In Akero Therapeutics' Phase 2b HARMONY Study, Both the 50mg and 28mg EFX Doses Achieved Statistical Significance on Primary and Secondary Histology Endpoints after 24 Weeks

September 13, 2022

50mg (41%) and 28mg (39%) groups demonstrated ≥1 stage improvement in fibrosis without worsening of NASH, double the placebo rate (20%)

50mg (76%) and 28mg (47%) groups demonstrated NASH resolution without worsening of fibrosis, three to five times the placebo rate (15%)

50mg (41%) and 28mg (29%) groups demonstrated fibrosis improvement AND resolution of NASH, six to eight times the placebo rate (5%)

EFX-treated patients also experienced statistically significant improvements in liver fat, liver enzymes, noninvasive fibrosis markers, glycemic control, lipoproteins, and body weight

Investor webcast at 8:00 am ET today to further discuss data

SOUTH SAN FRANCISCO, Calif., Sept. 13, 2022 (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 topline data from HARMONY, a 24-week Phase 2b study evaluating the efficacy and safety of its lead product candidate efruxifermin (EFX) in patients with pre-cirrhotic nonalcoholic steatohepatitis (NASH), fibrosis stage 2 or 3 (F2-F3). The study met its primary endpoint for both the 50mg and 28mg EFX dose groups, with 41% and 39% of EFX-treated patients, respectively, experiencing at least a one-stage improvement in liver fibrosis with no worsening of NASH by week 24, compared with 20% for the placebo arm.

The study also met a key secondary endpoint with 76% and 47% of patients treated with 50mg and 28mg, respectively, achieving NASH resolution without worsening of fibrosis, compared with 15% for placebo. In addition, 41% and 29% of patients treated with 50mg and 28mg, respectively, achieved both endpoints (NASH resolution and fibrosis improvement ≥1 stage), compared with 5% for placebo.

"The statistically significant histological improvements observed in the HARMONY study are among the strongest efficacy results reported in NASH to date and, together with strong results in secondary endpoints, show that EFX has the potential to treat the core facets of NASH," said Stephen Harrison, M.D., medical director of Pinnacle Clinical Research and the HARMONY study's principal investigator. "I believe the magnitude and general consistency of results observed across the Phase 2a BALANCED and Phase 2b HARMONY studies increase the probability of success in Phase 3 and position EFX to potentially be a foundational monotherapy for patients with NASH."

Patients in the HARMONY study exhibited characteristics of patients at high risk of disease progression. The mean body weight across dose groups was approximately 105 kilograms. Roughly 70% of patients across dose groups had Type 2 diabetes as well as NASH. Approximately twice as many patients in the HARMONY study had fibrosis stage 3 (66%) as fibrosis stage 2 (34%). Despite these indicators of more advanced disease, the study also demonstrated statistically significant effects in multiple secondary endpoints in both dose groups, including improvements in liver fat, liver enzymes, non-invasive fibrosis markers, HbA1c, lipoproteins, and body weight. Treatment with EFX was generally well-tolerated, with a tolerability profile comparable to that observed in Akero's Phase 2a BALANCED study.

"We believe today's results from the HARMONY study are an important milestone not only for Akero but for the entire NASH community," said Andrew Cheng, M.D., Ph.D., president and chief executive officer of Akero. "As the fastest growing cause of liver transplantation and liver cancer in the US and Europe, NASH represents a substantial and growing health burden. We believe the data are very compelling and show EFX's potential to meet the critical, global unmet need for patients by intervening across stages of disease progression, potentially addressing both early-stage metabolic drivers and later-stage inflammation and fibrosis."

Summary of Week 24 Biopsy Endpoints

Measure (Mean)	**Placebo (N=41)**	**28mg (N=38)**	**50mg (N=34)**
Improvement in at least one stage of fibrosis without worsening NASH (%)	20	39 *	41 *
Resolution of NASH without worsening of fibrosis (%)	15	47 **	76 ***
NASH resolution AND improvement in at least one stage of fibrosis (%)	5	29 **	41 ***

* p<0.05, ** p<0.01, *** p<0.001, versus placebo (Cochran-Mantel-Haenszel test)
Biopsy scored independently by two pathologists; third available to adjudicate was not needed

Summary of Week 24 Changes in Liver Fat and Key Markers of Fibrosis and Liver Injury

Measure (LS Mean Change From Baseline to Week 24)	**Placebo (N=40-42)**	**28mg (N=35-38)**	**50mg (N=34-36)**
Hepatic Fat Fraction (MRI-PDFF) (%)	-6	-52 ***	-64 ***
ALT (%)	-4	-38 ***	-47 ***
AST (%)	-2	-39 ***	-49 ***

Pro-C3 (µg/L)	+0.1	-5.1 ***	-5.2 ***
ELF Score	+0.1	-0.6 ***	-0.7 ***
Liver Stiffness (kPa) (FibroScan)	-0.7	-2.6 †	-4.3 **

** p<0.01, *** p<0.001, versus placebo (ANCOVA [Fat Fraction, Liver Stiffness]; MMRM [other endpoints])
† p<0.05, versus baseline (MMRM)

Summary of Key Cardio-Metabolic Biomarkers

Measure (LS Mean Change From Baseline)	**Placebo (N=42)**	**28mg (N=35-37)**	**50mg (N=35-36)**
HbA1c (%, absolute)	-0.0	-0.3 †	-0.4 *
Triglycerides (%)	+9	-25 ***	-29 ***
HDL Cholesterol (%)	-2	+24 ***	+30 ***
Non-HDL Cholesterol (%)	+8	-13 ***	-13 ***
LDL Cholesterol (%)	+9	-8 **	-8 **
Body Weight (kg)	-0.6	-0.2	-2.9 ††

* p<0.05, ** p<0.01, *** p<0.001, versus placebo (MMRM)
† p<0.05, †† p<0.01, versus baseline (MMRM)

EFX was reported to be generally well tolerated. Across both dose groups, the most frequent adverse events (AEs) were grade 1 or 2 gastrointestinal events (diarrhea, nausea, increased appetite, and frequent bowel movements), which were transient in nature. A total of five patients treated with EFX were discontinued due to AEs (two in the 28mg group and three in the 50mg group, one of which was reported to be unrelated to study drug), compared with none for placebo. A single drug-related serious adverse event (SAE) of esophagitis was experienced by a patient in the 50mg group who had a history of gastroesophageal reflux disease. Three other SAEs were reported as unrelated to study drug.

In July of 2021, Akero initiated the SYMMETRY study, a Phase 2b trial in biopsy-confirmed NASH patients with compensated cirrhosis (F4), Child-Pugh class A. Based on enrollment to date, Akero expects to report results from the ongoing Phase 2b SYMMETRY study in the second half of 2023. Results from a 12-week expansion cohort of the SYMMETRY study, evaluating treatment of EFX on top of GLP-1 therapy in patients with F1-F3 fibrosis, are expected in the first half of 2023.

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 the Akero website, with the recording and presentation available immediately following the event.

About NASH
NASH (non-alcoholic steatohepatitis) is a serious form of NAFLD (non-alcoholic fatty liver disease) that is estimated to affect 17 million Americans. NASH is characterized by an excessive accumulation of fat 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 eventually death. There are no approved treatments for the condition and NASH is the fastest growing cause of liver transplants and liver cancer in the US and Europe.

About the HARMONY Study
The Phase 2b HARMONY study is a multicenter, randomized, double-blind, placebo-controlled, dose-ranging trial in biopsy-confirmed adult NASH patients with fibrosis stage 2 or 3. The study enrolled a total of 128 patients, randomized to receive once-weekly subcutaneous dosing of 28mg or 50mg EFX, or placebo for 24-weeks. The primary efficacy endpoint for the study is the proportion of subjects who achieve at least a one-stage improvement in fibrosis without worsening of NASH at week 24. Secondary measures include NASH resolution, change from baseline in liver fat, liver enzymes, noninvasive markers of liver fibrosis, glycemic control, lipoproteins, and body weight at 24 weeks as well as safety and tolerability measures.

About Efruxifermin
Efruxifermin (EFX), formerly known as AKR-001, is Akero's lead product candidate for NASH, currently being evaluated in the ongoing Phase 2b HARMONY study. EFX is designed to reduce liver fat and inflammation, reverse fibrosis, increase insulin sensitivity and improve lipoproteins. This holistic approach offers the potential to address the complex, multi-system disease state of NASH, including improvements in lipoprotein risk factors linked to cardiovascular disease – the leading cause of death in NASH 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 non-alcoholic steatohepatitis (NASH), a disease without any approved therapies. Akero's lead product candidate, efruxifermin (EFX), is a differentiated Fc-FGF21 fusion protein that has been engineered to mimic the balanced biological activity profile of native FGF21, an endogenous hormone that alleviates cellular stress and regulates metabolism throughout the body. EFX is designed to offer convenient once-weekly subcutaneous dosing. The consistency and magnitude of observed effects position EFX to be a potentially best-in-class medicine, if approved, for treatment of NASH. EFX is currently being evaluated in two Phase 2b clinical trials: the HARMONY study in patients with pre-cirrhotic NASH (F2-F3 fibrosis), and the SYMMETRY study in patients with cirrhotic NASH (F4 fibrosis, compensated). EFX is also being evaluated in an expansion cohort of the SYMMETRY study, comparing the safety and tolerability of EFX to placebo when added to an existing GLP-1 receptor agonist in patients with pre-cirrhotic NASH (F1-F3 fibrosis) and Type 2 diabetes. Akero is headquartered in South San Francisco. Visit us at akerotx.com and follow us on LinkedIn and Twitter 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 efruxifermin (EFX), the therapeutic effects of EFX, as well as the dosing, safety and tolerability of EFX; and upcoming milestones, including the results, and expected timing to report such results of Akero's Phase 2b SYMMETRY study; and Akero's preparations for commercialization of EFX, if approved. 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: risks related to the impact of COVID-19 on Akero's ongoing and future operations, including potential negative impacts on Akero's employees, third-parties, manufacturers, supply chain and production as well as on global economies and financial markets; 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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