Akero Therapeutics' Phase 2b SYMMETRY Cohort D Study Met Safety & Tolerability Endpoints and Showed Adding EFX to GLP-1 Therapy Significantly Improved Non-Invasive Markers of NASH-Related Disease

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Patients treated with EFX for 12 weeks combined with GLP-1 achieved a 65% relative reduction in liver fat, compared to a 10% relative reduction for GLP-1 alone

88% of patients treated with EFX combined with GLP-1 had normalized liver fat at week 12, compared with 10% of those treated with GLP-1 alone

EFX-treated patients also experienced statistically significant improvements in liver enzymes and noninvasive markers of fibrosis, glycemic control, and lipids

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

SOUTH SAN FRANCISCO, Calif., June 5, 2023 -- 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 an expansion cohort (N=31) of the Phase 2b SYMMETRY study known as Cohort D. The primary aim of the 12-week study was to assess safety and tolerability of Akero's lead product candidate, efruxifermin (EFX), compared to placebo when added to an existing GLP-1 receptor agonist (GLP-1) in patients with Type 2 diabetes (T2D) and F1-F3 liver fibrosis due to non-alcoholic steatohepatitis (NASH).

EFX was reported to be generally well tolerated in Cohort D with comparable results for the EFX (N=21) and placebo (N=10) groups. The overall tolerability profile was similar to that observed in Akero's BALANCED and HARMONY studies. The most frequent adverse events for EFX-treated patients were grade 1 or 2 gastrointestinal events (diarrhea, nausea, and increased appetite). One patient treated with EFX discontinued due to nausea and one EFX-treated patient discontinued after withdrawing consent. There were no drug-related serious adverse events.

Cohort D also met all key secondary endpoints, including relative reduction of liver fat and proportion of patients whose absolute liver fat level normalized to 5 percent or less. We believe these data, together with statistically significant improvements across many other key NASH-related measures, show that EFX could be an important treatment for patients with NASH who are being treated with GLP-1 for T2D or obesity.

"A substantial portion of patients who have NASH are obese and have Type 2 diabetes, with utilization of GLP-1 therapies increasing rapidly to treat these underlying comorbidities", said Stephen Harrison, M.D., chairman and founder of Pinnacle Clinical Research and principal investigator for the SYMMETRY study. "With this in mind, it is highly encouraging that the Cohort D results not only showed that EFX combined with GLP-1 appeared to be adequately tolerated, but also the combination offered substantial benefit over GLP-1 therapy alone based on multiple key NASH endpoints. Hepatic steatosis was still present in patients on GLP-1 therapy, approximately two-thirds of whom were treated with GLP-1 for over one year, and 88% of patients resolved hepatic steatosis completely when EFX was added."

"We're highly encouraged by the strength and consistency of results across our Phase 2 studies to date," said Kitty Yale, chief development officer of Akero. "With the added support of this newest data set, we believe EFX has the potential to play an important role in treating patients with NASH who are receiving GLP-1 therapy in addition to the potential to be a foundational monotherapy for patients with NASH. We look forward to initiating two Phase 3 SYNCHRONY studies later this year to further our goal of addressing high unmet need across the globe for patients living with NASH."

Summary of Week 12 Changes in Liver Fat

Measure	**Placebo (N=10)**	**EFX 50mg (N=16)**
Hepatic Fat Fraction (MRI-PDFF) (%), LS Mean Relative Change from Baseline	-10	-65 ***
Proportion of patients achieving ≥50% Relative Reduction in Liver Fat (%)	0	88 ***
Proportion of patients with Normalized (≤5%) Liver Fat (%)	10	88***

*** p<0.001, versus placebo (ANCOVA [change from baseline] or CMH [proportion of patients])

Summary of Key Markers of Fibrosis and Liver Injury, LS Mean Absolute Change from Baseline to Week 12

Measure	**Placebo (N=10)**	**EFX 50mg (N=21)**
Pro-C3 (µg/L)	-2.7	-5.2 ††
ELF Score	+0.1	-0.6 **
Liver Stiffness (kPa) (FibroScan)	-1.1	-3.0 †††
FAST Score	+0.04	-0.16 ***
ALT (U/L)	-1.0	-10 *

AST (U/L)	+1.5	-5.3 *

* p<0.05, ** p<0.01, *** p<0.001, versus placebo (Mixed Model Repeated Measures [MMRM])

†† p<0.01, ††† p<0.001, versus baseline (ANCOVA [liver stiffness] or MMRM [all other endpoints])

Summary of Key Cardio-Metabolic Biomarkers, LS Mean Relative Change from Baseline to Week 12

Measure	Placebo (N=10)	EFX 50mg (N=21)
HbA1c (%, absolute)	-0.2	-0.5 †††
Insulin (%)	-13	-26
C-Peptide (%)	-3.5	-22 †
Adiponectin (%)	+16	+129 ***
Triglycerides (%)	-4.1	-42 ***
Non-HDL Cholesterol (%)	-6.8	-19 †††
Apolipoprotein B (%)	-4.5	-21 *
LDL Cholesterol (%)	-6.1	-8.0
HDL Cholesterol (%)	+2.5	+38 ***
Body Weight (kg)	-0.8	-1.2

** p<0.01, *** p<0.001, versus placebo (MMRM)

† p<0.05, ††† p<0.001, versus baseline (MMRM)

In July of 2021, Akero initiated the SYMMETRY main study, a Phase 2b trial in biopsy-confirmed NASH patients with compensated cirrhosis (F4), Child-Pugh class A. Akero expects to report results from the ongoing study in the fourth quarter 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 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 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 and SYMMETRY studies. EFX is designed to reduce liver fat and inflammation, reverse fibrosis, increase insulin sensitivity and improve lipids. 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 NASH, a disease without any approved therapies. Akero's lead product candidate, 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 EFX, the therapeutic effects of EFX, as well as the dosing, safety and tolerability of EFX, including in combination with GLP-1 therapies; and upcoming milestones, including the results, and expected timing to report such results of Akero's Phase 2b SYMMETRY study. 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, including Cohort D, 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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