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Leap Therapeutics Announces Publication of DeFianCe Study Results in Clinical Cancer Research

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- ***Peer-reviewed analyses establish baseline plasma DKK1 as a continuous quantitative biomarker predicting deepening sirexatamab benefit in 2L mCRC patients***

- ***In DKK1-high 2L mCRC patients, sirexatamab improved response, progression-free survival, and overall survival when added to bevacizumab and chemotherapy***

CAMBRIDGE, Mass., Aug. 12, 2026 /PRNewswire/ -- Leap Therapeutics, Inc., the biotechnology subsidiary of Cypherpunk Technologies Inc. (Nasdaq: CYPH), today announced the publication of results from the randomized Phase 2 DeFianCe study of sirexatamab (DKN-01), an anti-DKK1 monoclonal antibody, in *Clinical Cancer Research*.

The publication, "Sirexatamab in Combination with Bevacizumab and Chemotherapy as Second-Line Therapy for Advanced Colorectal Adenocarcinoma: the Phase II DeFianCe Trial," reports the complete efficacy, safety and biomarker analyses from the study and details the statistical basis for the DKK1 biomarker finding. It is available online at https://aacrjournals.org/clincancerres/article/doi/10.1158/1078-0432.CCR-26-1456/787049/Sirexatamab-in-Combination-with-Bevacizumab-and.

The peer-reviewed analyses establish that the benefit of sirexatamab increases as a patient's baseline plasma DKK1 level rises — a relationship confirmed by independent statistical approaches and reinforced by the observation that high DKK1 predicts poorer outcomes on standard of care alone. Together, these findings define DKK1-high mCRC as a biologically distinct population with high unmet need and provide the scientific foundation for a biomarker-selected Phase 3 trial. Additional information regarding the Company's regulatory plans and strategic process for sirexatamab is included in the second quarter 2026 financial results announcement issued today by Cypherpunk Technologies Inc.

"In second-line colorectal cancer, we urgently need novel biomarkers that inform patients' treatment options. The final data from the DeFianCe study show that baseline plasma DKK1 identifies patients with more aggressive disease, and it identifies the patients who benefit most from adding sirexatamab. Patients with high DKK1 do worse on standard of care, and they are the patients who gained the most in response and survival when sirexatamab was added," said Zev Wainberg, MD, Professor of Medicine at UCLA and co-director of the UCLA GI Oncology Program.

"Microsatellite-stable colorectal cancer remains one of the most difficult settings in gastrointestinal oncology, as patients whose disease progresses after first-line therapy have quite limited options. We need new liquid biopsy biomarkers that tell us effectively which patients will benefit from which therapy. These data support the utility of baseline plasma DKK1 as a liquid biomarker for improving response rates and survival with sirexatamab, making a compelling case for a biomarker-selected Phase 3 registrational trial," said Markus Moehler, MD, PhD, Head of GI Oncology, Senior Physician Gastroenterology & Endosonography Head at the Mainz University Clinic.

Key Findings from the Publication
DeFianCe (NCT05480306) was a two-part, randomized, open-label, multicenter Phase 2 study. Part B randomized 188 patients 1:1 to sirexatamab plus FOLFIRI or mFOLFOX6 and bevacizumab (Sirexatamab Arm) or to chemotherapy and bevacizumab alone (Control Arm). The primary endpoint was investigator-assessed progression-free survival (PFS); secondary endpoints included objective response rate (ORR) and overall survival (OS). Baseline plasma DKK1 was a prespecified candidate biomarker.

Sirexatamab benefit increased as baseline plasma DKK1 rose

- Three independent analyses — a continuous treatment-by-DKK1 interaction model, a permutation-tested Biomarker Adaptive Threshold (BAT) analysis, and median- and upper-quartile subgroup analyses — converged on the same conclusion: benefit rises with baseline plasma DKK1.
- The treatment-by-DKK1 interaction was statistically significant for both PFS (p=0.0129) and OS (p=0.0027), with DKK1 modeled as a continuous variable.
- The BAT analysis with permutation testing reached the same conclusion (PFS p=0.018; OS p<0.001), and the data-driven cut points aligned with the median and upper quartile of baseline plasma DKK1.

DKK1-high patients above the median (n=88)

- ORR was 38.0% in the Sirexatamab Arm compared with 23.7% in the Control Arm.
- Median PFS was 9.0 months versus 7.1 months; HR 0.61 (95% CI, 0.37–1.00); p=0.0255.
- Median OS was not reached versus 14.4 months; HR 0.42 (95% CI, 0.19–0.91); p=0.0118.

DKK1-high patients in the upper quartile (n=44)

- ORR was 44.0% in the Sirexatamab Arm compared with 15.8% in the Control Arm; p=0.0149.
- Median PFS was 9.4 months versus 5.9 months; HR 0.46 (95% CI, 0.22–0.96); p=0.0168.
- Median OS was not reached versus 9.5 months; HR 0.17 (95% CI, 0.05–0.53); p<0.001.

Higher baseline DKK1 was also prognostic of poor outcome

- In the Control Arm, median OS declined as DKK1 rose — not reached in the overall population, 14.4 months above the median, and 9.5 months in the upper quartile — consistent with published evidence linking elevated DKK1 to more aggressive disease.
- DKK1-high patients therefore represent a population with both poor prognosis on standard therapy and the greatest observed benefit from sirexatamab.

Plasma DKK1 is a practical, blood-based biomarker

- Baseline plasma DKK1 was detectable in 100% of patients across an approximately eight-fold dynamic range.
- Levels were concordant across two orthogonal platforms — an aptamer-based SomaScan assay and an antibody-based Meso Scale Discovery (MSD) assay (Spearman r=0.77).
- Tumoral DKK1 mRNA expression was low in most tissue samples, reinforcing that plasma — not tissue — reflects the systemic DKK1 burden relevant to colorectal cancer biology, and supporting a blood-based patient-selection test.

Results in the overall intent-to-treat (ITT) population

- The prespecified primary endpoint of PFS in the ITT population was not met. Median PFS was 9.2 months in the Sirexatamab Arm versus 8.3 months in the Control Arm; HR 0.84 (95% CI, 0.58–1.21). ORR was 35.1% versus 26.6%, and median OS was not reached in either arm; HR 0.83 (95% CI, 0.46–1.48).
- The final analysis included 119 investigator-assessed PFS events against the 145 events planned, leaving the ITT analysis underpowered in a biologically heterogeneous population.

Safety

- Sirexatamab in combination with chemotherapy and bevacizumab was generally well tolerated. Grade 3 or higher treatment-emergent adverse events (TEAEs) occurred in 59.3% of patients in the Sirexatamab Arm compared with 67.0% in the Control Arm, and serious TEAEs were comparable between arms (19.8% versus 19.3%).
- TEAEs leading to discontinuation of sirexatamab occurred in 4.4% of patients, indicating that adding sirexatamab did not meaningfully change the tolerability of standard of care.

About Sirexatamab (DKN-01)
Sirexatamab (DKN-01) is a humanized monoclonal antibody that binds and neutralizes Dickkopf-related protein 1 (DKK1), a secreted modulator of Wnt signaling associated with more aggressive disease, immune suppression, angiogenesis and poorer outcomes in colorectal and other cancers. In May 2026, the FDA granted Fast Track designation to sirexatamab in combination with fluoropyrimidine plus oxaliplatin- or irinotecan-based chemotherapy and bevacizumab for the treatment of patients with DKK1-high metastatic colorectal cancer whose disease has progressed following one prior systemic therapy.

About Leap Therapeutics
Leap Therapeutics, Inc. is the biotechnology research and development subsidiary of Cypherpunk Technologies Inc. (Nasdaq: CYPH), developing novel therapies for patients with cancer, including sirexatamab (DKN-01) and FL-501. For more information, visit www.leaptx.com.

About Cypherpunk Technologies
Cypherpunk Technologies is a privacy technology company. The Company's mission is to advance technologies that guarantee privacy for humans on the internet. Cypherpunk pursues this mission through two primary strategies: accumulating Zcash (ZEC); and investing in, acquiring, and building technologies that push the frontier of privacy forward. Additionally, through its subsidiary Leap Therapeutics, Inc., the Company is developing novel therapies for patients with cancer, continuing the development of sirexatamab and FL-501. For more information about the Company, visit our websites at http://www.cypherpunk.com and http://www.leaptx.com or view our public filings with the SEC that are available via EDGAR at http://www.sec.gov.

FORWARD-LOOKING STATEMENTS
This press release includes forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These forward-looking statements generally can be identified by the use of words such as "anticipate," "expect," "plan," "could," "may," "will," "believe," "estimate," "forecast," "goal," "intend," "project," and other words of similar meaning. Forward-looking statements in this release include, without limitation, statements regarding the potential clinical benefit of sirexatamab; the role of baseline plasma DKK1 as a predictive biomarker and the development of a companion diagnostic; the Company's plans for and the design, initiation, timing, conduct and potential results of a Phase 3 clinical trial of sirexatamab; the potential for objective response rate to support a filing for accelerated approval in the United States and for overall survival to support full approval in the United States and registration in other markets; the significance of the Company's Type C meeting with the FDA and any alignment reached with the Agency; the definition, validation and prevalence of the DKK1-high patient population and the anticipated size and enrollment of the Phase 3 trial; and the Company's strategic process and the potential for a financing, partnership, license, collaboration, sale or other transaction.

These statements are based on the Company's current expectations and are subject to substantial risks and uncertainties that could cause actual results to differ materially. Important factors include, among others: (i) the DeFianCe study did not meet its prespecified primary endpoint of progression-free survival in the intent-to-treat population; (ii) the DKK1 biomarker subgroup and interaction analyses were exploratory, were based on a limited number of patients, were not adjusted for multiplicity, and may not be replicated in a prospective clinical trial; (iii) the impact of imbalances between treatment arms in the DKK1 subgroups; (iv) the risk that alignment with the FDA on trial design does not constitute agreement that any trial will succeed or that any marketing application will be accepted or approved, and the FDA may change its position at any time; (v) accelerated approval, if pursued, requires that the surrogate endpoint be reasonably likely to predict clinical benefit and is subject to confirmatory trial requirements and possible withdrawal if such requirements are not satisfied; (vi) the Company's ability to initiate or complete the Phase 3 trial on the anticipated

timeline or at all; (vii) the Company's ability to obtain additional capital to advance sirexatamab on acceptable terms or at all; (viii) that risk that the strategic process may not result in any transaction or financing, may be terminated at any time, and any resulting transaction may not be on terms favorable to the Company or its stockholders; (ix) the Company's ability to develop and validate a companion diagnostic; (x) the success of competing therapies; (xi) the Company's ability to secure manufacturing capacity for sirexatamab; and (xii) the Company's ability to maintain and protect its intellectual property rights.

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. The Company 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 the Company's most recent Annual Report on Form 10-K filed with the SEC, or as may be included in other reports or information we file 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 the Company, 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 the Company's views as of any date subsequent to the date hereof.

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