Leap Therapeutics Reports Updated Clinical Data from Sirexatamab Colorectal Cancer Study and Announces Exploration of Strategic Alternatives

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Updated data from DeFianCe study continue to demonstrate statistically significant improvements in PFS among the DKK1-high, VEGF-naïve and liver metastasis subgroups

Board of Directors has initiated process to explore strategic alternatives to maximize shareholder value

CAMBRIDGE, Mass., June 23, 2025 /PRNewswire/ -- Leap Therapeutics, Inc. (Nasdaq:LPTX), a biotechnology company focused on developing targeted and immuno-oncology therapeutics, today reported updated results from Part B of the DeFianCe study (NCT05480306), a Phase 2 study of sirexatamab (DKN-01), an anti-DKK1 monoclonal antibody, in combination with bevacizumab and chemotherapy (Sirexatamab Arm) compared to bevacizumab and chemotherapy (Control Arm) in patients with advanced microsatellite stable (MSS) colorectal cancer (CRC) who have received one prior systemic therapy for advanced disease. Due to the Company's financial position, Leap's Board of Directors is taking further steps to preserve capital and has initiated a process to explore strategic options to preserve and maximize shareholder value.

"Sirexatamab demonstrated a statistically significant benefit in patients with high levels of DKK1, no prior exposure to anti-VEGF therapy, or liver metastasis, with a positive trend on ORR and PFS in the full second-line CRC population. With the additional patient follow-up, we believe that the objectives of the DeFianCe study have been achieved. On behalf of everyone at Leap, I thank all the patients and physicians who have participated in our sirexatamab clinical trials," said Douglas E. Onsi, President and Chief Executive Officer of Leap. "However, due to current market conditions, we have decided to wind-down the DeFianCe clinical trial and further reduce internal expenses. In parallel, we have initiated a review of the full range of strategic alternatives to maximize shareholder value."

DeFianCe Study Update

In the updated analysis as of May 22, 2025, sirexatamab demonstrated a positive trend on overall response rate (ORR), by investigator assessment (IA) and blinded independent central review (BICR), and progression-free survival (PFS) in the full second-line CRC population, driven by the statistically significant benefit in patients with high levels of DKK1, no prior exposure to anti-VEGF therapy, or liver metastasis.

- Across the intent-to-treat population (n=188):

	Sirexatamab Arm (n=94)	Control Arm (n=94)	
Median PFS	9.2 months	8.31 months	HR 0.84 95% CI: 0.57, 1.22 p = 0.1749
ORR by IA	35.1 %	26.6 %	p = 0.1009
ORR by BICR	33.0 %	20.2 %	P = 0.0203
Remaining on study drug	21	15	

- In patients with high DKK1 levels (upper quartile, n=44):

	Sirexatamab Arm (n=25)	Control Arm (n=19)	
Median PFS	9.36 months	5.88 months	HR 0.47 95% CI: 0.22, 1.01 p = 0.0237
ORR by IA	44.0 %	15.8 %	p = 0.0149
ORR by BICR	40.0 %	15.8 %	p = 0.0301
Median OS	Not Yet Reached	9.66 months	HR 0.19 95% CI: 0.05, 0.73 p = 0.0037
Remaining on study drug	7	1	

- In patients with DKK1 levels above the median (upper median, n=88):

	Sirexatamab Arm (n=50)	Control Arm (n=38)	
Median PFS	9.03 months	7.23 months	HR 0.56 95% CI: 0.33, 0.94 p = 0.0146
ORR by IA	38.0 %	23.7 %	p = 0.0706

ORR by BICR	40.0 %	15.8 %	p = 0.0039
Median OS	Not Yet Reached	14.39 months	HR 0.48 95% CI: 0.2, 1.16 p = 0.0475
Remaining on study drug	12	3	

- In patients who had not received prior anti-VEGF therapy (n=95):

	Sirexatamab Arm (n=49)	Control Arm (n=46)	
Median PFS	11.2 months	8.34 months	HR 0.61 95% CI: 0.35, 1.06 p = 0.0383
ORR by IA	55.1 %	32.6 %	p = 0.0116
ORR by BICR	44.9 %	26.1 %	p = 0.0252
Median OS	Not Yet Reached	Not Yet Reached	HR 0.47 95% CI: 0.14, 1.6 p = 0.1069
Remaining on study drug	15	5	

- In patients with liver metastases (n=138):

	Sirexatamab Arm (n=73)	Control Arm (n=65)	
Median PFS	9.03 months	7.26 months	HR 0.7 95% CI: 0.46, 1.06 p = 0.0443
ORR by IA	37.0 %	27.7 %	p = 0.1203
ORR by BICR	30.1 %	24.6 %	p = 0.233
Median OS	Not Yet Reached	15.74	HR 0.69 95% CI: 0.33, 1.43 p = 0.1584
Remaining on study drug	14	6	

Corporate Update

Leap is taking additional steps to reduce spending and preserve capital. Over the next two months as the DeFianCe study completes, the Company will implement a workforce reduction of approximately 75%. The total cash payments and costs related to this reduction in force, including severance payments, are estimated to be approximately $3.2 million. The majority of these costs will be recognized in the third quarter of 2025. The Company's cash and cash equivalents totaled $32.7 million as of March 31, 2025.

Leap has initiated a process to explore strategic alternatives to preserve and maximize shareholder value, including leveraging its cash balance and exploring potential sale or partnership opportunities for sirexatamab and FL-501. The Company's Board of Directors has approved the engagement of Raymond James & Associates, Inc. to serve as exclusive financial advisor to assist in the strategic evaluation process.

About Leap Therapeutic
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 and 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, including sirexatamab and FL-501; Leap's intention to implement a workforce reduction of approximately 75%, reduce clinical and operational activities, reduce spending and conserve cash, explore strategic alternatives to preserve and maximize shareholder value, including by leveraging its cash balance and potentially selling or partnering sirexatamab or FL-501; 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 sell or enter into partnerships for sirexatamab or FL-501; (ii) the cost and timeline to complete the DeFianCe Study and wind-down clinical operations; (iii) any regulatory feedback that Leap may receive from U.S. Food and Drug Administration (FDA) or equivalent foreign regulatory agency or from site institutional review boards; (iv) the magnitude, timing and costs associated with the implementation of a workforce reduction; and (v) the availability of strategic alternatives would preserve or generate any shareholder value.

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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