Akero Therapeutics Reports Preliminary Topline Results Showing Statistically Significant Reversal of Compensated Cirrhosis (F4) Due to MASH—by Both Completer and ITT Analyses—at Week 96 ir Phase 2b SYMMETRY Study

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Among patients with baseline and week 96 biopsies, 39% of the 50mg EFX group (p=0.009) demonstrated ≥1 stage improvement in fibrosis with no worsening of MASH, representing a 24% effect size over placebo at 15%

By ITT analysis, with all missing week 96 biopsies treated as failures, 29% of the 50mg EFX group (p=0.031) demonstrated ≥1 stage improvement in fibrosis with no worsening of MASH, representing a 17% effect size over placebo at 12%

Investor webcast at 8:00 am ET Monday, January 27, 2025

SOUTH SAN FRANCISCO, Calif., Jan. 27, 2025 (GLOBE NEWSWIRE) -- Akero Therapeutics, Inc. (Nasdaq: AKRO), a clinical-stage company developing transformational treatments for patients with serious metabolic disease marked by high unmet medical need, today released preliminary topline week 96 results from SYMMETRY, a Phase 2b study evaluating the efficacy and safety of its lead product candidate efruxifermin (EFX) in patients with biopsy-confirmed compensated cirrhosis (F4), Child-Pugh Class A, due to metabolic dysfunction-associated steatohepatitis (MASH). Among patients with baseline and week 96 biopsies (n=134), 39% of patients treated with 50mg EFX (n=46) (p=0.009) experienced reversal of cirrhosis with no worsening of MASH, compared to 15% for placebo (n=47). In the Intent to Treat (ITT) population (n=181), with all missing week 96 biopsies treated as failures, 29% of patients in the 50mg EFX group (n=63) (p=0.031) experienced reversal of cirrhosis with no worsening of MASH, compared to approximately 12% in the placebo group (n=61).

With more than a doubling of effect size from weeks 36 to 96 in the 50mg group (from 10% to 24%), the SYMMETRY study underscores the benefit of longer EFX treatment for patients with compensated cirrhosis (F4).

In a subgroup of patients with baseline and week 96 biopsies who were *not* taking GLP-1 at baseline (n=97), 45% in the 50mg EFX group experienced reversal of cirrhosis with no worsening of MASH (n=29) (p=0.009) compared to 17% for placebo (n=36), suggesting that the observed reversal of cirrhosis was not attributable to GLP-1 therapy.

“Until today, we’ve not had the prospect of an effective treatment for compensated cirrhosis due to MASH, which is associated with high rates of short-term morbidity and mortality,” said Mazen Nourredin, M.D., Professor of Medicine and Transplant Hepatologist at Houston Methodist Hospital, and principal investigator for the SYMMETRY study. “Now we have reason to be optimistic about the future potential of EFX as a much-needed treatment for cirrhosis, if approved. I’m so happy for my patients and patients all around the world.”

Summary of Week 96 Reversal of Cirrhosis Endpoint

	Primary Analysis (N=134)[1]			ITT Analysis (N=181)[2]		
Histology Endpoint[3] (Proportion of Patients)	**Placebo (N=47)**	**28mg (N=41)**	**50mg (N=46)**	**Placebo (N=61)**	**28mg (N=57)**	**50mg (N=63)**
≥1 stage fibrosis improvement without worsening MASH (%)	15	29	39 **	12	21	29 *

[1] All patients with baseline and week 96 biopsies

[2] The 47 randomized and dosed patients who had missing biopsies at week 96 are treated as failures in the ITT analysis (without imputation)

[3] Biopsies scored independently by two pathologists; third available to adjudicate (which was not required)

* p<0.05, ** p<0.01, versus placebo (Cochran-Mantel-Haenszel test (CMH))

“We believe today’s first-ever public report of reversal of cirrhosis due to MASH, whether by completer or ITT analysis, sets EFX apart from other approved or investigational treatments in the MASH landscape as a compound with transformational potential,” said Andrew Cheng, M.D., Ph.D., president and chief executive officer of Akero. “We look forward to continuing evaluation of 50mg EFX in our ongoing Phase 3 SYNCHRONY *Outcomes* study in patients with compensated cirrhosis due to MASH.”

The reversal of cirrhosis, as quantified by a consensus of two histopathologists, is supported by improvements in noninvasive measures of liver fibrosis and injury.

Summary of Week 96 Changes in Key Noninvasive Measures of Liver Fibrosis and Injury

Measure **(LS Mean Change From Baseline to Week 96)**	**Placebo (n=49)**	**28mg (n=40-41)**	**50mg (n=47)**
ELF Score	+0.22	-0.34 ***	-0.53 ***
Liver Stiffness (%) (FibroScan)	-8	-18	-24 *
ALT (U/L)	-6.8	-10.5	-11.1

AST (U/L)	-1.6	-8.1	-11.2 **

* p<0.05, *** p<0.001, versus placebo (MMRM)

EFX was reported to be generally well-tolerated. There were no deaths on EFX, but one death in the placebo arm due to pneumonia. None of the Serious Adverse Events were determined to be related to study drug. Across both EFX groups, the most frequent adverse events (AEs) were grade 1 or 2, gastrointestinal in origin (diarrhea, nausea, and increased appetite) and transient in nature.

Conference Call / Webcast Details
Akero will host a conference call and webcast with slide presentation at 8:00 a.m. ET today. The live webcast will be available on the Events & Presentations page of Akero's website, with the recording and presentation available immediately following the event.

About Cirrhosis Due to MASH
Cirrhosis due to MASH (metabolic dysfunction-associated steatohepatitis) is a life-threatening disease with high risk of liver failure, cancer and eventually death. By 2030, an estimated 3 million Americans are projected to have MASH cirrhosis, which is the fastest growing cause of liver transplants and liver cancer in the United States and Europe.

About the SYMMETRY Study
The Phase 2b SYMMETRY study is a multicenter, randomized, double-blind, placebo-controlled, dose-ranging trial in adult patients with biopsy-confirmed compensated cirrhosis (F4, Child-Pugh A) due to MASH. The study enrolled a total of 182 patients, randomized to receive once-weekly subcutaneous dosing of 28mg or 50mg EFX, or placebo for 36 weeks, 181 of whom received at least one study dose. The primary efficacy endpoint for the study was the proportion of patients who achieve at least one-stage fibrosis improvement without worsening of MASH at week 36. Week 96 secondary measures included ≥1 stage fibrosis improvement and no worsening of MASH, MASH resolution, change from baseline in liver enzymes, noninvasive markers of liver fibrosis, glycemic control, and lipoproteins, as well as safety and tolerability measures.

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 lipoprotein 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 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, EFX, is currently being evaluated in three ongoing Phase 3 clinical studies: SYNCHRONY *Histology* in patients with pre-cirrhotic MASH (F2-F3 fibrosis), SYNCHRONY *Outcomes* in patients with compensated cirrhosis 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 future plans or expectations for EFX and ongoing clinical studies, the therapeutic effects of EFX, as well as the dosing, safety and tolerability of EFX; and the future potential of EFX following the preliminary topline week 96 results of Akero's Phase 2b SYMMETRY study, which are subject to audit and verification procedures and additional data that could result in material changes in the final data. 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 a clinical study 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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