRs, 7 SDs)
  - Preliminary median PFS of 9.4 months (6 patients continuing on therapy within subgroup)
  - Higher baseline plasma DKK1 levels correlated with improved responses
- DKN-01 plus bevacizumab and chemotherapy was well-tolerated, with a majority of DKN-01 related events being low grade (Grade 1/2)
- Randomized controlled Part B of the study is underway with 54 patients currently enrolled

Conference Call:
Leap's management team, together with Dr. Pelster and Dr. Wainberg, will host a conference call on Tuesday, January 23, 2024 at 8:30 a.m. Eastern Time to further discuss the data. The conference call will be broadcast live in listen-only mode and can be accessed via the website URL: https://edge.media-server.com/mmc/p/q5zrz568. A replay of the event will also be available for a limited time on the Investors page of the Company's website at https://investors.leaptx.com/.

About the DeFianCe Study
The DeFianCe study (NCT05480306) is a Phase 2, open-label, global study of DKN-01 in combination with standard of care bevacizumab and chemotherapy in patients with advanced CRC who have received one prior systemic therapy for advanced disease. The Part A cohort enrolled 33 patients, including significant numbers of patients who had early progression on first-line therapy, previous exposure to bevacizumab, tumors with Ras mutations, or liver metastases. The study has expanded into a 130-patient Part B randomized controlled trial. The primary objective of the study is progression free survival. Secondary objectives include overall response rate, duration of response, and overall survival.

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. FL-301, is a humanized monoclonal antibody targeting Claudin18.2, being developed in patients with gastric and pancreatic cancer. Leap also has preclinical antibody programs targeting Claudin18.2/CD137 and GDF15. 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 the federal securities laws. Such statements are based upon current plans, estimates and expectations of the management of Leap that are subject to various risks and uncertainties that could cause actual results to differ materially from such statements. The inclusion of forward-looking statements should not be regarded as a representation that such plans, estimates and expectations will be achieved.

All statements, other than historical facts, including statements regarding the anticipated timing for completion of or success of enrollment in the DeFianCe study or any other clinical trial, the release of clinical data, and any outcomes of such trials; the potential, safety, efficacy, and regulatory and clinical progress of Leap's product candidates, including DKN-01; and any assumptions underlying any of the foregoing, are forward-looking statements. Important factors that could cause actual results to differ materially from Leap's plans, estimates or expectations could include, but are not limited to: (i) Leap's ability to successfully execute its clinical trials and the timing of enrollment in and cost of such clinical trials; (ii) the results of Leap's clinical trials and pre-clinical studies; (iii) Leap's ability to successfully enter into new strategic partnerships for DKN-01 or any of its other programs; (iv) whether any Leap clinical trials and products will receive approval from the U.S. Food and Drug Administration or equivalent foreign regulatory agencies; (v) exposure to inflation, currency rate and interest rate fluctuations, as well as fluctuations in the market price of Leap's traded securities; and (vi) that the initiation, conduct, and completion of clinical trials, laboratory operations, manufacturing campaigns, and other studies may be delayed, adversely affected, or impacted by global conflict, or supply chain related issues. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. No representations or warranties (expressed or Implied) are made about the accuracy of any such forward-looking statements. Leap may not actually achieve the forecasts disclosed in such forward-looking statements, and you should not place undue reliance on such forward-looking statements. Such forward-looking statements are subject to a number of material risks and uncertainties including but not limited to those set forth under the caption "Risk Factors" in Leap's most recent Annual Report on Form 10-K filed with the SEC, as well as discussions of potential risks, uncertainties, and other important factors in its subsequent filings with the SEC. Any forward-looking statement speaks only as of the date on which it was made. Neither Leap, nor any of its affiliates, advisors or representatives, undertake any obligation to publicly update or revise any forward-looking statement, whether as result of new information, future events or otherwise, except as required by law. These forward-looking statements should not be relied upon as representing Leap's views as of any date subsequent to the date hereof.

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