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Leap Therapeutics to Present Preclinical Data of FL-501, a Novel GDF-15 Neutralizing Antibody, at the AACR 2025 Annual Meeting

April 25, 2025

FL-501 fully restored body composition and reversed key indicators of cachexia in preclinical models

Findings confirm GDF-15's role in cachexia and support advancing FL-501 into the clinic

CAMBRIDGE, Mass., April 25, 2025 /PRNewswire/ -- Leap Therapeutics, Inc. (Nasdaq:LPTX), a biotechnology company focused on developing targeted and immuno-oncology therapeutics, today announced it will present preclinical data of FL-501 in a poster presentation at the American Association for Cancer Research (AACR) Annual Meeting taking place April 25-30 in Chicago, Illinois.

FL-501 is a potential best-in-class monoclonal antibody targeting growth differentiation factor 15 (GDF-15), a cytokine that is implicated in multiple diseases and therapeutic areas, including cancer cachexia.

"Cancer cachexia is a devasting and potentially life-threatening condition characterized by significant weight loss, muscle wasting, fatigue, and severely reduced quality of life. It is a major contributor to cancer-related mortality, and unfortunately there are no effective treatment options available to patients," said Jason Baum, PhD, Chief Scientific Officer of Leap. "These data not only demonstrate that FL-501 is a novel and potential best-in-class anti-GDF-15 antibody, but also capable of fully restoring body composition in preclinical models that is comparable or better than other, clinical-stage antibodies. We look forward to progressing the development of FL-501 and bringing the asset into the clinic in 2026."

Key Findings:

- In humanized FcRn mouse studies, FL-501 demonstrated a 2-3-fold longer half-life and 50% reduced clearance compared to its wild-type precursor and ponsegromab
- In mouse cachexia models using GDF-15-overexpressing colorectal cancer cells, FL-501 fully restored body composition, comparably or better than clinical-stage antibodies visugromab and ponsegromab
- In a non-small cell lung cancer patient-derived xenograft model, FL-501 effectively countered cisplatin-induced weight loss, restoring body weight, composition, and condition scores
- These findings confirm GDF-15's role in cachexia and support FL-501's advancement in development

Poster Details:

Title: FL-501 is a potential best in class GDF-15 inhibitor with extended half-life and potent anti-cachexia activity in preclinical models
Presenter: Roma Kaul, PhD, Leap Therapeutics
Session Category: Experimental and Molecular Therapeutics
Session Title: New and Emerging Cancer Drug Targets
Date and Time: Tuesday, April 29, 2025, 9:00 a.m. – 12:00 p.m. CT
Poster Board Number: 15
Published Abstract Number: 4258

About FL-501
FL-501 is a potential best-in-class monoclonal antibody in preclinical development that targets growth differentiation factor-15 (GDF-15), a cytokine that is produced at elevated levels in response to various stresses, including chronic inflammation, obesity, cardiovascular diseases, cancers, and chemotherapy treatment. High GDF-15 expression is associated with cancer cachexia including loss of appetite, nausea and weight loss. FL-501 was engineered for higher affinity to GDF-15 and longer plasma half-life compared to competing therapies. In addition to cachexia, FL-501 may be able to reverse immunosuppression in cancers where elevated GDF-15 is correlated with poor survival, as well as play a role in treating other GDF-15-related diseases. FL-501 is being developed through a collaboration agreement with Adimab.

About Leap
Leap Therapeutics (Nasdaq: LPTX) is focused on developing targeted and immuno-oncology therapeutics. Leap's most advanced clinical candidate, sirexatamab (DKN-01), is a humanized monoclonal antibody targeting the Dickkopf-1 (DKK1) protein. Sirexatamab is being studied in patients with colorectal cancer. Leap's pipeline also includes FL-501, a humanized monoclonal antibody targeting the growth differentiation factor 15 (GDF-15) protein, in preclinical development. 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. Words such as "anticipate," "expect," "project," "intend," "believe," "may," "will," "should," "plan," "could," "continue," "target," "contemplate," "estimate," "forecast," "guidance," "predict," "possible," "potential," "pursue," "likely," and words and terms of similar substance used in connection with any discussion of future plans, actions or events identify forward-looking statements.

All statements, other than historical facts, including statements regarding the potential safety, efficacy, and regulatory and clinical progress of Leap's product candidates; the anticipated timing for initiation or completion of clinical trials and release of clinical trial data and the expectations surrounding

the outcomes thereof; Leap's future clinical or preclinical product development plans for any of Leap's product candidates; Leap's estimations of projected cash runway; 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) the results of Leap's clinical trials and pre-clinical studies, including the final data from Part B of the DeFianCe study and additional preclinical data for FL-501, (ii) Leap's ability to successfully finance or enter into new strategic partnerships for sirexatamab or FL-501; (iii) any regulatory feedback that Leap may receive from U.S. Food and Drug Administration (FDA) or equivalent foreign regulatory agency with respect to the sirexatamab or FL-501; (v) whether any Leap products will receive approval from the FDA or equivalent foreign regulatory agencies; and (vi) exposure to inflation and interest rate fluctuations, as well as fluctuations in the market price of Leap's traded securities. 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 a 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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