



Akerio Therapeutics Reports Statistically Significant Histological Improvements at Week 96 in Phase 2b HARMONY Study

March 4, 2024

50mg (75%, $p < 0.001$) and 28mg (46%, $p = 0.07$) EFX groups demonstrated ≥ 1 stage improvement in fibrosis without worsening of MASH, approximately three- and two-fold the placebo rate (24%)

50mg (36%, $p < 0.01$) and 28mg (31%, $p < 0.01$) EFX groups demonstrated ≥ 2 stage improvement in fibrosis without worsening of MASH, more than 10-fold the placebo rate (3%)

EFX-treated patients experienced statistically significant improvements on nearly all histological endpoints by ITT analysis as well as the primary analysis of patients with week 96 biopsies

Investor webcast at 8:00 am ET Monday, March 4, 2024

SOUTH SAN FRANCISCO, Calif., March 04, 2024 (GLOBE NEWSWIRE) -- Akerio 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 HARMONY, a Phase 2b study evaluating the efficacy and safety of its lead product candidate efruxifermin (EFX) in patients with pre-cirrhotic metabolic dysfunction-associated steatohepatitis (MASH), fibrosis stage 2 or 3 (F2-F3). The study previously met its primary endpoint of ≥ 1 stage improvement in fibrosis with no worsening of MASH after 24 weeks of treatment for both the 50mg EFX (41%) and 28mg EFX (39%) dose groups, compared to 20% for the placebo arm. At week 96, the response rates on this endpoint increased to 75% ($p < 0.001$) for 50mg EFX and 46% ($p = 0.07$) for 28mg EFX, compared to 24% for placebo.

The study also met additional histology endpoints at week 96—notably 36% ($p < 0.01$) and 31% ($p < 0.01$) of patients treated with 50mg EFX and 28mg EFX experienced a 2-stage improvement in fibrosis without worsening of MASH—which is more than 10-fold the placebo rate of 3%. Results for all of the histological endpoints are summarized in the table below, based on either the primary analysis (patients with baseline and week 96 biopsies) or intent-to-treat (ITT) analysis (all randomized and dosed patients, with missing data imputed as non-response).

Summary of Week 96 Biopsy Endpoints

Histology Endpoint ³ (Proportion of Patients)	Primary Analysis ¹			ITT Analysis ²		
	Placebo (N=34)	28mg (N=26)	50mg (N=28)	Placebo (N=43)	28mg (N=40)	50mg (N=43)
≥ 1 stage fibrosis improvement without worsening MASH (%)	24	46	75 ^{***}	19	30	49 ^{**}
≥ 2 stage fibrosis improvement without worsening MASH (%)	3	31 ^{**}	36 ^{***}	2	20 ^{**}	23 ^{**}
Resolution of MASH without worsening of fibrosis (%)	24	62 ^{**}	57 ^{**}	19	40 [*]	37 [*]
MASH resolution AND ≥ 1 stage fibrosis improvement (%)	9	42 ^{**}	54 ^{***}	7	28 ^{**}	35 ^{**}

¹ All patients with baseline and week 96 biopsies

² All randomized and dosed patients, with missing data imputed as non-response

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

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, versus placebo (Cochran-Mantel-Haenszel test [CMH])

“Notwithstanding inherent limitations in making cross-trial comparisons, the statistically significant results for ≥ 1 - and 2-stage fibrosis improvement and no worsening of MASH observed for 50mg EFX at week 96 are the largest response rates reported publicly to date for these endpoints in any MASH population,” 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 in patients with pre-cirrhotic MASH are reasons to be optimistic about results of the ongoing Phase 3 SYNCHRONY Histology study and the potential for EFX to be an important MASH medicine, if approved.”

The placebo-adjusted effect size on fibrosis improvement without worsening of MASH (EFX response rate minus placebo response rate) more than doubled between week 24 and week 96 for the 50mg EFX group, with a slight increase observed for the 28mg EFX group. Specifically, the placebo-adjusted effect sizes for fibrosis improvement without worsening of MASH grew from 21% to 52% between week 24 and week 96 for 50mg EFX and from 20% to 22% for 28mg EFX. Highly statistically significant results for 50mg EFX at week 96 are notable because (1) the study was not fully powered at week 96 and (2) the placebo rate increased rather than decreased. An increase in treatment rate for placebo means that the increases in effect size are attributable to higher EFX treatment responses rather than a decline in placebo rate.

Analysis of the evolution of responses between weeks 24 and 96 indicated not only broader fibrosis improvement without worsening of MASH but also sustained response, particularly at 50mg EFX. Among those patients with available week 96 biopsies whose fibrosis improved at week 24, 92% and 83% of the 50mg and 28mg EFX groups remained responders, respectively, compared to 40% for placebo.

Analysis of a subset of patients with baseline F3 fibrosis who had week 96 biopsies showed EFX’s potential to treat patients with more advanced fibrosis, who are generally considered to be at higher risk of progression to cirrhosis. For this advanced F3 patient population, 68% ($p < 0.001$) and 40%

(p=0.053) of the 50mg EFX and 28mg EFX groups, respectively, experienced at least a one-stage improvement in fibrosis without worsening of MASH, compared to 14% for placebo.

"We believe the statistically significant 2-stage improvement in fibrosis without worsening of MASH observed in approximately one in three EFX-treated patients sets EFX apart," said Andrew Cheng, M.D., Ph.D., president and chief executive officer of Akero. "Today's results show that longer exposure to EFX has the potential to yield sustained fibrosis improvement as well as widening anti-fibrotic treatment responses across the treated patient populations. We look forward to continuing our evaluation of EFX in patients with pre-cirrhotic MASH and cirrhosis due to MASH in our ongoing Phase 3 SYNCHRONY program, in which two out of three studies are actively enrolling."

Summary of Changes in Effect Size from Week 24 to Week 96 for ≥1 Stage Fibrosis Improvement Without Worsening of MASH (%)¹

Measure (Mean)	Placebo		28mg EFX		50mg EFX	
	Week 24 (N=41)	Week 96 (N=34)	Week 24 (N=38)	Week 96 (N=26)	Week 24 (N=34)	Week 96 (N=28)
≥1 stage fibrosis improvement without worsening of MASH, n (%)	8 (20)	8 (24)	¹ 15 (39) [*]	12 (46)	14 (41) [*]	21 (75) ^{***}
Placebo-adjusted effect size (%)	NA	NA	20	22	21	52

¹ All patients with baseline and week 96 biopsies

^{*} p<0.05, ^{***} p<0.001, versus placebo (CMH)

Summary of Breadth and Durability of Treatment Response for ≥1 Stage Fibrosis Improvement Without Worsening of MASH

Sustained ¹ vs. New ² Response Among Week 96 Responders	Placebo (N=34)	28mg (N=26)	50mg (N=28)
All week 96 responders, n (%)	8 (24%)	12 (46%)	21 (75%) ^{***}
Sustained response at week 96, n (%) ³	2 (6%)	10 (38%)	11 (39%)
New response at week 96, n (%) ³	6 (18%)	2 (8%)	10 (36%)
Proportion of week 24 responders with sustained response, n (%) ³	2 of 5 (40%)	10 of 12 (83%)	11 of 12 (92%)
Proportion of week 24 non-responders with new response, n (%) ³	6 of 29 (21%)	2 of 14 (14%)	10 of 16 (63%)

^{***} p<0.001, versus placebo (CMH)

¹ Sustained response refers to patients who were responders at week 24 and remained responders at week 96.

² New response refers to patients who were non-responders at week 24 but became first-time responders at week 96.

³ Not analyzed for statistical significance.

Fibrosis Improvement Among Patients with Advanced Fibrosis (F3)

Patients with F3 Baseline Fibrosis and Week 96 Biopsies	Placebo (N=22)	28mg (N=15)	50mg (N=19)
≥1 stage fibrosis improvement without worsening MASH (%)	3 (14%)	6 (40%)	13 (68%) ^{***}

^{***} p<0.001, versus placebo (CMH)

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

Measure	Placebo (n=33-35)	28mg (n=27)	50mg (n=25-28)
(LS Mean Change From Baseline to Week 96)			
Pro-C3 (µg/L) (GEN2 ELISA)	†-17†	†††-40†††	** -51**
ELF Score	-0.1	** -0.7**	** -0.8**
Liver Stiffness (kPa) (FibroScan)	-0.6	* -4.0*	*** -7.2***
ALT (%)	-10	*** -44***	** -37**
AST (%)	-4	* -30*	** -38**

^{*} p<0.05, ^{**} p<0.01, ^{***} p<0.001, versus placebo (MMRM)

††† p<0.001, versus baseline (MMRM)

Summary of Week 96 Changes in Key Cardio-Metabolic Biomarkers

Measure	Placebo (n=34-35)	28mg (n=25-28)	50mg (n=26-27)
(LS Mean Change From Baseline to Week 96)			
Triglycerides (%)	+8	*** -15***	*** -20***
HDL Cholesterol (%)	+5	* +18*	** +27***
Non-HDL Cholesterol (%)	+3	** -2	** -2

LDL Cholesterol (%)	+4	+3	+5
C-peptide (%)	+8	-2	** -20**
HOMA-IR (%)	+7	-11	** -33**
Adiponectin (%)	+17	† +28†	** +63**
Body Weight (kg)	-1.5	-0.3	† -3.5†

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

† p<0.05, versus baseline (MMRM)

EFX was reported to be generally well-tolerated. There were no deaths. Fifteen serious adverse events were reported, which were generally balanced across dose groups. Across both EFX groups, the most frequent adverse events (AEs) were grade 1 or 2 gastrointestinal events (diarrhea, nausea, and increased appetite), which were transient in nature. A total of three patients treated with EFX were discontinued due to AEs between week 24 and week 96 (two in the 28mg group and one in the 50mg group), compared with none for placebo.

In October of 2023, Akero reported week 36 results for the SYMMETRY study, a Phase 2b trial in patients with compensated cirrhosis (F4) due to MASH, Child-Pugh class A. The SYMMETRY study was designed to include a second biopsy after 96 weeks of treatment, for which the results remain on track to be reported in the first quarter of 2025.

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 MASH

MASH (metabolic-associated steatohepatitis) is a serious form of MASLD (metabolic-associated steatotic liver disease) that is estimated to affect more than 17 million Americans. MASH 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 MASH is the fastest growing cause of liver transplants and liver cancer in the United States 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 MASH 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, 126 of whom received at least one study dose. The primary efficacy endpoint for the study was the proportion of subjects who achieve at least one-stage fibrosis improvement without worsening of MASH at week 24. Week 96 secondary measures included ≥1 stage fibrosis improvement and no worsening of MASH, 2-stage fibrosis improvement without worsening of MASH, at least one-stage fibrosis improvement and MASH resolution, change from baseline in liver enzymes, noninvasive markers of liver fibrosis, glycemic control, lipoproteins, and body weight as well as safety and tolerability measures.

About EFX

Efruxifermin (EFX), is Akero's lead product candidate for MASH, currently being evaluated in the ongoing Phase 2b SYMMETRY, Phase 3 SYNCHRONY Histology, and Phase 3 SYNCHRONY Real-World studies. EFX has been observed to reduce liver fat and inflammation, reverse fibrosis, increase insulin sensitivity and improve lipoproteins in multiple clinical trials. This holistic profile offers the potential to address the complex, multi-system disease state of MASH, including improvements in lipoprotein risk factors linked to cardiovascular disease – the leading cause of death in 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), a disease without any approved therapies. Akero's lead product candidate, EFX, is currently being evaluated in two ongoing Phase 3 clinical trials: the SYNCHRONY Histology study in patients with pre-cirrhotic MASH (F2-F3 fibrosis) and the SYNCHRONY Real-World study in patients with MASH or MASLD. A third clinical trial, the SYNCHRONY Outcomes study in patients with cirrhosis due to MASH, is expected to be initiated in the first half of 2024. 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 cirrhosis due to MASH. 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; the timing and enrollment of Akero's Phase 3 SYNCHRONY program and upcoming milestones, including the results, and expected timing to report the long-term follow-up 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 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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