Study Published in Nature Medicine Shows Investigational NASH Drug Reduced Liver Fat to Normal Levels and Reversed Fibrosis After 16 Weeks of Treatment

July 8, 2021

Efruxifermin (EFX) also improved markers of liver injury, inflammation, lipoproteins, and glycemic control

SOUTH SAN FRANCISCO, Calif., July 08, 2021 (GLOBE NEWSWIRE) -- Akero Therapeutics, Inc. (Nasdaq: AKRO), a cardio-metabolic biotechnology company developing transformational treatments for non-alcoholic steatohepatitis (NASH), today announced that full results of the main portion of its Phase 2a BALANCED trial in biopsy-confirmed NASH patients with F1-F3 fibrosis have been published in *Nature Medicine*.

The manuscript, available at this link, provides a comprehensive analysis showing that pre-cirrhotic NASH patients treated for 16 weeks with Akero's investigational drug, efruxifermin (EFX), an FGF21 analog, achieved substantial reductions in liver fat, associated with decreases in markers of liver injury and inflammation, and reversal of fibrosis after only 16 weeks treatment. Numerous endpoints are reported for the first time in *Nature Medicine*.

"This disclosure of EFX data in *Nature Medicine* marks the first published clinical evidence of fibrosis regression with an FGF21 analog and what we believe are the largest reductions in liver fat publicly reported to date across all NASH investigational drug classes," said Kitty Yale, chief development officer of Akero. "We're pleased to contribute to the field of NASH clinical research with publication of these data. We extend gratitude to the trial participants who made this study possible."

NASH is a serious, potentially life-threatening condition that is a leading cause of liver failure and liver transplantation globally. An estimated 17.3 million Americans had NASH in 2016, a number that is expected to increase to 27.0 million by 2030. There are currently no approved therapies for NASH. Weight loss of 10 percent or more has been shown to reverse NASH by restoring normal levels of liver fat and reducing insulin resistance. Unfortunately, achieving this degree of weight loss through lifestyle change is very challenging.

"The holy grail for NASH drug development is a therapy that treats the whole person, addressing liver fat accumulation, insulin resistance, and liver cell stress that drive the disease, as well as reducing inflammation, and reversing fibrosis," said Stephen Harrison, MD, medical director of Pinnacle Clinical Research and lead author. "The magnitude and consistency of positive effects in all of these areas demonstrate potential for EFX to be a foundational NASH monotherapy."

The BALANCED study was a randomized, controlled Phase 2a trial across 27 U.S. sites that enrolled 80 biopsy-confirmed, pre-cirrhotic NASH patients (F1 to F3 fibrosis stage) who received either placebo or EFX for 16 weeks as a weekly subcutaneous injection in one of three doses: 28 mg, 50 mg, or 70 mg. The study met its primary endpoint of absolute change from baseline in hepatic fat fraction measured at week 12, with 48 percent of EFX patients across dose groups achieving normal levels of liver fat (defined as less than 5 percent liver fat), compared with 5 percent of placebo patients. Reductions in liver fat were associated with substantial decreases in markers of liver injury and fibrosis. Consistent with these observations, 50 percent of EFX patients who had F2/F3 fibrosis at baseline and repeat biopsies after 16 weeks of treatment achieved a two-stage regression of fibrosis. Reflecting EFX's potential to have a beneficial impact on whole body metabolism, EFX patients were reported to have significantly improved levels of triglyceride, non HDL-cholesterol and HbA1c, along with a trend toward lower body weight.

EFX was reported to be generally well tolerated. There were two Serious Adverse Events, one of which occurred prior to dosing, and there were no deaths in the study. Across EFX groups, the most frequent AEs were grade 1 or 2 gastrointestinal events, which were transient in nature.

The BALANCED study also incorporated a 30-patient expansion cohort in late-stage (F4) cirrhotic NASH. Substantial improvements in fibrosis were evident after 16 weeks of treatment among patients with end-of-treatment biopsies, with 58 percent of EFX patients meeting one of two key biopsy endpoints. Specifically, 4 of 12 patients who received 50mg EFX achieved a one-stage improvement in fibrosis without worsening of NASH[1] and 3 of 12 achieved NASH resolution[2], in each case compared with 0 of 5 placebo patients. The expansion cohort data are not included in the *Nature Medicine* publication and will be submitted for potential publication in the future. Topline results are reported here.

About Akero Therapeutics
Akero Therapeutics is a clinical-stage cardio-metabolic company developing transformational treatments for 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 a Phase 2b clinical trial in NASH patients with F2/F3 fibrosis, the HARMONY study. Akero is headquartered in South San Francisco. Visit www.akerotx.com 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, upcoming milestones, and therapeutic effects of EFX, as well as the dosing, safety and tolerability of EFX; Akero's Phase 2a BALANCED clinical trial, including additional analysis of its data and potential therapeutic benefits; Akero's Phase 2b HARMONY clinical trial; and the potential impact of COVID-19 on strategy, future operations, enrollment and clinical trials. 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, as filed with the Securities and Exchange Commission (SEC) and quarterly reports on Form 10-Q filed with the 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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[1] No worsening of NASH mean no increase in NAFLD Activity Score (NAS) for ballooning, inflammation, or steatosis.

[2] NASH resolution is defined as having a NAS of 0 or 1 for lobular inflammation and a score of 0 for ballooning, out of a total possible NAS of 8 (0-3 for steatosis, 0-3 for lobular inflammation, and 0-2 for hepatocyte ballooning).