UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of The Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): June 5, 2023

Akero Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-38944**	**81-5266573**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

601 Gateway Boulevard, Suite 350
South San Francisco, CA **94080**
(Address of principal executive offices) **(Zip Code)**

Registrant's telephone number, including area code (650) 487-6488

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	AKRO	The Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 2.02 Results of Operation and Financial Condition.

On June 5, 2023, Akero Therapeutics, Inc. (the "Company") provided an update regarding the amount of cash, cash equivalents and short-term marketable securities it had on hand as of June 2, 2023. Although the Company has not finalized its financial results for such period, the Company currently anticipates that its cash, cash equivalents and short-term marketable securities were approximately $660 million as of June 2, 2023. This information is unaudited and does not present all information necessary for an understanding of the Company's financial condition as of June 2, 2023.

Item 7.01. Regulation FD Disclosure.

On June 5, 2023, the Company issued a press release titled "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." A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The Company from time to time presents and/or distributes to the investment community slide presentations to provide updates and summaries of its business. A copy of its corporate slide presentation is being furnished herewith as Exhibit 99.2 to this Current Report on Form 8-K. The Company undertakes no obligation to update, supplement or amend the materials attached hereto as Exhibit 99.2.

The information under this Item 7.01, including Exhibit 99.1 and Exhibit 99.2 hereto, is being furnished herewith and shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall such information be deemed incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 8.01. Other Events.

On June 5, 2023, the Company 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 its 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 the Company'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.

On June 5, 2023, the Company also announced that it has cash, cash equivalents and short-term marketable securities sufficient to fund its current operating plan into 2026.

Forward-Looking Statements

This Current Report on Form 8-K and certain materials furnished or filed herewith contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, implied and express statements regarding: the Company's business plans and objectives, including future plans or expectations for EFX, the therapeutic effects and clinical benefits of EFX, as well as the dosing, safety and tolerability of EFX; and expectations regarding its uses of capital, expenses and financial results, including the expected cash runway.

Any forward-looking statements 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 public health epidemics affecting countries or regions in which we have operations or do business, such as COVID-19, which has been labelled a pandemic by the World Health Organization, including potential negative impacts on the Company's employees, manufacturers, supply chain and production as well as on global economies and financial markets; the company'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 risks related to the competitive landscape. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause the Company's actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in the Company's annual report on Form 10-K filed, with the United States 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 the Company's other filings with the SEC. All forward-looking statements contained in this presentation speak only as of the date on which they were made. The Company undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release issued by Akero Therapetuics, Inc. on June 5, 2023.
99.2	Corporate slide presentation of Akero Therapeutics, Inc., furnished herewith
104	Cover Page Interactive Data File (embedded within Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: June 5, 2023

AKERO THERAPEUTICS, INC.

By: /s/ Andrew Cheng
Andrew Cheng, M.D., Ph.D.
President and Chief Executive Officer

Exhibit 99.1

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

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)

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 (MMRM)

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.

Investor Contact:
Christina Tartaglia
212.362.1200
IR@akerotx.com

Media Contact:
Sarah O'Connell
732.456.0092
soconnell@vergescientific.com

akero

Restoring Balance. Renewing Life.

Corporate Presentation

June 2023

» Safe Harbor and Legal Disclaimers

This presentation may contain “forward-looking statements” of Akero Therapeutics, Inc. (“we,” “us,” “our,” “Akero” or the “Company”) within the meaning of the Private Securities Litigation Reform Act of 1995 relating to our business, operations, and financial conditions, including but not limited to current express or implied beliefs, expectations and assumptions regarding: the future of our business; future plans and strategies, including our expectations around the therapeutic potential and clinical benefits of Efruxifermin (“EFX”), including in combination with GLP-1 receptor agonist therapies; our development plans for EFX, including our belief in the unique potential of EFX as a foundational NASH therapy; our preclinical and clinical results, including our safety/tolerability, laboratory measures and histology data from our Phase 2a BALANCED study, Phase 2b HARMONY study, and the Cohort D expansion of our Phase 2b SYMMETRY study; the potential benefits resulting from the PRIME, Breakthrough Therapy and Fast Track designations of EFX; the Phase 2b SYMMETRY study, including the Cohort D expansion and expected timing to report preliminary results, and other related milestones; the SYNCHRONY Phase 3 program, including the SYNCHRONY *Histology* and SYNCHRONY *Real-World* studies and design of trials and expected timing thereof; the availability of a new drug product formulation to support Phase 3 clinical trials; risks related to the competitive landscape; the timing and potential benefits of our regulatory interactions; our use of capital, expenses and other future financial results, including the expected cash runway; and the potential impact of COVID-19 on strategy, our employees, supply chain, future operations and clinical trials. Words such as, but not limited to, “look forward to,” “believe,” “expect,” “anticipate,” “estimate,” “intend,” “plan,” “would,” “should” and “could,” and similar expressions or words, identify forward-looking statements. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the section entitled “Risk Factors” in our most recent annual report on Form 10-K filed with the Securities and Exchange Commission (the “SEC”), as well as discussions of potential risks, uncertainties, and other important factors in our other subsequent filings with the SEC. All information in this presentation is as of the date hereof, and we undertake no duty to update this information unless required by law.

Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and the Company’s own internal estimates and research. While the Company believes these third-party sources to be reliable as of the date of this presentation, it has not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, all of the market data included in this presentation involves a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source.

» Corporate Highlights

akero

1 Potential First-in-Class & Best-in-Class NASH Drug

- Substantial potential market opportunity
- Differentiated mechanism of action
- Strongest reported efficacy data among FGF21s, including:
  - Fibrosis improvement
  - NASH Resolution
  - Improved glycemic control

Ph3 SYNCHRONY program announced

2 Building Momentum Toward Phase 3 Pivotal Trials

- Two parallel Phase 2b trials underway
  - HARMONY (F2-F3)
  - SYMMETRY (F4, compensated)
- Regulatory designations
  - Breakthrough Therapy (US FDA)
  - Fast Track (US FDA)
  - PRIME (European EMA)
- Commercial product-device for Ph3

SYMMETRY readout expected 4Q'23

3 Experienced & Validated Team with Substantial Resources

- Involved in 20+ FDA approvals
- ~$660M cash, cash equivalents and short-term marketable securities on hand as of June 2, 2023, including proceeds in April and May from the ATM and a Registered Direct offering.

Cash runway into 2026

Extensive Development and Commercialization Experience Involved in 20+ Medicine Approvals

Andrew Cheng, MD, PhD | President & CEO

- 19 years at Gilead
- Chief Medical Officer & HIV Division Head
- Major role in 11 NDA/MAA approvals

Tim Rolph, D.Phil | Co-Founder & Chief Scientific Officer

- Over 30 years at Pfizer & Glaxo
- CSO of Pfizer's cardiovascular and metabolic disease unit
- Head of Groton & UK Discovery Research, Pfizer
- Major role in discovery and early clinical evaluation of two medicines: Selzentry (HIV) and Steglatro (Diabetes)

Jonathan Young, PhD, JD | Co-Founder & COO

- Over 15 years in biotechnology product development, law and regulatory policy
- General Counsel and VP Policy, Braeburn
- Partner and General Counsel, FoxKiser

Kitty Yale | Chief Development Officer

- Over 25 years at Gilead, Roche, Pfizer
- VP, Gilead Worldwide Clinical Operations
- Major role in 8 global approvals NDA, MAA, JNDA and CFDA

Patrick Lamy | SVP, Commercial Strategy

- Over 20 years of commercial experience at Gilead, Iovance and other small biotech
- Most Recently, VP Commercial at Iovance
- Five product launches is liver disease including global launch lead for Gilead's HCV franchise

William White | CFO & Head of Corporate Development

- 18 years in life sciences investment banking at Goldman Sachs, Citigroup and Deutsche Bank
- Most recently, Head of US Life Sciences Investment Banking at Deutsche Bank
- Advised on more than $70bn in M&A and $25bn in financing transactions

» Providing a Potentially Effective Treatment for NASH

Reducing liver fat is critical to remove disease driver

Peripheral fat is the largest source of liver fat in patients with NASH

30 Million US patients with NASH expected by 2030

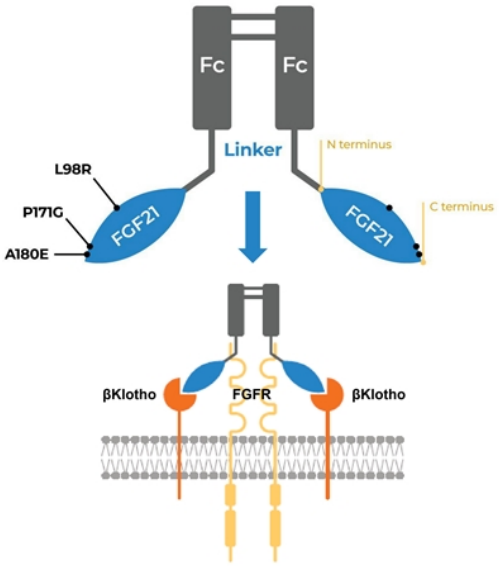
Insulin resistance and Type 2 Diabetes drives liver caloric burden

Achieving >10% weight loss is challenging for patients who are obese

Reversing fibrosis is key to avoiding transplant, cancer, death

Dyslipidemia drives cardiovascular disease, the #1 cause of mortality in the US

EFX Engineering Potentially Optimal for NASH Efficacy, With Convenient Once-weekly Dosing



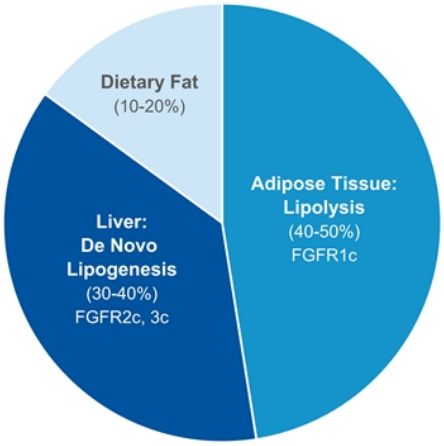
Key attributes

- Akero proprietary Fc-FGF21, Point mutations
- Increases half-life from < **2 hours** to ~**3 days**
- **High affinity** for β-Klotho
- Better translation to **human** pharmacology
- **Balanced potency** at FGFR1c, 2c, 3c
- **Inactive** at FGFR4

Stanislaus, S *et al.* (2017) *Endocrinology* 158(5): 1314-27; Lee, S *et al.* (2018) *Nature* 553: 501-505; Kharitonenkov, A *et al.* (2007) Endocrinology 148(2)774-781

EFX Acts on Two Major Sources of Liver Fat With Potential for Optimal Reduction

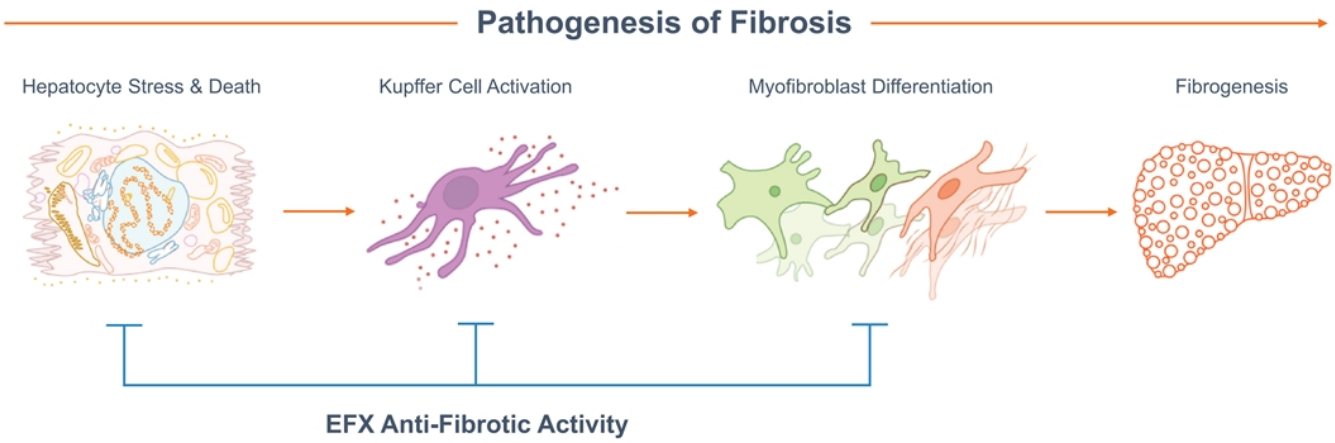
Sources of Fat Flowing into and Through Liver for Patients with NASH



Acting on both hepatic and peripheral sources of liver fat is key to optimizing liver fat reduction

Source of Liver Fat	FGF Receptor	EFX Activity
Lipolysis	FGFR1c	✓
De Novo Lipogenesis	FGFR2c FGFR3c	✓

» EFX Direct And Indirect Anti-fibrotic Effects



Bao, L *et al.* (2018) *Br J Pharmacol* 175:3379-3393; Fisher, FM *et al.* (2014) *Gastroenterology* 147:1073-1083.e6; Jimenez, V *et al.* (2018) *EMBO Mol Med* 10:e8791; Lee, JH *et al.* (2016) *Am J Transl Res* 8:4750-4763; Sanyal, A *et al.* (2018) *Lancet* 392:2705-2717; Le, CT *et al.* (2018) *PLOS one* 13:e0192146; Xu, P *et al.* (2016) *Toxicol Appl Pharmacol* 290:43-53; Yu, Y *et al.* (2016) *Int Immunopharmacol* 38:144-152

**Cited literature available on company website*

» Key Regulatory Designations Based on EFX Therapeutic Profile

akero

Breakthrough Therapy (US FDA - 2022)

- Enables expedited development
- Signifies potential for substantial improvement over available therapy on clinically significant endpoints
- Based on Phase 2b HARMONY data

Fast Track (US FDA - 2021)

- Enables more frequent regulatory interactions to resolve development issues with potential eligibility for priority review
- Signifies potential to fill an unmet medical need
- Based on Phase 2a BALANCED data

PRIME (EMA - 2020)

- Enables enhanced regulatory support
- Signifies potential to offer a major therapeutic advantage over existing treatments or benefit patients without treatment options
- Based on Phase 2a BALANCED data

Efruxifermin was the first investigational NASH drug to receive all three designations

FDA, Guidance for Industry: Expedited Programs for Serious Conditions – Drugs and Biologics (2014);
European Medicines Agency, Reflection paper on a proposal to enhance early dialogue to facilitate accelerated assessment of priority medicines (PRIME) (Draft 2015)

HARMONY

STATISTICALLY SIGNIFICANT EFFECTS AFTER 24 WEEKS

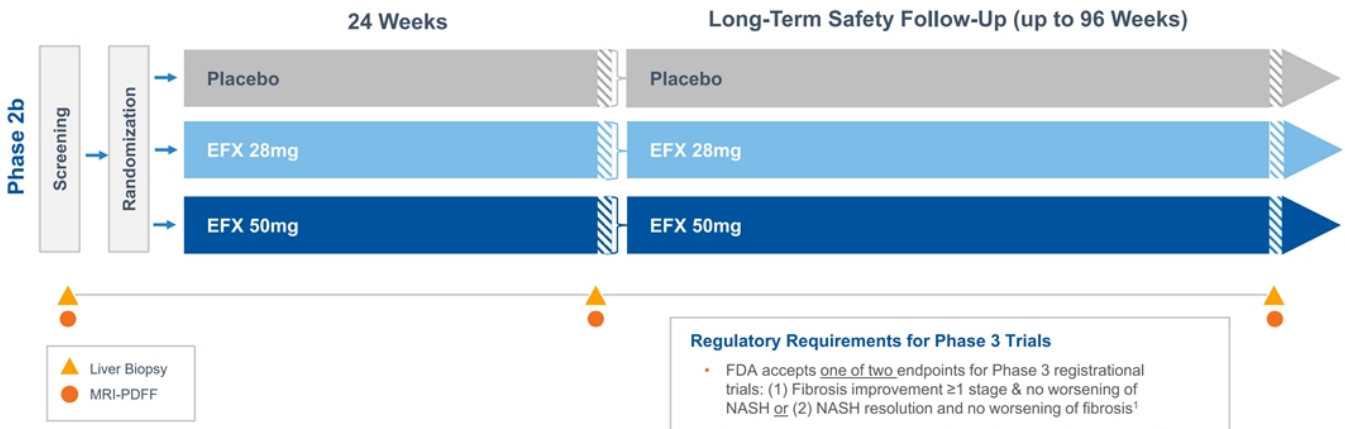
» HARMONY Trial Design: Pre-Cirrhotic (F2-F3) NASH

akero

Key Inclusion Criteria
- F2-F3 NASH
- NAS ≥4
- Liver Fat (MRI-PDFF) ≥8%

Phase 2b Primary Endpoint
- ≥ 1-stage fibrosis improvement without worsening of NASH

Key Secondary Efficacy Endpoints
- NASH Resolution & No Worsening of Fibrosis
- Fibrosis Markers
- Lipoproteins
- Glycemic Control
- Weight Change
- MRI-PDFF
- Liver Injury Markers

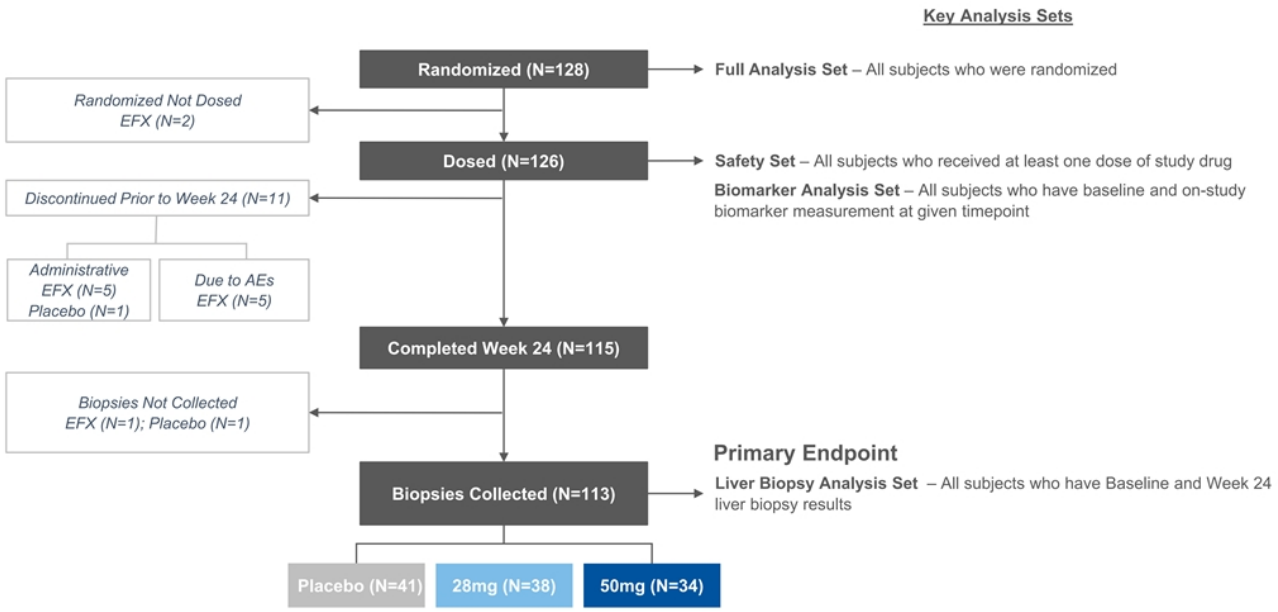


Regulatory Requirements for Phase 3 Trials
- FDA accepts one of two endpoints for Phase 3 registrational trials: (1) Fibrosis improvement ≥1 stage & no worsening of NASH or (2) NASH resolution and no worsening of fibrosis[1]
- EMA requires both endpoints to be met for marketing approval[2]

[1] FDA Draft Guidance, Noncirrhotic Nonalcoholic Steatohepatitis With Liver Fibrosis: Developing Drugs for Treatment (2018)

[2] EMA, Draft Reflection paper on regulatory requirements for the development of medicinal products for chronic non-infectious liver diseases (PBC, PSC, NASH) (2018)

» Week 24 Patient Disposition & Analysis Sets



» Baseline Demographics

Parameter (Mean)	Placebo (N=43)	EFX 28mg (N=42)	EFX 50mg (N=43)
Age (Years)	55	57	52
Sex (% Female)	63	69	53
Weight (kg)	108	104	103
Type 2 Diabetes (%)	65	76	70
Fibrosis Stage (% F3)[1]	70	64	63
Enhanced Liver Fibrosis (ELF) Score	9.8	9.7	9.8
Pro-C3[2] (µg/L)	16.5	15.3	18.4
Liver Stiffness by VCTE[3] (FibroScan) (kPa)	15	14	16
Hepatic Fat Fraction by MRI-PDFF[4] (%)	17.1	18.5	17.5
NAFLD Activity Score (NAS)	5.4	5.1	5.6
Alanine Aminotransferase (ALT) (U/L)	62	50	63
Aspartate Aminotransferase (AST) (U/L)	57	42	52
HbA1c (%)	6.8	6.8	6.7
Triglycerides (mg/dL)	170	158	154
LDL-Cholesterol (mg/dL)	94	96	111

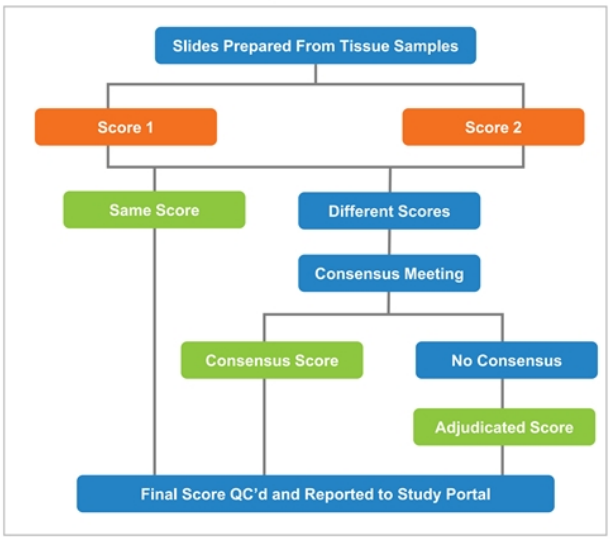
[1] All patients either fibrosis stage 2 (F2) or stage 3 (F3); [2] Procollagen 3 N-Terminal Propeptide; [3] Vibration-controlled transient elastography; [4] Magnetic Resonance Imaging Proton Density Fat Fraction

Consensus Reading of Biopsies: Rigorous Approach to Histopathology Based on FDA Input to Minimize Variability

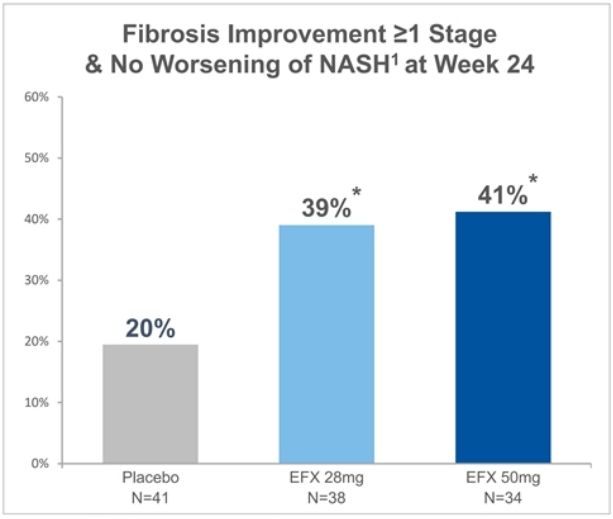
Key Features of EFX Biopsy Analysis Plan

- Biopsies independently scored by two pathologists, with a third pathologist available to adjudicate in absence of consensus
- Pathologists underwent protocol-specific training to align on NASH-CRN scoring interpretation
- Pathologists blinded to subject, treatment, and sequence
- No paired biopsy reads (i.e., pre- and on-treatment biopsies not read side-by-side)

Consensus Biopsy Analysis Flow Chart



Both EFX Doses Achieved Statistical Significance on Primary Endpoint (Fibrosis Improvement)



* p<0.05, versus placebo (Cochran–Mantel–Haenszel test [CMH])

[1] Per FDA guidance, this endpoint is defined as: "Improvement in liver fibrosis greater than or equal to one stage (NASH CRN fibrosis score) **and** no worsening of steatohepatitis (defined as no increase in NAS for ballooning, inflammation, or steatosis)"
FDA Draft Guidance, Noncirrhotic Nonalcoholic Steatohepatitis With Liver Fibrosis: Developing Drugs for Treatment (2018), p.7

Source Data: Liver Biopsy Analysis Set

EFX Fibrosis Improvement in Context: Pre-Cirrhotic NASH
(≥1 Stage Improvement in Fibrosis and No Worsening of NASH)

Efruxifermin
Phase 2b (F2-F3)
66% F3
24 Wks / Completers[1]
Consensus Readers

Pegozafermin
Phase 1b/2a (F2-F3)
65% F3
24 Wks / Completers[4]
Consensus Readers

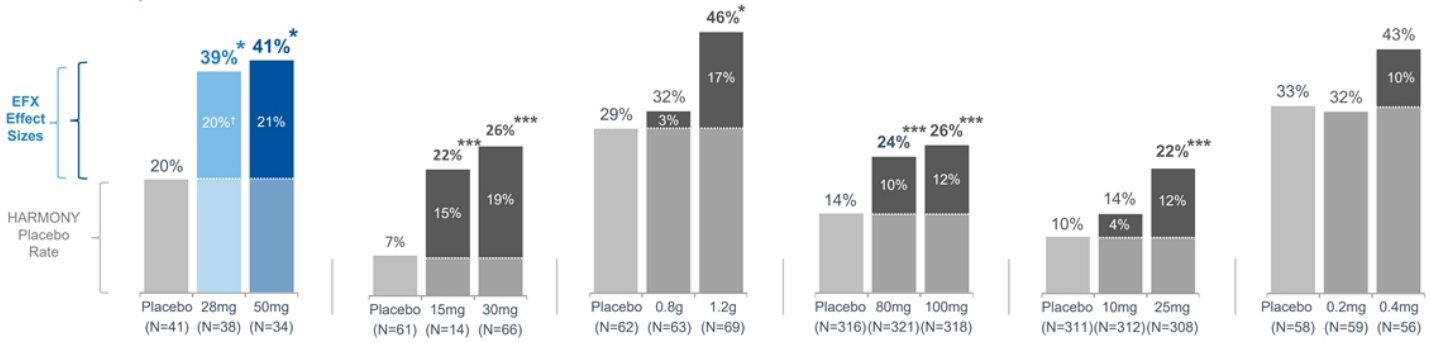
Lanifibranor
Phase 2b (F1-F3)
% F3 Not Reported
24 Wks / Completers[2]
Single Reader

Resmetirom
Phase 3 (F1-F3)
62% F3
52 Wks / ITT[3]
Two Readers
(Combined Statistically)

Obeticholic Acid
Phase 3 (F2-F3)
54% F3
72 Wks / ITT[3]
Consensus Readers

Semaglutide
Phase 2b (F2-F3)
69% F3
72 Wks / ITT[3]
Consensus Readers

By Reported Effect Size (Treatment Minus Placebo)



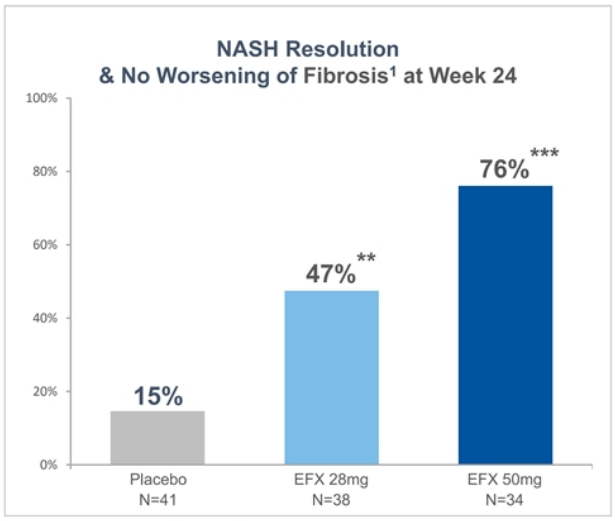
Note: These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.

[1] Baseline and Week 24 biopsies available; [2] End-of-study biopsy available with no major protocol deviations; [3] Missing biopsies were imputed as non-responders; [4] End-of-study biopsy available.

Pegozafermin - 89Bio (2023) March 22 Corporate Presentation; Lanifibranor - Francque et al. (2021) New Engl J Med 385, 1547–1558; Obeticholic acid - Intercept (2022) July 7 Press Release; Semaglutide - Newsome et al. (2020) New Engl J Med 384, 1113-24; Resmetirom – Madrigal (2022) December 19 Press Release. All trademarks are the property of their respective owners.

† 39.47 - 19.51 = 19.96 * p<0.05, *** p<0.001, versus placebo

Both EFX Doses Achieved Statistical Significance on Key Secondary Endpoint (NASH Resolution)



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

[1] Per FDA guidance, this endpoint is defined as: "Resolution of steatohepatitis on overall histopathological reading **and** no worsening of liver fibrosis on NASH CRN fibrosis score. Resolution of steatohepatitis is defined as absent fatty liver disease or isolated or simple steatosis without steatohepatitis and a NAS score of 0–1 for inflammation, 0 for ballooning, and any value for steatosis"
FDA Draft Guidance, Noncirrhotic Nonalcoholic Steatohepatitis With Liver Fibrosis: Developing Drugs for Treatment (2018), p.7

Source Data: Liver Biopsy Analysis Set

EFX NASH Resolution in Context: Pre-Cirrhotic NASH
(NASH Resolution and No Worsening of Fibrosis)

Efruxifermin
Phase 2b (F2-F3)
66% F3
24 Wks / Completers[1]
Consensus Readers

Semaglutide
Phase 2b (F2-F3)
69% F3
72 Wks / ITT[2]
Consensus Readers

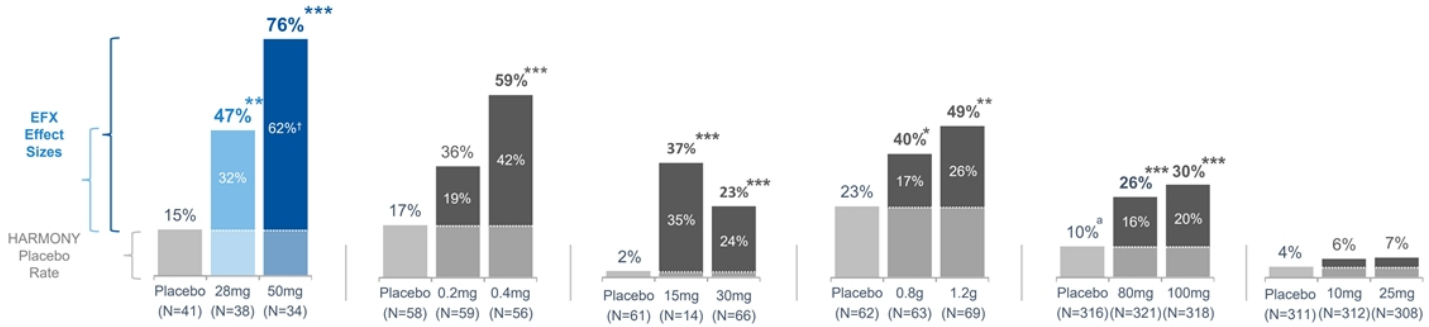
Pegozafermin
Phase 1b/2a (F2-F3)
65% F3
24 Wks / Completers[4]
Consensus Readers

Lanifibranor
Phase 2b (F1-F3)
% F3 Not Reported
24 Wks / Completers[3]
Single Reader

Resmetirom
Phase 3 (F1-F3)
62% F3
52 Wks / ITT[3]
Two Readers
(Combined Statistically)

Obeticholic Acid
Phase 3 (F2-F3)
54% F3
72 Wks / ITT[2]
Consensus Readers

By Reported Effect Size (Treatment Minus Placebo)



Note: These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.

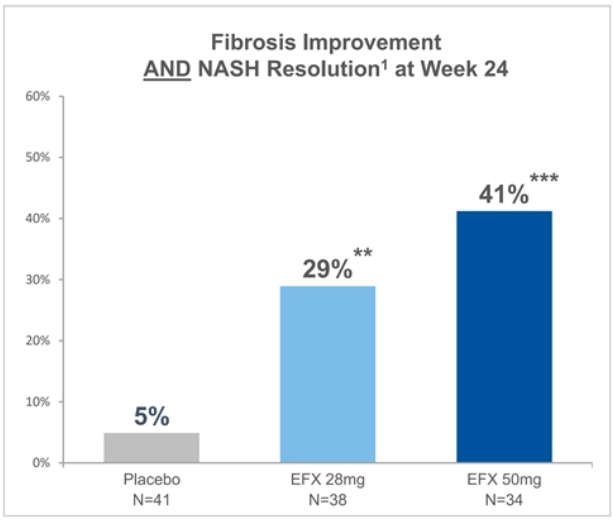
[1] Baseline and Week 24 biopsies available; [2] Missing biopsies were imputed as non-responders; [3] End-of-study biopsy available with no major protocol deviations; [4] End-of-study biopsy available.
[a] Modified definition of NASH resolution (requiring ≥2 point reduction in NAS) might lead to lower placebo response rate

Semaglutide - Newsome et al. (2020) New Engl J Med 384, 1113–1124; Pegozafermin - 89Bio (2023) March 22 Corporate Presentation; Lanifibranor - Francque et al. (2021) New Engl J Med 385, 1547–1558; Resmetirom – Madrigal (2022) December 19 Press Release; Obeticholic acid - Intercept (2022) July 7 Press Release. All trademarks are the property of their respective owners.

† 76.47 - 14.63 = 61.84

* p<0.05, ** p<0.01, *** p<0.001, versus placebo

Both EFX Doses Achieved Statistical Significance on Composite Endpoint (Fibrosis Improvement and NASH Resolution)



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

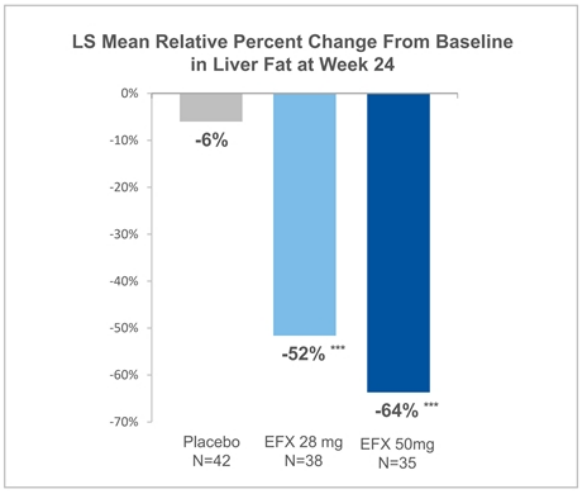
Patients Achieving Fibrosis Improvement ≥2 Stages and No Worsening of NASH at Week 24

Placebo (N=41)	EFX 28mg (N=38)	EFX 50mg (N=34)
5%	16%	15%

[1] Per FDA guidance, this endpoint is defined as: "Both resolution of steatohepatitis and improvement in fibrosis…. Resolution of steatohepatitis is defined as absent fatty liver disease or isolated or simple steatosis without steatohepatitis and a NAS score of 0–1 for inflammation, 0 for ballooning, and any value for steatosis…. Improvement in liver fibrosis greater than or equal to one stage (NASH CRN fibrosis score)"
FDA Draft Guidance, Noncirrhotic Nonalcoholic Steatohepatitis With Liver Fibrosis: Developing Drugs for Treatment (2018), p.7-8

Source Data: Liver Biopsy Analysis Set

Magnitude of Reduction and Normalization of Liver Fat Comparable to Phase 2a BALANCED Study[1]



*** p<0.001, versus placebo (ANCOVA)

Proportion of Patients Achieving Fat Reduction Thresholds at Week 24

Endpoint	Placebo (N=42)	EFX 28mg (N=38)	EFX 50mg (N=35)
Relative Reduction in Liver Fat			
≥50%	2%	63% ***	77% ***
Normalization of Liver Fat Content			
≤5%	2%	34% ***	51% ***

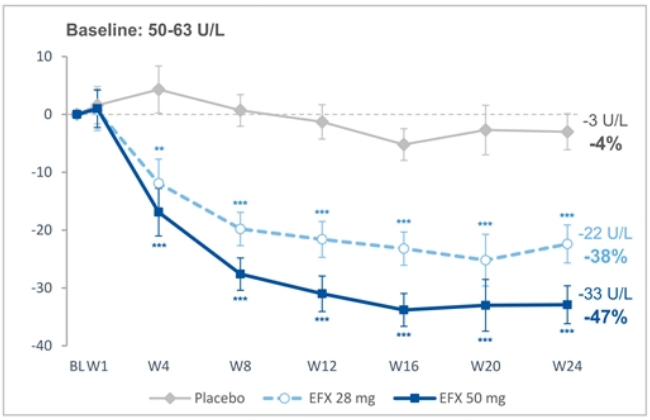
*** p<0.001, versus placebo (CMH)

[1] The Phase 2a BALANCED study was a 12-week randomized clinical trial in patients with F1-F3 NASH

Source Data: MRI-PDFF Analysis Set (All subjects who have Baseline and Week 24 liver fat measurements)

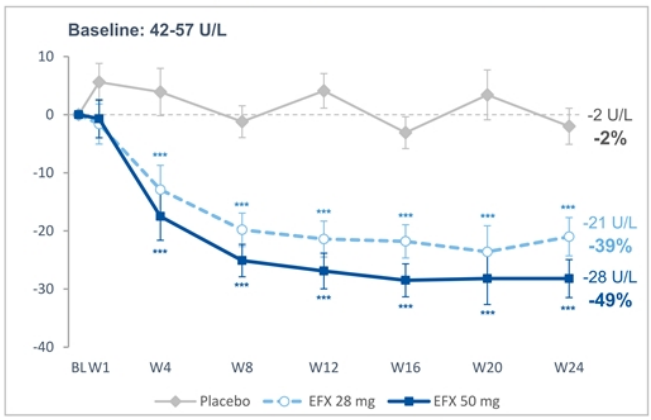
Rapid and Sustained Statistically Significant Improvements in Markers of Liver Injury

ALT
LS Mean [SE] Change from Baseline (U/L)



** p<0.01, *** p<0.001, versus placebo (MMRM[1])

AST
LS Mean [SE] Change from Baseline (U/L)



*** p<0.001, versus placebo (MMRM[1])

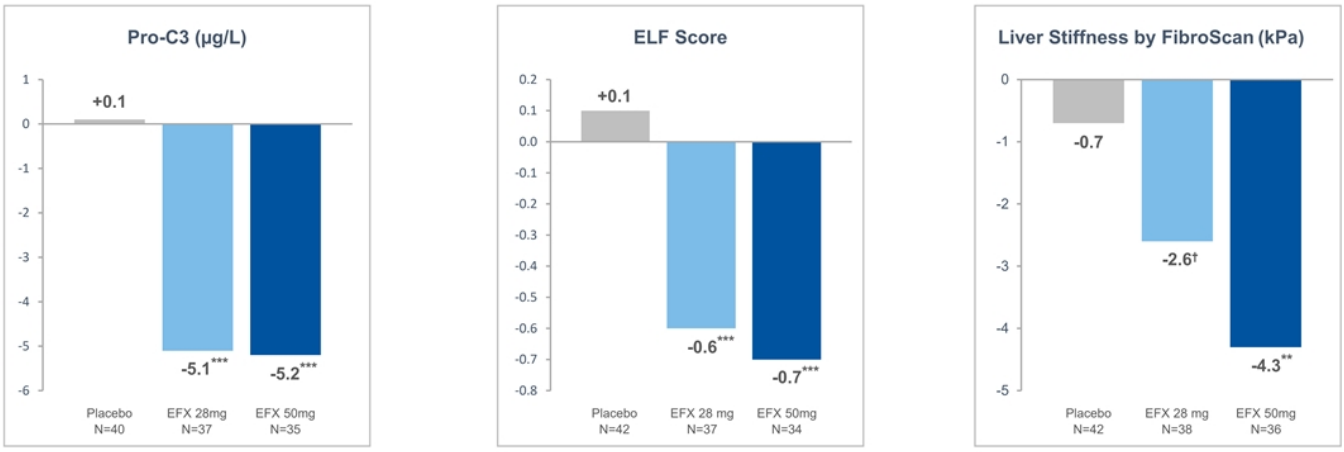
Statistically significant improvements also observed for GGT & ALP

[1] Mixed Model Repeated Measures

Source Data: Full Analysis Set

Statistically Significant Reductions in Non-Invasive Markers Reflect Histological Improvement in Fibrosis

LS Mean Change From Baseline to Week 24



*** p<0.001, versus placebo (MMRM[1])

*** p<0.001, versus placebo (MMRM[1])

** p<0.01, versus placebo (ANCOVA[2])
† p<0.01, versus baseline (ANCOVA[2])

[1] Mixed Model Repeated Measures; [2] Analysis of Covariance

Source Data: Biomarker Analysis Set (Pro-C3 and ELF); Full Analysis Set (Liver Stiffness) (non-missing values only, no imputation)

» Treatment-Emergent Adverse Events (TEAE)

akero

TEAE Overview	Placebo (N=43)	EFX 28mg (N=40)	EFX 50mg (N=43)
TEAE Leading to Death	0 (0%)	0 (0%)	0 (0%)
Drug-Related Serious Adverse Event (SAE)	0 (0%)	0 (0%)	1 (2%)[a,b]
Drug-Related TEAE Leading to Discontinuation	0 (0%)	2 (5%)[c]	2 (5%)[d,e]
Most Frequent (≥15%) Drug-Related TEAEs	**Placebo**	**EFX 28mg**	**EFX 50mg**
Diarrhea	6 (14%)	14 (35%)	14 (33%)
Nausea	5 (12%)	10 (25%)	14 (33%)
Increased Appetite	2 (5%)	7 (18%)	10 (23%)
Frequent Bowel Movements	1 (2%)	8 (20%)	0 (0%)
Injection Site Erythema	5 (12%)	6 (15%)	7 (16%)
Injection Site Bruising	1 (2%)	6 (15%)	3 (7%)

[a] (1) Esophagitis
[b] There were three additional non-drug-related SAEs: (1) Edema; (2) Covid-19; (3) Pancreatitis
[c] (1) Increased appetite & weight gain; (2) diarrhea
[d] (1) Esophagitis & vomiting; (2) Nausea
[e] There was one additional non-drug-related SAE: Lymphadenopathy (not drug-related)

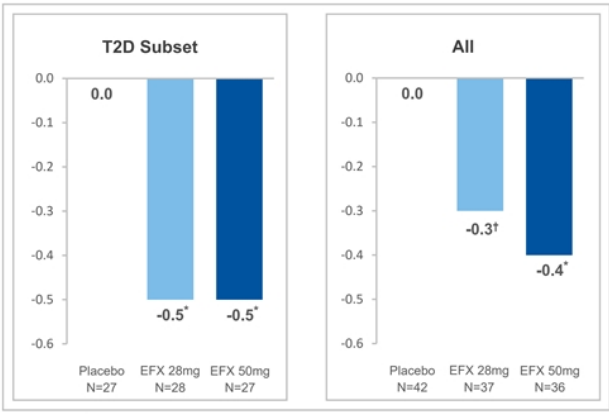
Source Data: Safety Set

Clinically Meaningful Improvements Observed in Glycemic Control and Insulin Sensitivity, Particularly in Patients with T2D

akero

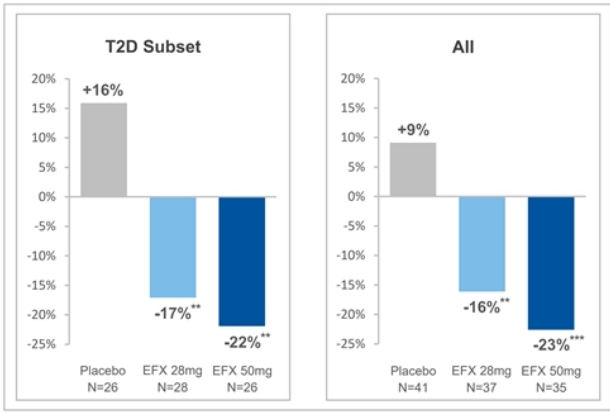
LS Mean Change From Baseline to Week 24[2]

HbA1c(%)[1]



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

C-Peptide[3]

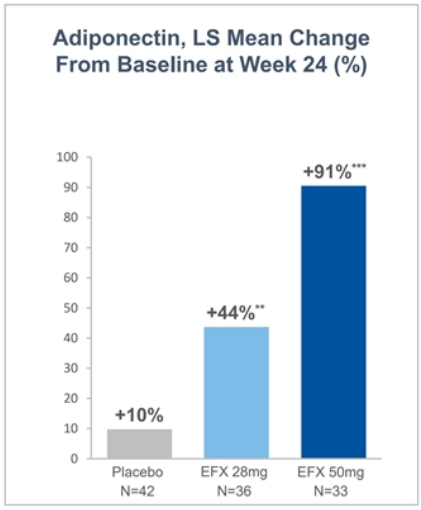


** p<0.01, *** p<0.001, versus placebo (MMRM)

[1] Absolute change from baseline, %; [2] Patients remained on diabetic medications; [3] Relative percent change from baseline

Source Data: Biomarker Analysis Set

Substantial Increases Observed in Adiponectin, a Marker of Insulin Sensitizing Action of EFX



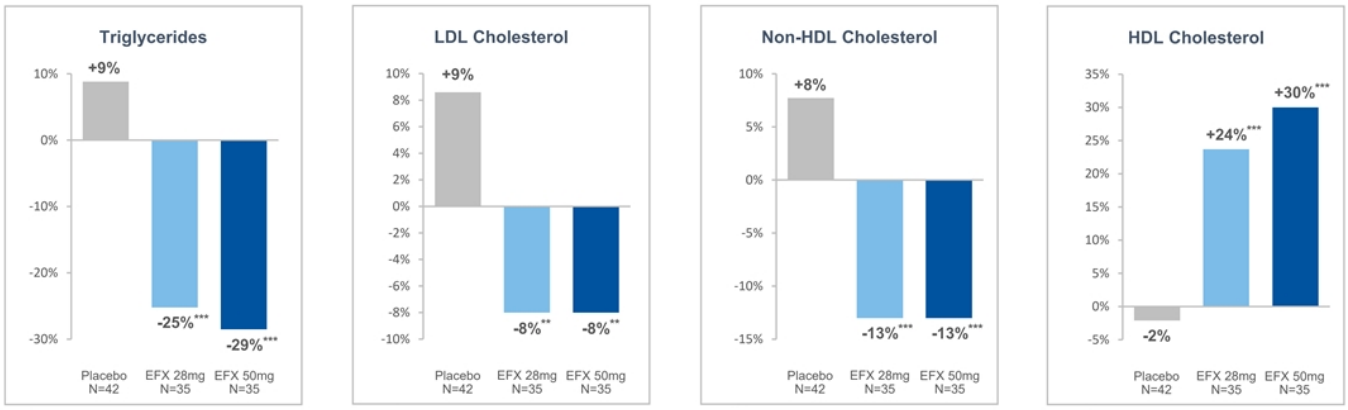
** p<0.01, *** p<0.001, versus placebo (MMRM)

Source Data: Full Analysis Set, non-missing values only, no imputation

» Statistically Significant Improvements Observed in Lipoprotein Profile

akero

LS Mean Change From Baseline to Week 24 (%)



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

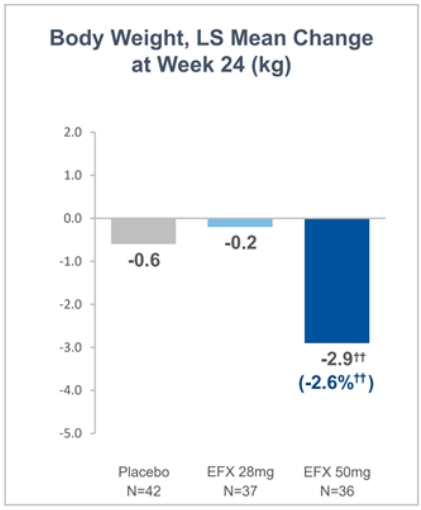
** p<0.01, versus placebo (MMRM)

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

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

Source Data: Full Analysis Set, non-missing values only, no imputation

» Weight Loss Observed for 50mg EFX Dose Group



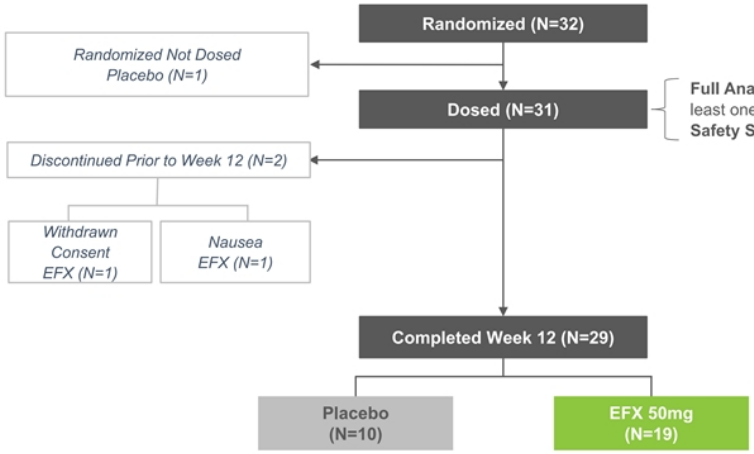
†† p<0.01, versus baseline (MMRM)

Source Data: Full Analysis Set, non-missing values only, no imputation

Cohort D Study Design

[a] Approximately two-thirds of randomized patients were on a stable dose of GLP-1 for more than one year; all patients were on a stable dose for at least three months.

» Week 12 Patient Disposition & Key Analysis Sets



Full Analysis Set – All patients who were randomized and received at least one dose of study drug
Safety Set - All subjects who received at least one dose of study drug

» Baseline Demographics

Parameter (Mean)	Placebo (N=10)	EFX 50mg (N=21)
Age (Years)	55	59
Sex (% Female)	90	43
Weight (kg)	96	101
Fibrosis Stage (% F1 / F2 / F3)	40 / 10 / 50	38 / 33 / 29
Hepatic Fat Fraction by MRI-PDFF[1] (%)	15	11
Pro-C3[2] (µg/L)	34	33
Enhanced Liver Fibrosis (ELF) Score	9.6	9.2
Liver Stiffness by VCTE[3] (FibroScan) (kPa)	12	10
Alanine Aminotransferase (ALT) (U/L)	31	35
Aspartate Aminotransferase (AST) (U/L)	24	26
HbA1c (%)	6.5	7.0
Triglycerides (mg/dL)	171	163
LDL-Cholesterol (mg/dL)	98	73
Statin Use (%)	50	81

[1] Magnetic Resonance Imaging Proton Density Fat Fraction; [2] Procollagen 3 N-Terminal Propeptide; [3] Vibration-controlled transient elastography

» Concomitant Diabetic Medications at Baseline

GLP-1s	Placebo (N=10)	EFX 50mg (N=21)
Semaglutide	60%	43%
Dulaglutide	30%	52%
Liraglutide	10%	5%
Tirzepatide[1]	0%	0%
Other Diabetic Medications	**Placebo**	**EFX 50mg**
Metformin	70%	76%
Insulin	30%	48%
SGLT-2	20%	33%
Sulfonylureas	20%	24%
DPP-IV	0%	10%

[1] With one exception, all patients remained on their baseline GLP-1 therapy through Week 12; one patient entered treatment on a stable dose of semaglutide but switched to tirzepatide after the Week 10 visit due to unavailability of semaglutide.

Source Data: Safety Analysis Set

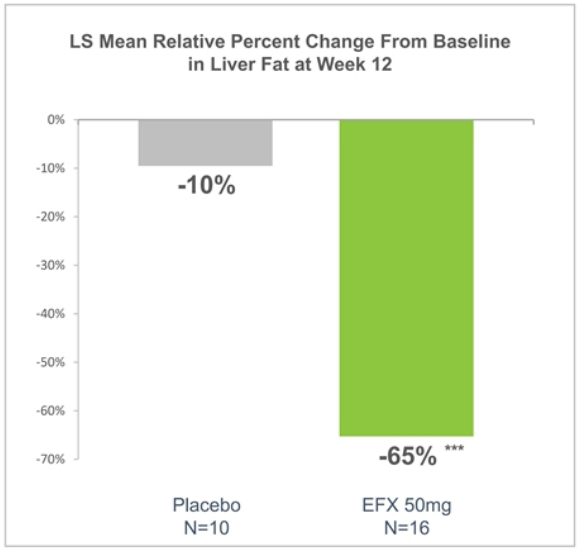
Primary Endpoint: Comparable Safety and Tolerability Across Both Treatment Groups

Treatment-Emergent Adverse Event (TEAE) Overview	Placebo (N=10)	EFX 50mg (N=21)
TEAE Leading to Death	0 (0%)	0 (0%)
Drug-Related Serious Adverse Event (SAE)	0 (0%)	0 (0%)[a]
Drug-Related TEAE Leading to Discontinuation	0 (0%)	1 (5%)[b]
Most Frequent (≥15%) Drug-Related TEAEs	**Placebo**	**EFX 50mg**
Diarrhea	3 (30%)	4 (19%)
Nausea	1 (10%)	7 (33%)
Increased Appetite	0 (0%)	5 (24%)
Decreased Appetite	2 (20%)	3 (14%)

[a] Two SAEs in the EFX group were not drug related: post-procedural hemorrhage and uterine cancer.
[b] Nausea

Source Data: Safety Analysis Set

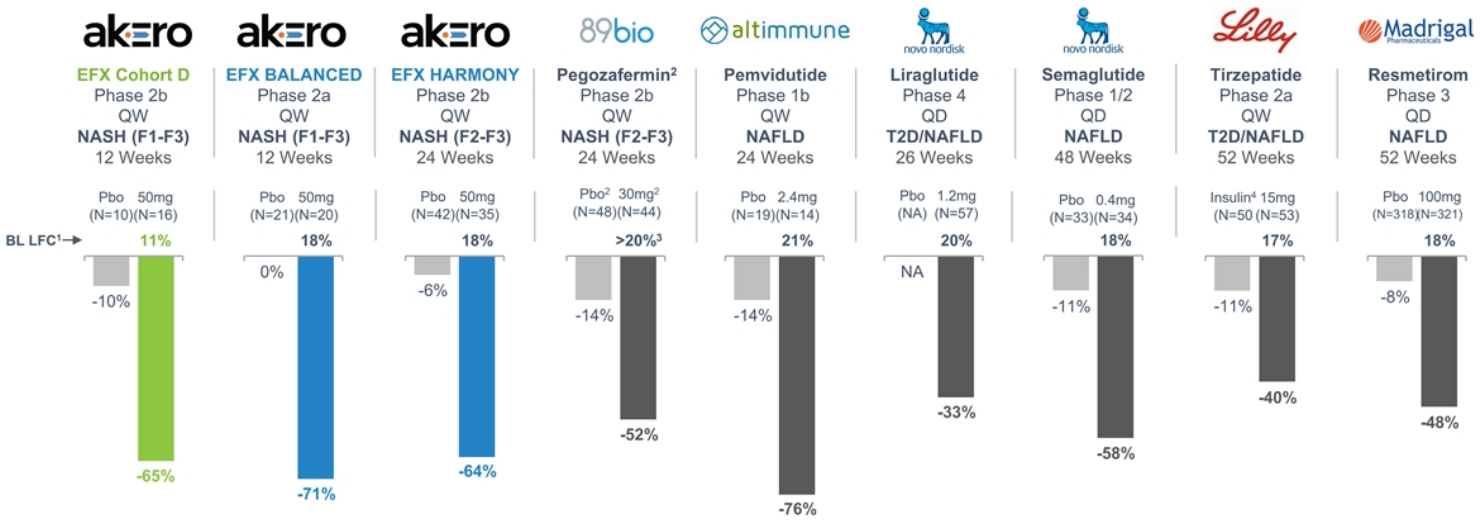
Significantly Greater Relative Reductions in Liver Fat by MRI-PDFF for EFX Combined with GLP-1 than GLP-1 Alone



*** p<0.001, versus placebo (ANCOVA[1])
[1] Analysis of Covariance

Source Data: MRI-PDFF Analysis Set (all subjects with baseline and on-study measurements assessed by MRI-PDFF [N=26]); Topline preliminary data

» EFX Liver Fat Reduction in Context: NAFLD & Pre-Cirrhotic NASH



[1] Baseline Liver Fat Content

Note: These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.

[2] Reported reductions only for subset of patients with liver fat content ≥10% at baseline

[3] Estimated for subset of patients with LFC ≥10% at baseline

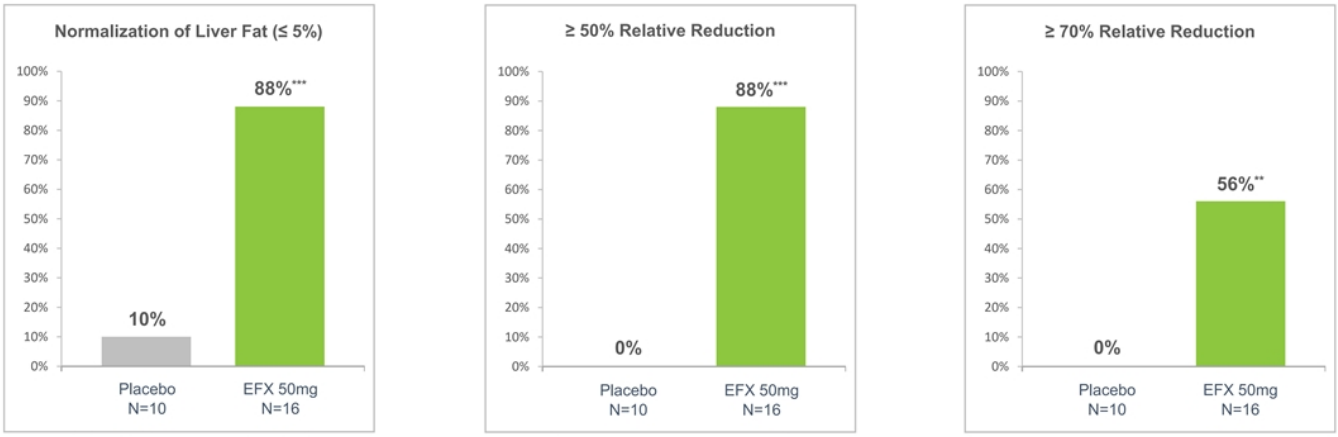
[4] Insulin Degludec

Pegozafermin - 89Bio (2023) May 6 Corporate Presentation; Pemvidutide - Altimmune (2023) March Evercore NASH Renaissance Presentation; Liraglutide - Petit et al (2017) J Clin Endocrinol Metab 102(2):407-15; Tirzepatide - Gastaldelli et al (2022) Lancet Diabetes Endocrinol 10(6):P393-406; Resmetirom - Madrigal (2023) May Corporate Presentation; Semaglutide - Flint et al. (2021) Aliment Pharmacol Ther 54(9):1150-61. All trademarks are the property of their respective owners.

More Patients Treated with EFX Combined with GLP-1 Met Higher Thresholds of Liver Fat Reduction and Normalization than GLP-1 Alone

akero

Proportion of Patients Achieving Liver Fat Reduction Thresholds at Week 12



*** p<0.001, versus placebo (CMH)

*** p<0.001, versus placebo (CMH[1])

** p<0.01, versus placebo (CMH)

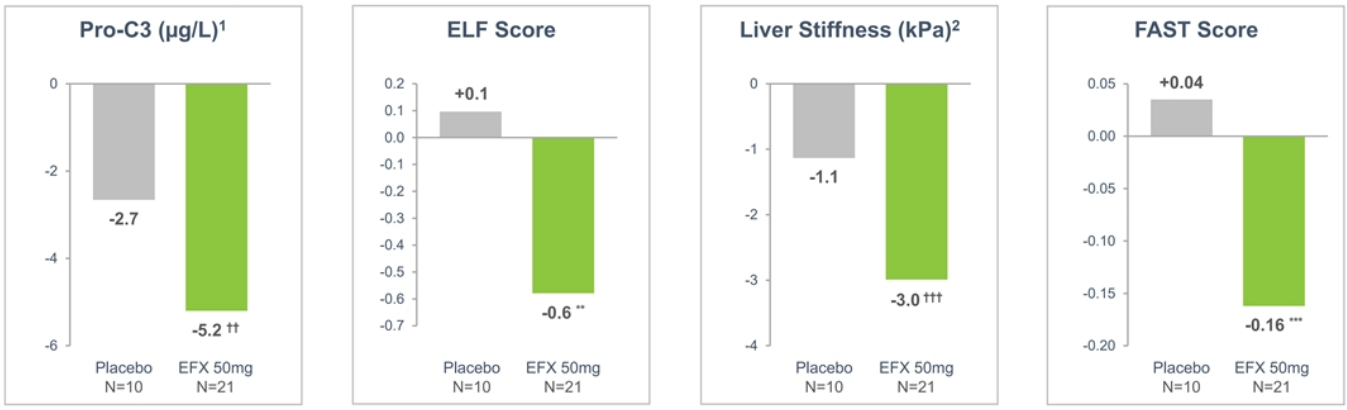
In the HARMONY Study, patients whose liver fat was normalized had 3-fold higher odds of achieving NASH Resolution and Fibrosis Improvement

[1] Cochran–Mantel–Haenszel test

Source Data: MRI-PDFF Analysis Set; Topline preliminary data

Greater Reductions in Markers of Fibrosis for EFX Combined with GLP-1 than GLP-1 Alone

LS Mean Change From Baseline to Week 12



†† p<0.01, versus baseline (MMRM)[1]

** p<0.01, versus placebo (MMRM)

††† p<0.001, versus baseline (MMRM)

[2] Measured by FibroScan

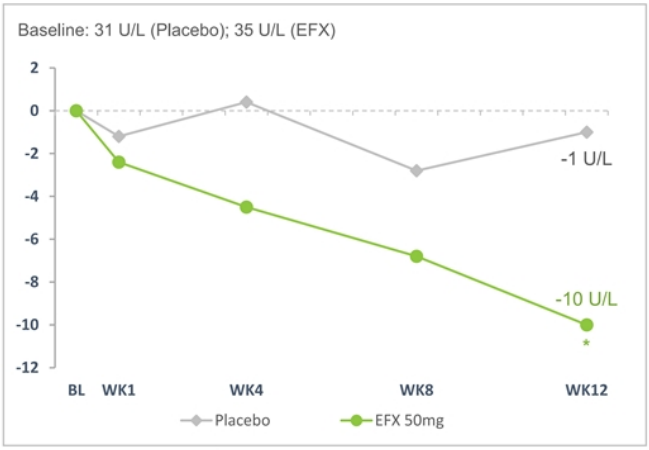
*** p<0.001, versus placebo (MMRM)

[1] Mixed Model Repeated Measures (MMRM)

Source Data: Full Analysis Set; Topline preliminary data

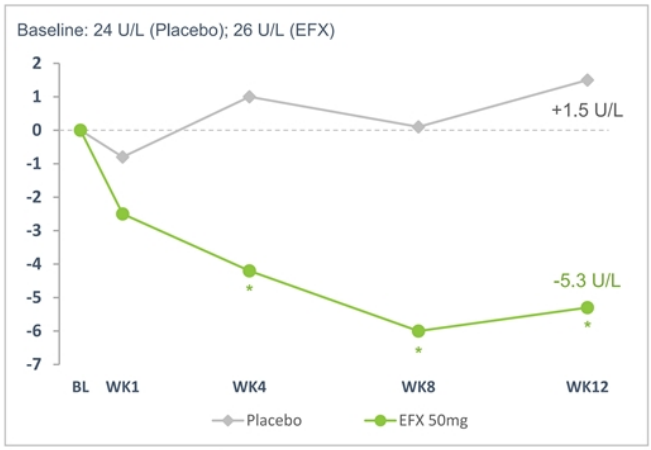
Greater Reductions in Markers of Liver Injury for EFX Combined with GLP-1 than GLP-1 Alone

ALT
LS Mean Change from Baseline (U/L)



* p<0.01, versus placebo (MMRM)

AST
LS Mean Change from Baseline (U/L)



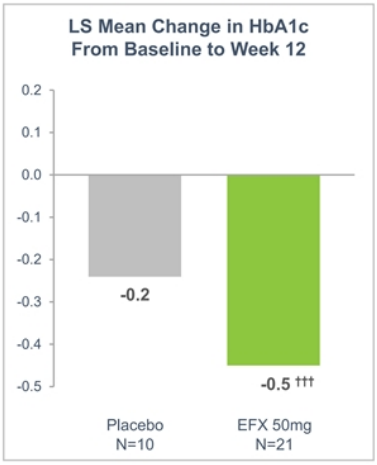
* p<0.01, versus placebo (MMRM)

Source Data: Full Analysis Set; Topline preliminary data

» Clinically Meaningful Improvements in HbA1c after Only 12 Weeks

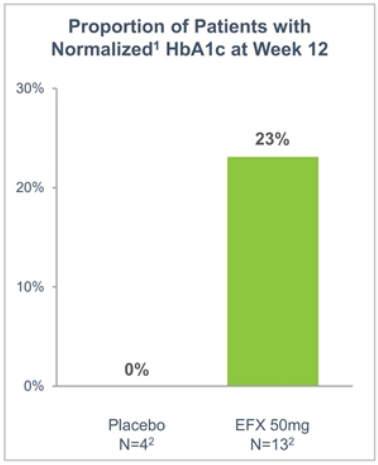
akero

HbA1c



††† p<0.001, versus baseline (MMRM)

HbA1c Normalization[1]

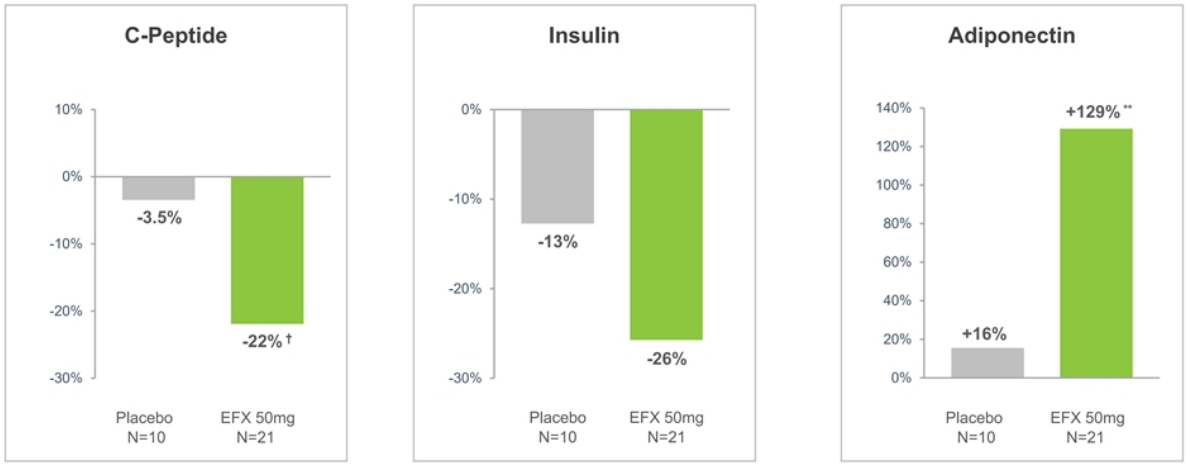


[1] Normalization of HbA1c defined as an HbA1c of ≥6.5 at baseline and <6.5 at week 12
[2] Number of patients with HbA1c ≥6.5 at baseline

Source Data: Full Analysis Set; Topline preliminary data

» EFX Complements GLP-1 by Increasing Sensitivity to Insulin

LS Mean Change From Baseline to Week 12



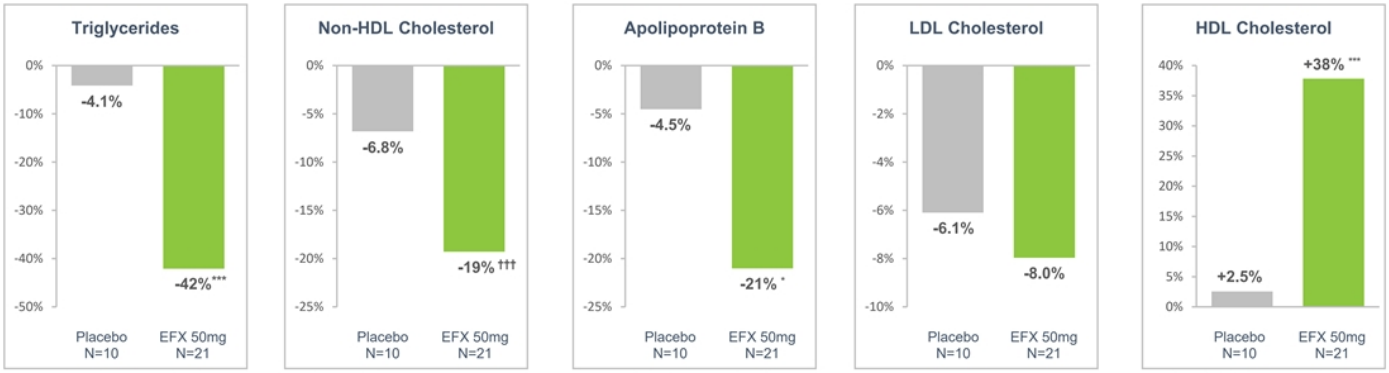
† p<0.001, versus baseline (MMRM)

** p<0.01, versus placebo (MMRM)

Source Data: Full Analysis Set; Topline preliminary data

Much Greater Improvements in Lipids for Patients Treated with EFX in Combination with GLP-1 than GLP-1 Alone

LS Mean Percent Change From Baseline to Week 12



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

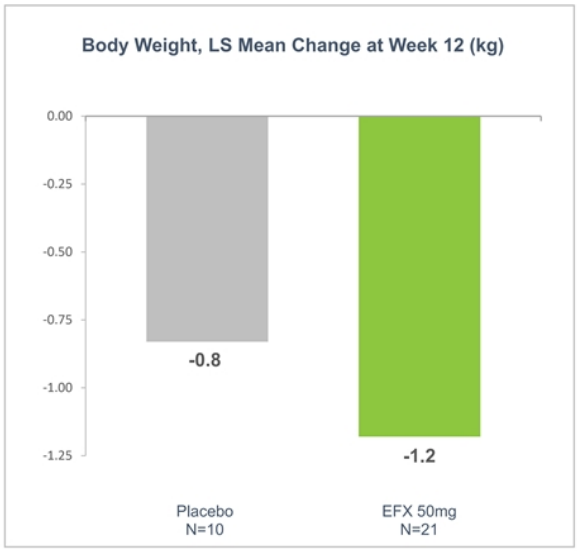
††† p<0.01, versus baseline (MMRM)

* p<0.05, versus placebo (MMRM)

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

Source Data: Full Analysis Set; Topline preliminary data

» Weight Loss Maintained for EFX Combined with GLP-1



Source Data: Full Analysis Set; Topline preliminary data

Cohort D Adds to a Growing Body of Evidence for EFX's Potential as a Cornerstone NASH Treatment

Key Take-Aways

- EFX and GLP-1 have complementary mechanisms of action.
- Addition of EFX to GLP-1 in patients with NASH and type 2 diabetes was well tolerated, without additive GI side effects.
- EFX with GLP-1 showed multiple benefits over GLP-1 alone: reduced markers of liver steatosis, injury and fibrosis with improved glycemic control, dyslipidemia and weight loss maintained.
- The Cohort D EFX profile was comparable to that seen in the previous BALANCED and HARMONY studies with EFX.

Complementing GLP-1

Potential for EFX on Top of GLP-1 to be More Effective than GLP-1 Alone

symmetry
FOR CIRRHOTIC NASH

Building on Encouraging 16-Week Data in Patients with F4 Fibrosis

58%[a] Achieved

FIBROSIS IMPROVEMENT

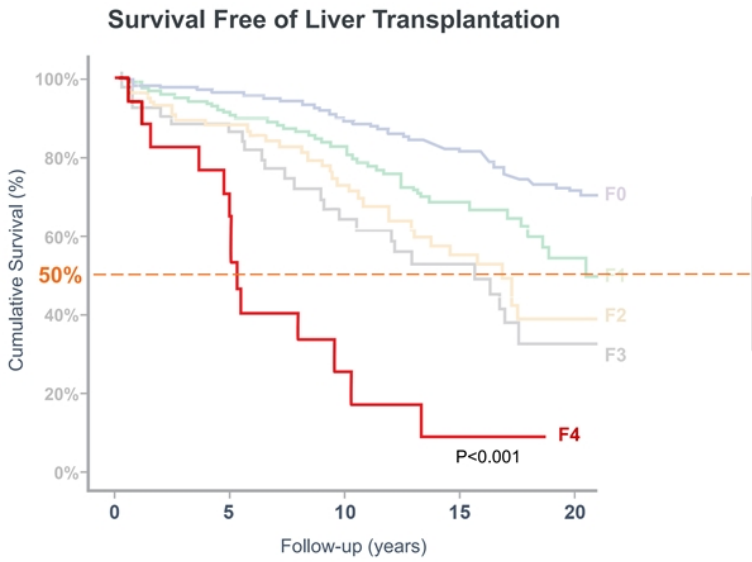
or

NASH RESOLUTION

in Phase 2a

[a] 7 of 12 (58%) patients treated with EFX 50mg in a 16-week expansion cohort (Cohort C) of the Phase 2a BALANCED study achieved either a one-stage improvement in fibrosis without worsening of NASH or NASH resolution without worsening of fibrosis, compared to 0% of placebo patients

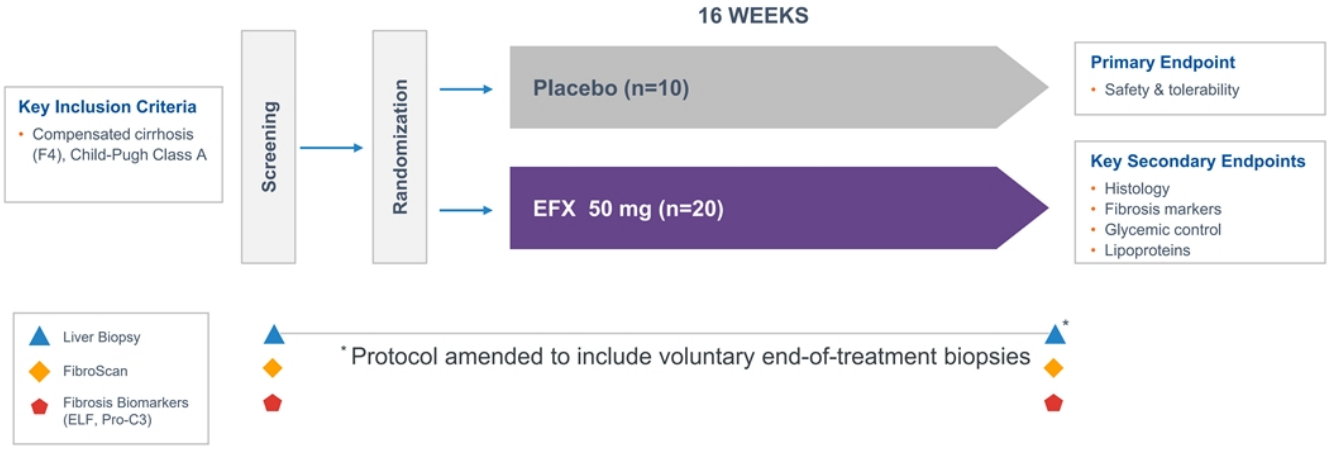
» Value of Preventing Progression to & Reversing From Cirrhosis



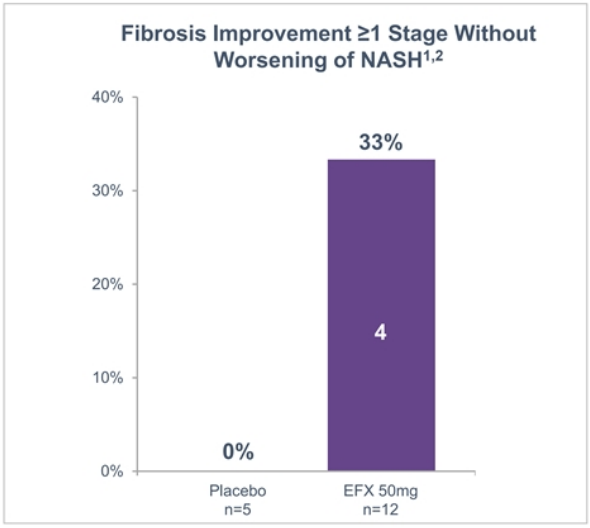
~50%
5-year mortality
without liver transplant
for **F4 patients**

Angulo, P et al. (2015) Gastroenterology 149:389-397

» Design of Phase 2a Proof-of-Concept Trial for Cirrhotic NASH (F4)



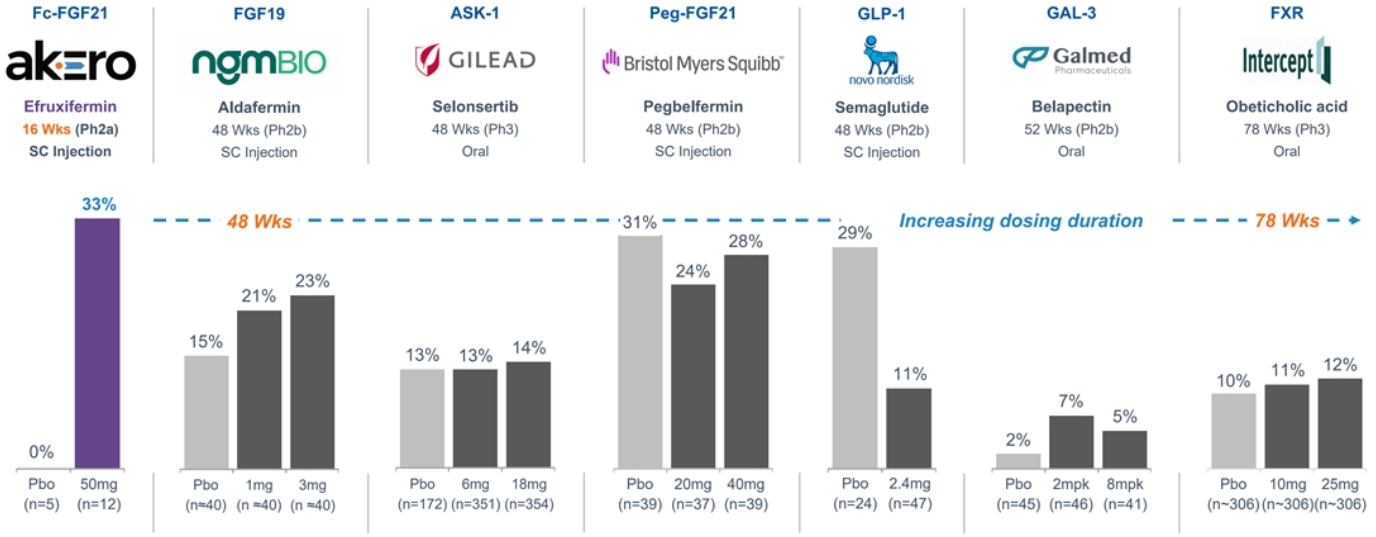
High Rate of Fibrosis Improvement After Only 16 Weeks Among Patients with Cirrhosis (F4 NASH)



[1] No increase in NAS for ballooning, inflammation, or steatosis; [2] Study not powered to assess statistical significance of changes in histological endpoints

Source Data: Liver Biopsy Analysis Set, F4

» EFX Results In Context: Fibrosis Improvement* (F4)

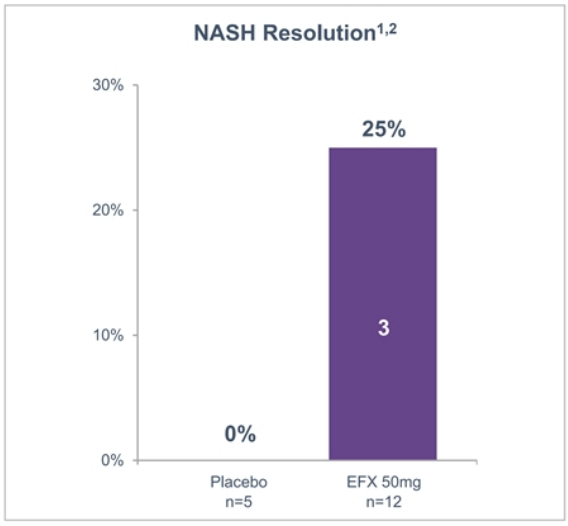


** Includes results from publicly reported NASH studies for single agents in F4 patients reporting either ≥ 1-stage fibrosis improvement (belapectin and simtuzumab) or ≥ 1-stage fibrosis improvement and no worsening of NASH (EFX, selonsertib, Pegbelfermin and obeticholic acid); numerical values represent percent responders*

Aldafermin – NGM Bio (2023) May 4 Press Release; Selonsertib – Harrison, SH et al. (2020) J Hepatol 73(1):26-39; Pegbelfermin – Abdelmalek, MF et al. (2021) AASLD Poster LP-8; Semaglutide – Loomba, R et al. (2022) EASL Presentation; Belapectin – Chalasani, N et al. (2020), Gastro 158:1334–45; Obeticholic acid - Intercept (2022) September 30 Press Release

Note: These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. No head-to-head clinical trials have been conducted.

NASH Resolution Also Observed in Patients with Cirrhosis (F4 NASH)



[1] NAS score of 0 or 1 for lobular inflammation and a score of 0 for ballooning
[2] Study not powered to assess statistical significance of histological endpoints

Change in NAS among Subjects Achieving NASH Resolution

EFX Subject	Baseline NAS	Week 16 NAS
A	7	1
B	3	1
C	6	1

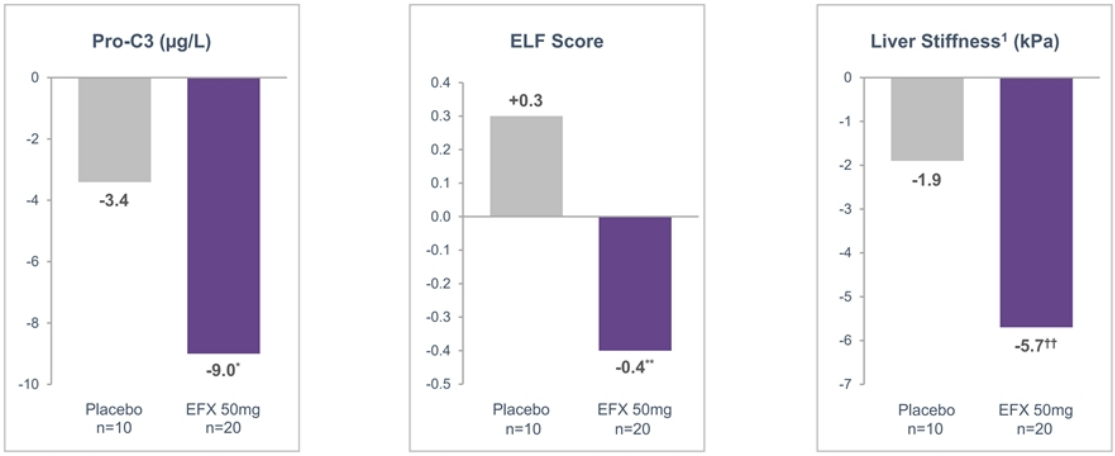
Proportion of Subjects with ≥2 Point NAS Reduction

Placebo	EFX 50mg
1 (20%)	7 (58%)

Source Data: Liver Biopsy Analysis Set, F4

Improvements in Fibrosis Biomarkers in Patients with Cirrhosis Support Histology Results (F4 NASH)

LS Mean Change From Baseline to Week 16



* p<0.05, versus placebo (ANCOVA)

** p<0.01, versus placebo (ANCOVA)

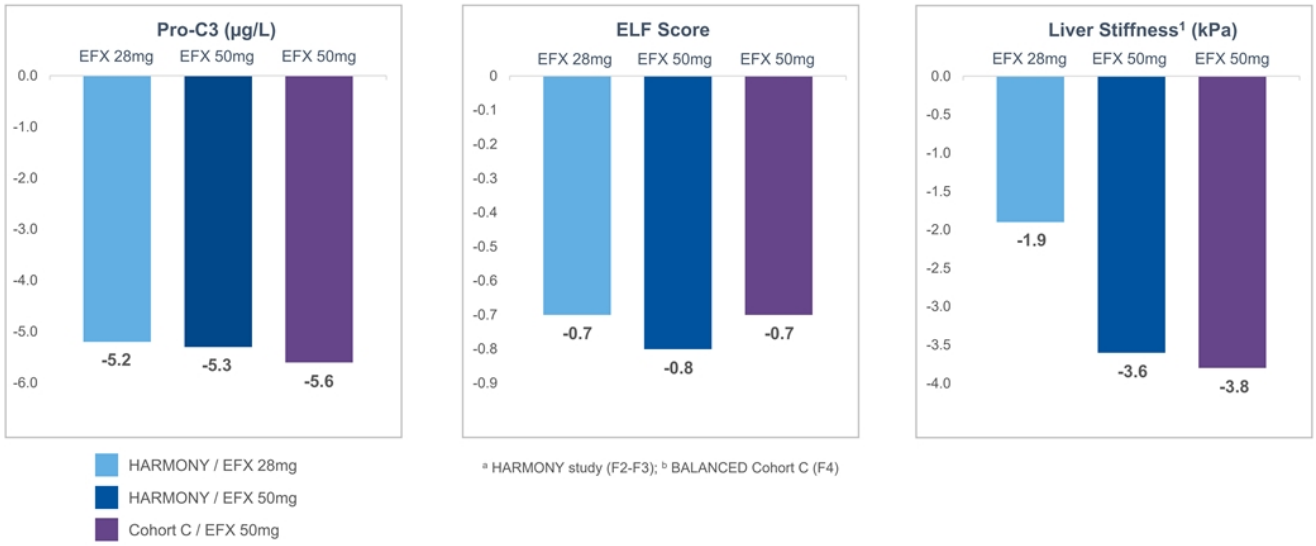
[1] Measured by FibroScan

†† p<0.01, versus baseline (ANCOVA)

Source Data: Biomarker Analysis Set, F4 (all Cohort C subjects with baseline and interpretable on-study measure of ELF or pro-C3, respectively); Liver Stiffness Analysis Set, F4 (all Cohort C subjects with baseline and interpretable on-study measure of Liver Stiffness); Topline preliminary data

Placebo-Corrected Reductions in Cohort C (F4) Fibrosis Markers Consistent with Magnitude Observed for HARMONY (F2-F3)

LS Mean Placebo-Corrected Change From Baseline to Week 24[a] or Week 16[b]



[a] HARMONY study (F2-F3); [b] BALANCED Cohort C (F4)

HARMONY (F2-F3) Source Data: Biomarker Analysis Set (Pro-C3 and ELF); Full Analysis Set (Liver Stiffness) (non-missing values only, no imputation)
Cohort C (F4) Source Data: Biomarker Analysis Set (Pro-C3 and ELF); Liver Stiffness Analysis Set, F4

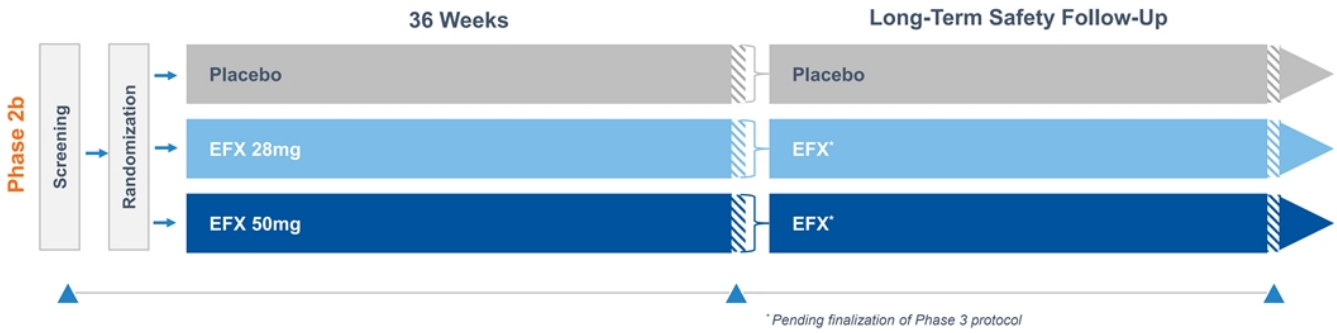
» SYMMETRY Trial Design: Cirrhosis Due to NASH (F4)

akero

Key Inclusion Criteria
- F4 NASH

Phase 2b Primary Endpoint
- Fibrosis Improvement (Cirrhosis reversal)

Key Secondary Efficacy Endpoints
- NASH Resolution
- Fibrosis Markers
- Lipoproteins
- Glycemic Control
- Weight Change
- Liver Injury Markers

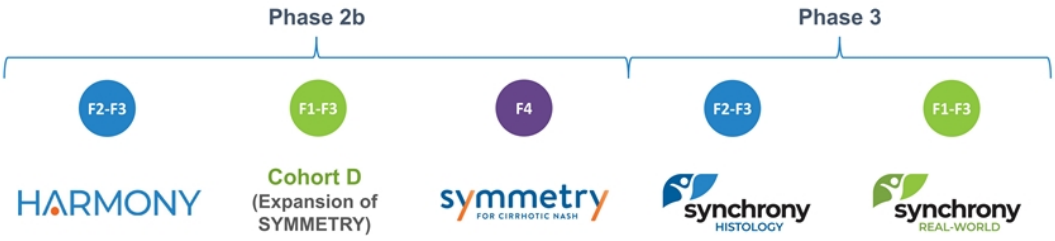


Enrollment completed in December 2022
Readout expected in Q4'23

akero

Looking Ahead

Looking Ahead to Phase 2b SYMMETRY Readout in Patients with Cirrhosis and Initiation of Phase 3 SYNCHRONY Studies



Status	Primary Endpoint Completed	Completed	Enrollment Complete; Readout expected in 4Q'23	Initiation Expected in 2H'23	Initiation Expected in 2H'23
Duration	24 Weeks	12 Weeks	36 Weeks	TBD	TBD
EFX Doses	28, 50mg	50mg	28, 50mg	28, 50mg	28, 50mg
Placebo-Controlled	✓	✓	✓	✓	✓

» Introducing the SYNCHRONY Phase 3 Program

akero

Three Planned Parallel Randomized, Placebo-Controlled Clinical Trials

synchrony HISTOLOGY

- Biopsy confirmed F2-F3 NASH
- Primary endpoint: ≥ 1-stage fibrosis improvement AND resolution of NASH
- 28 and 50mg EFX

synchrony REAL-WORLD

- Non-invasively diagnosed NASH/NAFLD
- Primary endpoint: safety & tolerability

synchrony OUTCOMES

Design to be finalized following SYMMETRY Phase 2b results

The duration of and total number of subjects to be enrolled in the SYNCHRONY ***Histology*** and ***Real-World*** trials are subject to confirmation with the FDA

» Supplying API and Drug Product/Device for Phase 3

akero

Drug Substance (API)

Boehringer Ingelheim

- ✓ Commercial scale
- ✓ Released for Phase 3
- ✓ Comparability demonstrated

Drug Product/Device Combination

VETTER

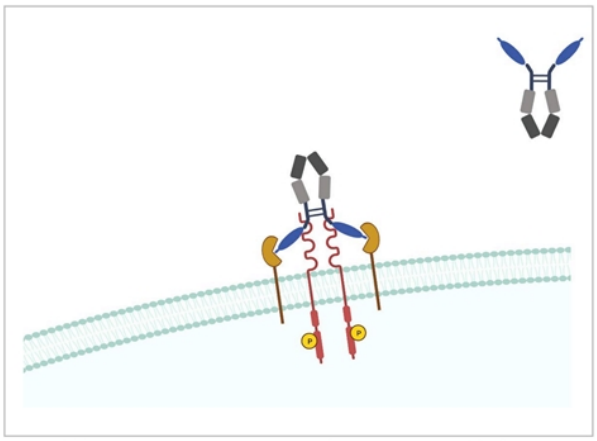
- ✓ Commercially precedented
- ✓ Released for Phase 3
- ✓ 1 mL SC weekly injection
- ✓ Self-administered, stable at 2-8ºC

akero

Backup Slides

EFX's Four Attachment Points to Cellular Surface May Contribute to Stronger Receptor Binding and Enhanced Efficacy

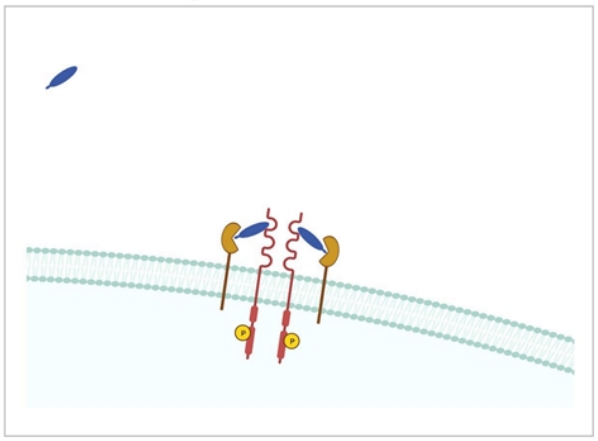
EFX



Dimer structure may enable cooperative binding and enhance avidity effects

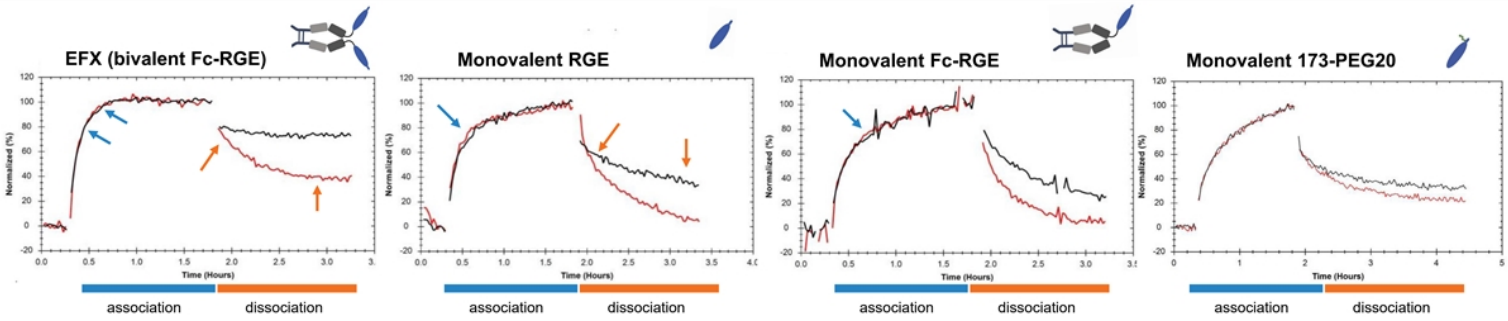
VS

Single-chain FGF21



Two independent binding events preclude cooperative binding or avidity effects

» Supportive Evidence for EFX's Cooperative Binding to Cell Surface



— No chase (labeled ligand removed)
— Chase with 10x unlabeled excess

Single-chain FGF21 has slower association, faster and more complete dissociation

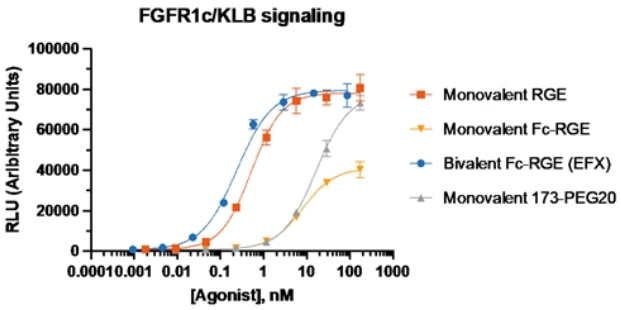
Addition of Fc or 20 kDa PEG to single-chain FGF21 analog further slows association

FGF21 Analog	k_a (1/[M*s])	k_d (1/s)	K_D (M)
EFX	1.8×10^{5}	3.3×10^{-6}	1.8×10^{-11}
Monovalent RGE	4.7×10^{4}	1.4×10^{-4}	3.0×10^{-9}
Monovalent Fc-RGE	2.1×10^{4}	1.1×10^{-4}	5.4×10^{-9}
Monovalent 173-PEG20	1.7×10^{4}	8.3×10^{-5}	4.8×10^{-9}

>100-fold tighter binding (K_D) of EFX vs. all monovalent analogs, i.e., RGE, Fc-RGE, or 173-PEG20:
- faster rate of association [k_a] AND
- much slower rate of dissociation [k_d]

FITC-labeled FGF21 analog binding analysis to the surface of FGFR1c/KLB-expressing HEK293

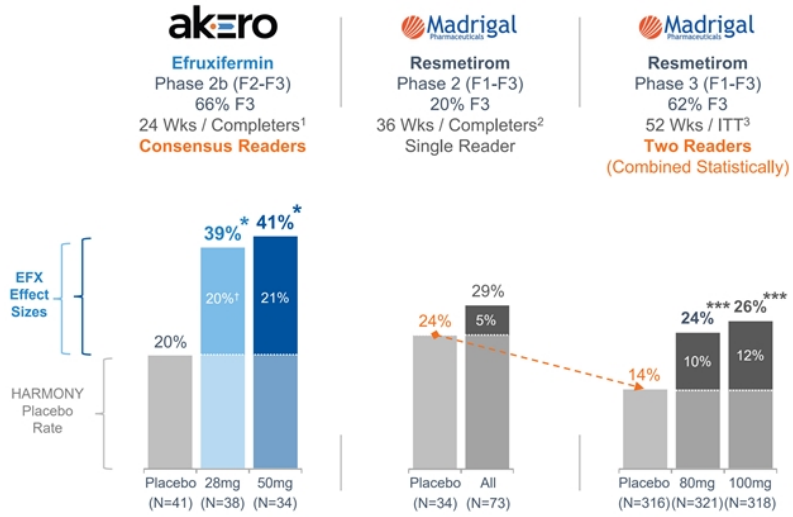
Single FGF21 chain analogs fused to “half-life extenders” are **15- to 30-Fold** Less Potent than EFX with two FGF21 chains’ or “unmodified FGF21”



	Bivalent Fc-RGE (EFX)	Monovalent RGE	Monovalent Fc-RGE	Monovalent 173-PEG20
Half-life extension	Fc-fusion	minimal	Fc-fusion	20 kDa PEG at residue 173
FGF21-receptor hindrance	N-terminus linked to IgG1 Fc	none	N-terminus linked to IgG1 Fc	20 kDa PEG at residue 173
mol. FGF21 / mol. analog	2	1	1	1
K_D (affinity) on live cells	**.018 nM**	3 nM	5.4 nM	4.8 nM
EC_{50} (potency), cell-based bioassay	0.24 nM	0.52 nM	7.93 nM	16.2 nM

- Monovalent Fc-RGE is **less potent** (higher EC_{50}) and a **partial agonist** (smaller fold induction) than Monovalent RGE
  - *Likely steric hindrance effect due to Fc*
- Adding a second FGF21(RGE) to monovalent Fc-RGE, forming bivalent Fc-RGE (EFX) restores **full agonism** and is **much more potent** (lower EC_{50})
  - *More than overcomes steric hindrance of Fc*
- Addition of 20 kDa PEG at residue 173 appears to maintain **full agonism** but is associated with **lower potency** (higher EC_{50})

Potential for Translation from Phase 2 to Phase 3: Fibrosis Improvement



Note: These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.

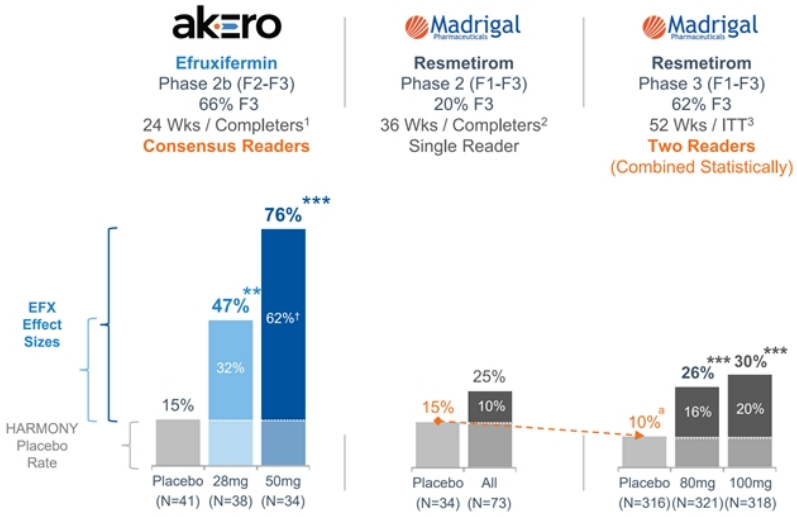
[1] Baseline and Week 24 biopsies available; [2] Completed 36 weeks of treatment and had end-of-study biopsy; [3] Missing biopsies were imputed as non-responders.

Resmetirom (Phase 2) - Harrison, S et al. (2019) Lancet 394(10213):2012-24; (Resmetirom Phase 3) – Madrigal (2022) December 19 Press Release. All trademarks are the property of their respective owners.

† 39.47 - 19.51 = 19.96 * p<0.05, *** p<0.001, versus placebo

Potential for Translation from Phase 2 to Phase 3: NASH Resolution

akero



Note: These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.

[1] Baseline and Week 24 biopsies available; [2] Completed 36 weeks of treatment and had end-of-study biopsy; [3] Missing biopsies were imputed as non-responders.
[a] Modified definition of NASH resolution (requiring ≥2 point reduction in NAS) might lead to lower placebo response rate

Resmetirom (Phase 2) - Harrison, S et al. (2019) Lancet 394(10213):2012-24; (Resmetirom Phase 3) – Madrigal (2022) December 19 Press Release. All trademarks are the property of their respective owners.

† 76.47 - 14.63 = 61.84

* p<0.05, ** p<0.01, *** p<0.001, versus placebo

From BALANCED to HARMONY

		Placebo	EFX 28mg		EFX 50mg	
% Responders, Histology and Liver Fat Normalization		**HARMONY**	**BALANCED**	**HARMONY**	**BALANCED**	**HARMONY**
Fibrosis improvement ≥ 1 stage and no worsening of NASH		20	46	39	62	41
NASH resolution and no worsening of fibrosis		15	46	47	54	76
Fibrosis improvement AND resolution of NASH		5	31	29	39	41
Normalization of liver fat to ≤5%		5	21	34	45	51
Non-Invasive Tests			**BALANCED[a]**	**HARMONY[b]**	**BALANCED[a]**	**HARMONY[b]**
Placebo-Adjusted LS Mean Absolute Change	Pro-C3 (µg/L)		-5.3	-5.2	-3.9	-5.3
	ELF Score		-0.7	-0.7	-0.8	-0.8
	Liver Stiffness (kPa)		n/a[#]	-1.9	-3.8[#]	-3.6
	Body Weight (kg)		-0.2	0.4	-2.2	-2.3
	HbA1c, % (T2D subset)		0.1	-0.5	-0.6	-0.6
Placebo-Adjusted LS Mean Relative Change (%)	C-peptide		-44.9	-25.2	-42.9	-31.7
	Adiponectin		72.8	33.9	92.2	80.8
	Liver Fat Content		-63.0	-45.5	-70.6	-57.6
	ALT		-41.2	-34.1	-50.8	-43.6
	AST		-40.1	-37.6	-45.5	-47.4
	Triglycerides		-43.0	-34.0	-51.4	-37.2
	LDL Cholesterol		-15.6	-16.9	-2.1	-16.2
	Non-HDL Cholesterol		-20.6	-20.2	-13.1	-20.7
	HDL Cholesterol		29.8	25.8	34.6	32.1

[a] Change from baseline to week 12 (ELF, Liver Fat) or week 16 (all other endpoints); [b] Change from baseline to Week 24; [#] Change in Liver Stiffness in BALANCED was only assessed in Cohort C in patients with cirrhotic NASH

» High Level of Consistency Across Four Clinical Studies of EFX

akero

Endpoints Non-Invasive Tests		EFX 50mg BALANCED[1] F1-F3 16 Weeks	EFX 50mg Cohort C[2] F4 16 Weeks	EFX 50mg HARMONY[3] F2-F3 24 Weeks	EFX 50mg Cohort D[4] F1-F3 12 Weeks
LS Mean Absolute Change	**Pro-C3 (µg/L)**	-4.7	-9.5	-5.2	-5.2
	ELF Score	-0.7	-0.4	-0.7	-0.6
	Liver Stiffness (kPa)	NT	-5.7	-4.3	-3.0
	Body Weight (kg)	-1.7	-2.2	-2.9	-1.2
	HbA1c, % (T2D Patients Only)	-0.6	-0.5	-0.5	-0.5
LS Mean Relative Change (%)	**Insulin**	-16	-48	NT	-26
	C-peptide	-22	-20	-23	-22
	Adiponectin	+80	+95	+91	+129
	Liver Fat Content	-71	NT	-64	-65
	ALT	-51	-22	-47	-24
	AST	-44	-26	-49	-17
	Triglycerides	-48	-40	-29	-42
	Non-HDL Cholesterol	-15	-14	-13	-19
	Apolipoprotein B	-12	-11	-3.9	-21
	LDL Cholesterol	-2.3	-8	-8	-8
	HDL Cholesterol	+39	+33	+30	+38

[1] Change from baseline (CFB) to week 12 (ELF, Liver Fat) or week 16 (all other endpoints); [2] CFB to week 16; [3] CFB to Week 24; [4] CFB to Week 12 NT = Not Tested

Note: These data are derived from different clinical trials with differences in patient populations, study duration, trial design, baseline demographics, and placebo rates.

NASDAQ: AKRO

AKERO THERAPEUTICS
601 Gateway Boulevard
Suite 350
South San Francisco, CA 94080