Leap Therapeutics and Flagship Biosciences Develop Image Analysis RNAscope Assay for Prospective Trial Enrollment

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CAMBRIDGE, Mass. and WESTMINSTER, Colo., May 12, 2021 /PRNewswire/ -- Leap Therapeutics (Nasdaq: LPTX), a biotechnology company focused on developing targeted and immuno-oncology therapeutics, and Flagship Biosciences, the leader in data-centric pathology and tissue analysis, today announced that they have developed an image analysis RNAscope® assay that is being used successfully for prospective patient enrollment in a clinical trial. To the companies' knowledge, this is the first example of an RNAscope assay using a digital image analysis solution for patient enrollment. The findings were published in an article, "Validation of a DKK1 RNAscope chromogenic in situ hybridization assay for gastric and gastroesophageal junction adenocarcinoma tumors," on Monday, May 10 in *Scientific Reports.* It can be viewed at https://rdcu.be/ckjl5.

Co-authored by a collaborative team from Leap Therapeutics, Flagship Biosciences, and Athenaeum Pathology Consulting, the article highlights how Leap is identifying patients likely to benefit from DKN-01, its anti-Dickkopf-1 (DKK1) antibody, and Flagship's ability to validate and implement complex biomarker assays using digital image analysis. Leap and Flagship's work centered on the development and validation of a DKK1 RNAscope chromogenic in situ hybridization (CISH) assay and digital image analysis solution. DKK1 is a secreted modulator of Wnt signaling that is frequently overexpressed in tumors and associated with a poor prognosis for patients. DKN-01 is a humanized monoclonal therapeutic antibody that binds to and blocks the activity of DKK1 and has demonstrated clinical activity in gastric/gastroesophageal junction (G/GEJ) adenocarcinoma patients with elevated tumoral expression of DKK1 RNA. Leap and Flagship have validated the DKK1 RNAscope assay and accompanying digital image analysis solution as specific, sensitive, accurate, and reproducible according to Clinical Laboratory Improvement Amendments (CLIA) guidelines, and their work is currently being applied to prospectively identify G/GEJ patients with elevated tumoral expression of DKK1 for treatment with a DKN-01 plus tislelizumab combination (Leap Therapeutics; NCT04363801). Additionally, the companies are using the DKK1 RNAscope assay and digital image analysis solution for a retrospective analysis of G/GEJ patients treated with DKN-01 in combination with tislelizumab and chemotherapy.

Biomarkers are increasingly prominent in drug development and are often applied in clinical trial design to determine the patients who are most likely to benefit from a specific therapeutic or treatment regimen. To use a biomarker strategy to prospectively identify patients, the biomarker test must be robust and precise. Because of the challenges in manual semi-quantification of RNAscope tissue staining, Leap and Flagship developed the novel digital image analysis algorithm that identifies tumor cells and quantifies DKK1 signal.

"A potential challenge with RNAscope is manual scoring, which requires a pathologist to score the tissue at a high magnification to visualize and count the number of stained dots that appear in tumor cells," said Michael Kagey, Ph.D., Senior Director of Translational Medicine at Leap Therapeutics. "Since this can lead to slow, inaccurate, and non-reproducible scoring, we worked with Flagship to develop a digital algorithm. The digital algorithm reduces pathologist time, potential variability from manual scoring and allows us to reliably screen for patients who may benefit from our therapy."

In addition to the prospective screening of patients, the work is also further advancing the companion diagnostic development of the RNAscope assay and could generally be used as a guide for the validation of RNAscope CISH assays with digital image quantification.

"Our technology, combined with our scientific process and pathology oversight allows you to quickly find the right patients and get to your endpoints more rapidly," said Trevor Johnson, CEO of Flagship Biosciences. "Image analysis also provides a superior return on investment by saving time and helping get drugs to market more quickly. Our ability to take a completely novel pathology approach and turn it into a CLIA-validated diagnostic test to help our clients is extremely gratifying."

"Our clinical development has been enhanced by the rapid, prospective patient screening that has happened as a result of using the DKK1 RNAscope CISH assay and digital image analysis solution," said Douglas E. Onsi, President and CEO of Leap Therapeutics. "As a result of the partnership between Leap and Flagship, the patients who we believe will best benefit from our drug are now being included in our trial. We look forward to further collaborating with Flagship Biosciences."

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 https://www.leaptx.com or view our public filings with the SEC that are available via EDGAR at https://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.

About Flagship Biosciences
Founded in 2009 and headquartered in Westminster, Colorado, Flagship Biosciences, Inc. is a technology-driven tissue analysis services company delivering the most accurate and informative data available. We are revolutionizing tissue analysis to improve drug development and diagnostics using the power of AI with a consultative approach. Our services and technology dramatically improve on the data and interpretation from traditional pathology methods, eliminating variability associated with typical tissue assessments, and bringing new insights to tissue analysis results. We provide expert scientific consultation for every client. Our team interprets results, contextualizes tissue biology, and identifies the best course for success.
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