Akero Therapeutics Announces Lancet Publication of the Phase 2b HARMONY Clinical Trial Demonstrating 96 Weeks Treatment with EFX Reduced Liver Fibrosis in Patients with Pre-cirrhotic MASH

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Results support potential of efruxifermin (EFX) to reduce risk of fibrosis progression in patients with pre-cirrhotic (F2-F3) MASH

SOUTH SAN FRANCISCO, Calif., Aug. 14, 2025 (GLOBE NEWSWIRE) -- Akero Therapeutics, Inc. (Nasdaq: AKRO), a clinical-stage company developing transformational treatments for patients with serious metabolic diseases marked by high unmet medical need, today announced publication of 96-week results from the Phase 2b HARMONY trial in *The Lancet*.

The publication reports final results from HARMONY, a 96-week multicenter, randomized, double-blind, placebo-controlled trial that evaluated efruxifermin (EFX) in adults with biopsy-confirmed metabolic dysfunction-associated steatohepatitis (MASH) and moderate (F2) or advanced (F3) fibrosis. Continued treatment with EFX from 24 to 96 weeks resulted in more participants exhibiting improvements in fibrosis and MASH, such that there was near complete reversal of disease in almost one-third of participants treated with the 50mg dose of EFX. EFX-treated participants also exhibited improvements in markers of liver injury and whole-body metabolic health.

"The HARMONY results published in *The Lancet* provide encouraging evidence of EFX's potential to reverse liver fibrosis and resolve steatohepatitis in patients with pre-cirrhotic MASH. The sustained and increased magnitude of response observed with longer treatment underscores the importance of therapies capable of longer-term use to address the underlying drivers of MASH," said Kitty Yale, chief development officer at Akero. "These results, combined with the exciting topline data from the 96-week SYMMETRY trial that demonstrated significant disease reversal in participants with cirrhosis due to MASH, paint an encouraging picture of the potential for EFX to transform patient outcomes, especially in those with a high fibrosis burden and greater risk of hepatic decompensation."

In the modified intent-to-treat (mITT) population at week 96, 49% of participants who received 50mg EFX achieved at least one stage fibrosis improvement without worsening of MASH evaluated by liver histology (the primary endpoint), compared to 19% for placebo (p=0.0030). This improvement was confirmed by digital pathology and corroborated by improvements in non-invasive markers, including liver stiffness and ELF score. Notably, fibrosis improvements were also observed in people with more advanced disease. The primary endpoint was analyzed in the mITT population (all randomized participants who received at least one dose of study drug) with missing biopsies imputed as non-responders.

The secondary endpoint of MASH resolution without fibrosis worsening was achieved by 40% of participants receiving 28mg EFX and 37% receiving 50mg EFX in the mITT population at week 96, compared to 19% for placebo (p=0.020 and p=0.039, respectively). A composite endpoint of both MASH resolution and ≥1-stage fibrosis improvement was met by 35% and 28% of participants in the 50mg and 28mg EFX treatment groups, respectively, versus 7% for placebo (p=0.0013 and p=0.0065, respectively).

Analysis of primary endpoint responders at week 24 and week 96 in the 50mg EFX group indicated that almost all (92%) week 24 responders maintained their response status at week 96, while a majority (63%) of week 24 non-responders became responders at week 96.

EFX was generally well tolerated, with a safety profile consistent with previous trials. The most frequent adverse events were mild to moderate gastrointestinal events (e.g., diarrhea, nausea, increased appetite), which occurred at similar rates in the 28mg and 50mg groups. The rate of treatment discontinuation was similar for both doses but was greater than that for placebo. A small reduction in bone mineral density compared with placebo was observed after 96 weeks of EFX treatment. The relevance of this observation remains to be determined, as poor or declining bone health is common in adults with MASH.

The sustained reductions in fibrosis as well as MASH, the underlying disease driver, observed in this trial reflects an overall improvement in whole body metabolic health as evident by reduced dyslipidemia and increased insulin sensitivity. Furthermore, the magnitude of fibrosis improvement supports the potential of EFX to reduce disease progression and improve clinical outcomes, even in patients with high fibrosis burden. Confirmation of these potential benefits of EFX is being evaluated in the ongoing Phase 3 SYNCHRONY clinical trial program.

About EFX

Efruxifermin (EFX), Akero's lead product candidate for MASH, is currently being evaluated in three ongoing Phase 3 studies. In multiple Phase 2 studies, EFX has been observed to reverse fibrosis (including compensated cirrhosis), resolve MASH, reduce non-invasive markers of fibrosis and liver injury, and improve insulin sensitivity and lipoprotein profile. This holistic profile offers the potential to address the complex, multi-system disease state of all stages of MASH, including improvements in multiple risk factors linked to cardiovascular disease – the leading cause of death among MASH patients. Engineered to mimic the biological activity profile of native FGF21, EFX is designed to offer convenient once-weekly dosing and has been generally well-tolerated in clinical trials to date.

About MASH

MASH is a serious form of MASLD that is estimated to affect 17 million Americans. MASH is characterized by excess fat accumulation in the liver that causes stress and injury to liver cells, leading to inflammation and fibrosis, which can progress to cirrhosis, liver failure, cancer, and death. Approximately 20% of patients with MASH will progress to cirrhosis, which has a higher

risk of mortality. There are no approved treatments for cirrhosis due to MASH and MASH is the fastest growing cause of liver transplants and liver cancer in the US and Europe.

About HARMONY

HARMONY was a Phase 2b multicenter, randomized, double-blind, placebo-controlled trial in adult participants with biopsy-confirmed MASH and fibrosis stage 2 or 3. The trial enrolled and randomized 128 patients to once-weekly subcutaneous dosing of 28mg or 50mg EFX, or placebo for 96 weeks, 126 of whom received at least one dose of study drug and were included in the modified intent to treat (mITT) population. The primary efficacy endpoint was the proportion of participants with ≥1-stage fibrosis improvement without worsening of MASH. The trial continued for up to 96 weeks. Secondary endpoints included MASH resolution without fibrosis worsening, improvement in liver fibrosis, change from baseline in noninvasive markers of liver injury and fibrosis, glycemic control, lipoproteins, and body weight as well as safety and tolerability.

About Akero Therapeutics

Akero Therapeutics is a clinical-stage company developing transformational treatments for patients with serious metabolic diseases marked by high unmet medical need, including metabolic dysfunction-associated steatohepatitis (MASH). Akero's lead product candidate, efruxifermin (EFX), is currently being evaluated in three ongoing Phase 3 clinical studies: SYNCHRONY Histology in patients with pre-cirrhotic (F2-F3 fibrosis) MASH, SYNCHRONY Outcomes in patients with compensated cirrhosis (F4) due to MASH, and SYNCHRONY Real-World in patients with MASH or MASLD (metabolic dysfunction-associated steatotic liver disease). The Phase 3 SYNCHRONY program builds on the results of two Phase 2b clinical trials, the HARMONY study in patients with pre-cirrhotic MASH and the SYMMETRY study in patients with compensated cirrhosis due to MASH. Akero is headquartered in South San Francisco. Visit us at akerotx.com and follow us on LinkedIn and X for more information.

Forward Looking Statements

Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements, including, but not limited to, statements regarding Akero's business plans and objectives, including the ongoing Phase 3 SYNCHRONY clinical trial; and the potential therapeutic effects and anti-fibrotic activity of EFX, as well as the dosing, safety and tolerability of EFX. Any forward-looking statements in this press release are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking

statements. Risks that contribute to the uncertain nature of the forward-looking statements include: the success, cost, and timing of Akero's product candidate development activities and planned clinical trials; Akero's ability to execute on its strategy; positive results from any of its clinical studies may not necessarily be predictive of the results of future or ongoing clinical studies; regulatory developments in the United States and foreign countries; Akero's ability to fund operations; as well as those risks and uncertainties set forth more fully under the caption "Risk Factors" in Akero's most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q, as filed with the Securities and Exchange Commission (SEC) as well as discussions of potential risks, uncertainties and other important factors in Akero's other filings and reports with the SEC. All forward-looking statements contained in this press release speak only as of the date on which they were made. Akero undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

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