akero

Phase 2b SYMMETRY Readout

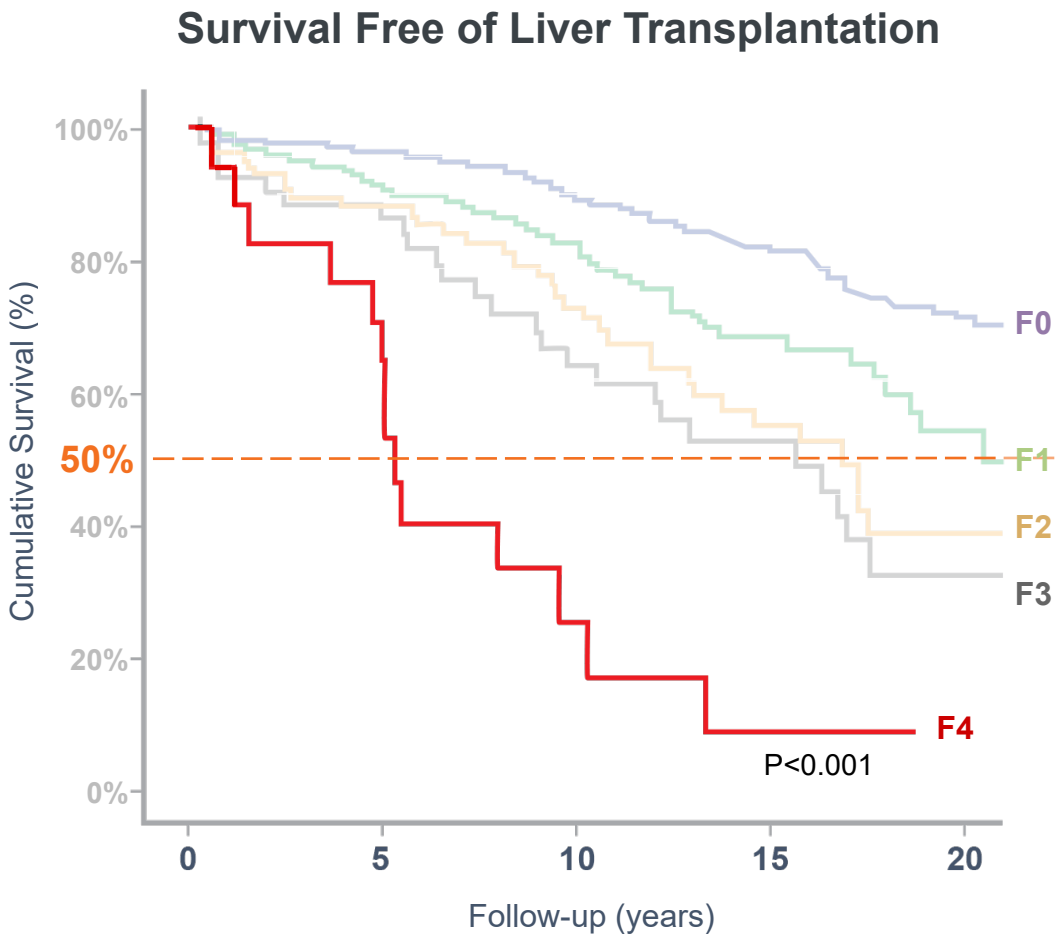
October 10, 2023

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”); 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 2b SYMMETRY study, 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; 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.

High Risk of Mortality Associated with Cirrhosis Due to NASH



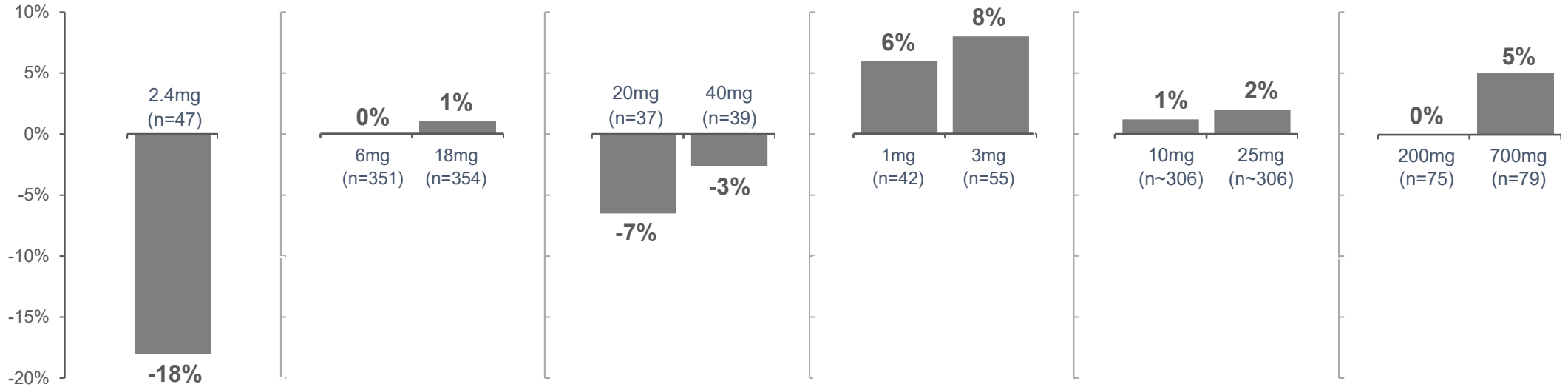
~50%
5-year mortality
without liver transplant
for **F4 patients**

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

Landscape for Cirrhosis Due to NASH:
Placebo-Corrected Fibrosis Improvement With No Worsening of NASH

	GLP-1	ASK-1	Peg-FGF21	FGF19	FXR	LOXL-2
	Semaglutide	Selonsertib	Pegbelfermin	Aldafermin	Obeticholic acid	Simtuzumab
	48 Wks / Ph2b	48 Wks / Ph3	48 Wks / Ph2b	48 Wks / Ph2b	78 Wks / Ph3	96 Wks / Ph2b
	Active	Discontinued	Discontinued	Discontinued	Discontinued	Discontinued
Placebo Rate	29%	13%	31%	15%	10%	8%

By Treatment Duration



Includes results from publicly reported placebo-controlled studies in patients with compensated cirrhosis due to NASH reporting either ≥ 1-stage fibrosis improvement and no worsening of NASH (semaglutide, selonsertib, pegbelfermin, obeticholic acid) or only ≥ 1-stage fibrosis improvement (aldafermin, simtuzumab); numerical values represent percent responders

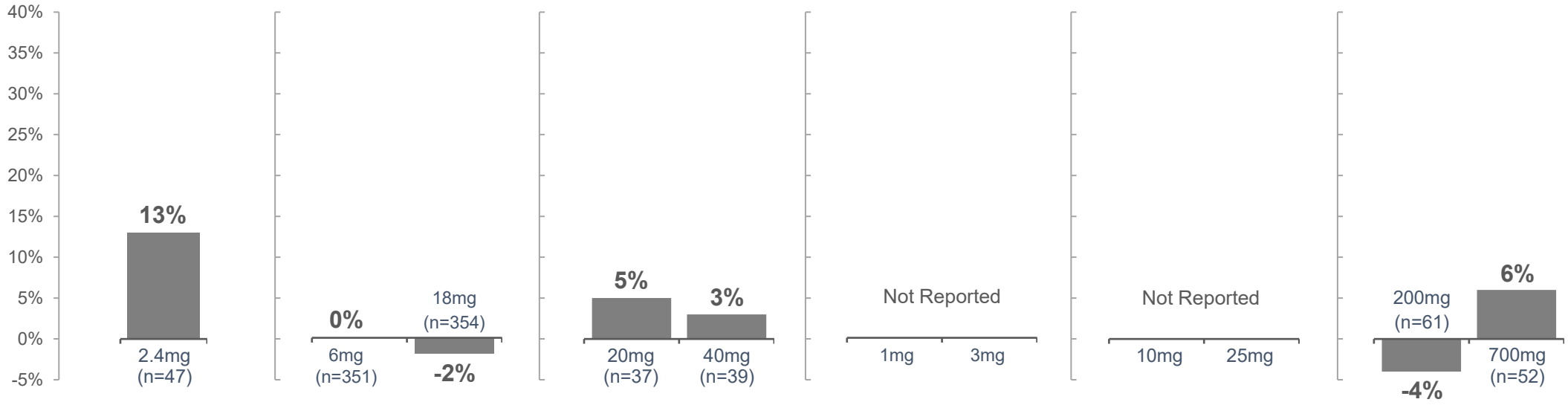
Semaglutide – Loomba, R et al. (2023) Lancet Gastro Hep 8:511-22; Selonsertib – Harrison, SH et al. (2020) J Hepatol 73(1):26-39; Pegbelfermin – Abdelmalek, MF et al. (2023) Clinical Gastro Hep 23:S1542-3565; Aldafermin – NGM Bio (2023) September Corporate Overview; Obeticholic acid - Intercept (2022) September 30 Press Release; Simtuzumab – Harrison, SA et al. (2018) Gastroenterology 155:1140–1153

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.

Landscape for Cirrhosis Due to NASH:
Placebo-Corrected NASH Resolution

	GLP-1	ASK-1	Peg-FGF21	FGF19	FXR	LOXL-2
	Semaglutide	Selonsertib	Pegbelfermin	Aldafermin	Obeticholic acid	Simtuzumab
	48 Wks / Ph2b	48 Wks / Ph3	48 Wks / Ph2b	48 Wks / Ph2b	78 Wks / Ph3	96 Wks / Ph2b
	Active	Discontinued	Discontinued	Discontinued	Discontinued	Discontinued
Placebo Rate	21%	4%	0%	NA	NA	6%

By Treatment Duration



Includes results from publicly reported placebo-controlled studies in patients with compensated cirrhosis due to NASH reporting either ≥ 1-stage fibrosis improvement and no worsening of NASH (semaglutide, selonsertib, pegbelfermin, obeticholic acid) or only ≥ 1-stage fibrosis improvement (aldafermin, simtuzumab); numerical values represent percent responders

Semaglutide – Loomba, R et al. (2023) Lancet Gastro Hep 8:511-22; Selonsertib – Harrison, SH et al. (2020) J Hepatol 73(1):26-39; Pegbelfermin – Abdelmalek, MF et al. (2023) Clinical Gastro Hep 23:S1542-3565; Aldafermin – NGM Bio (2023) September Corporate Overview; Obeticholic acid - Intercept (2022) September 30 Press Release; Simtuzumab – Harrison, SA et al. (2018) Gastroenterology 155:1140–1153

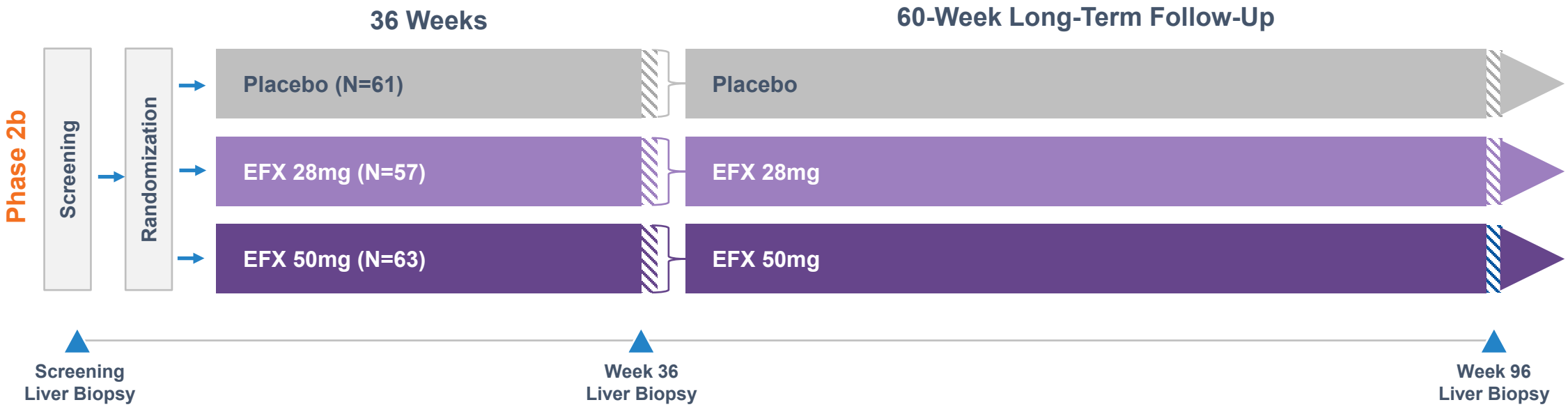
Note: These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. No head-to-head clinical trials have been conducted.

SYMMETRY Trial Design: Cirrhosis Due to NASH (F4)

Key Inclusion Criteria[1]
- F4 NASH
- T2D or 2 of 4 components of metabolic syndrome

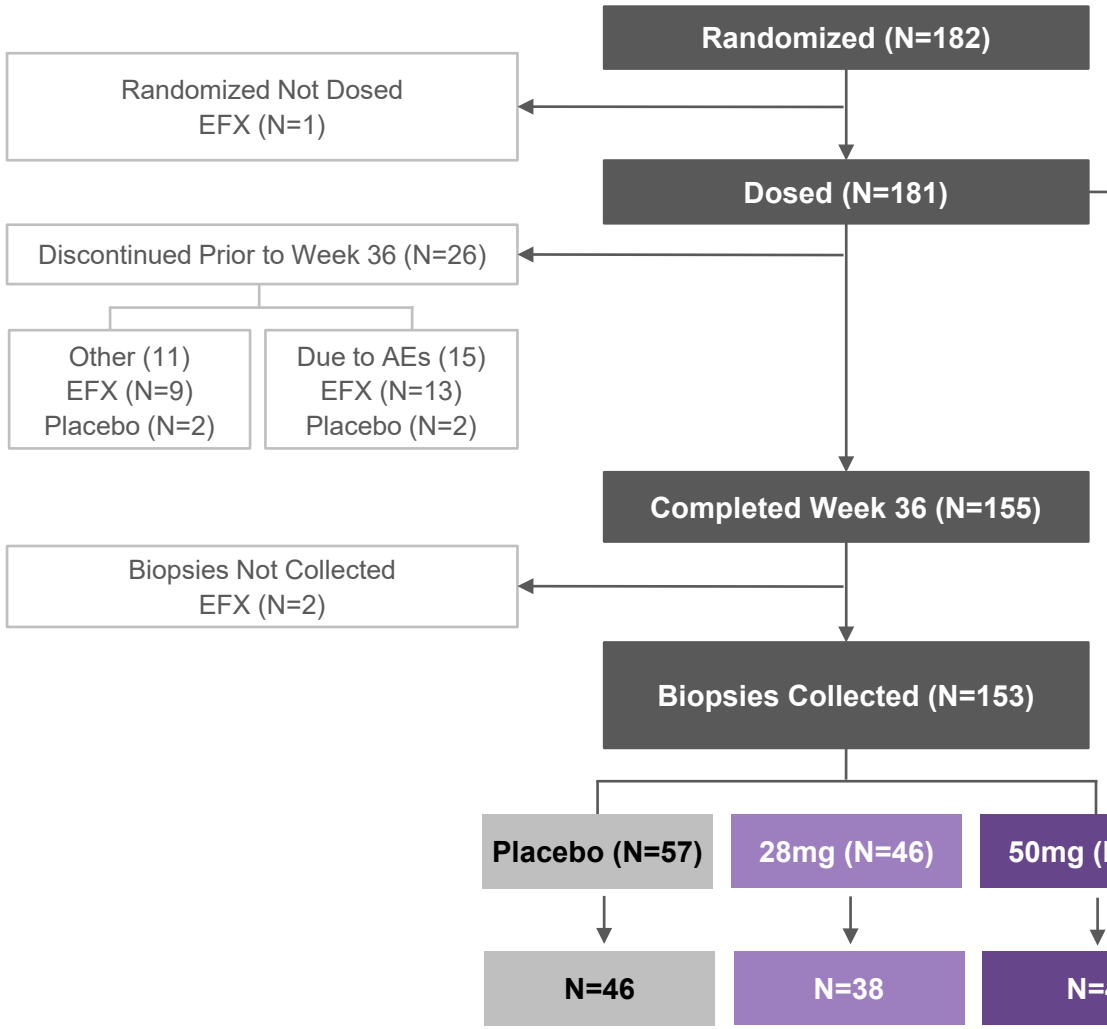
Phase 2b Primary Endpoint
- ≥1 Stage Fibrosis Improvement with no Worsening of NASH

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



[1] All patients had biopsy-proven compensated cirrhosis (fibrosis stage 4) due to definitive NASH or cryptogenic cirrhosis presumed secondary to NASH. Subjects with cryptogenic cirrhosis were limited to approximately 20% of the total study population.

Week 36 Patient Disposition & Key Analysis Sets



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

Primary Endpoint
Liver Biopsy Analysis Set
All subjects who have Baseline & Week 36 liver biopsy results

Secondary Histological Endpoints
Liver Biopsy Analysis Set (Definitive NASH[1] Only)
Excludes all subjects with cryptogenic cirrhosis

[1] NAS ≥ 3 with a score of ≥ 1 for each of steatosis, inflammation and ballooning

Baseline Demographics

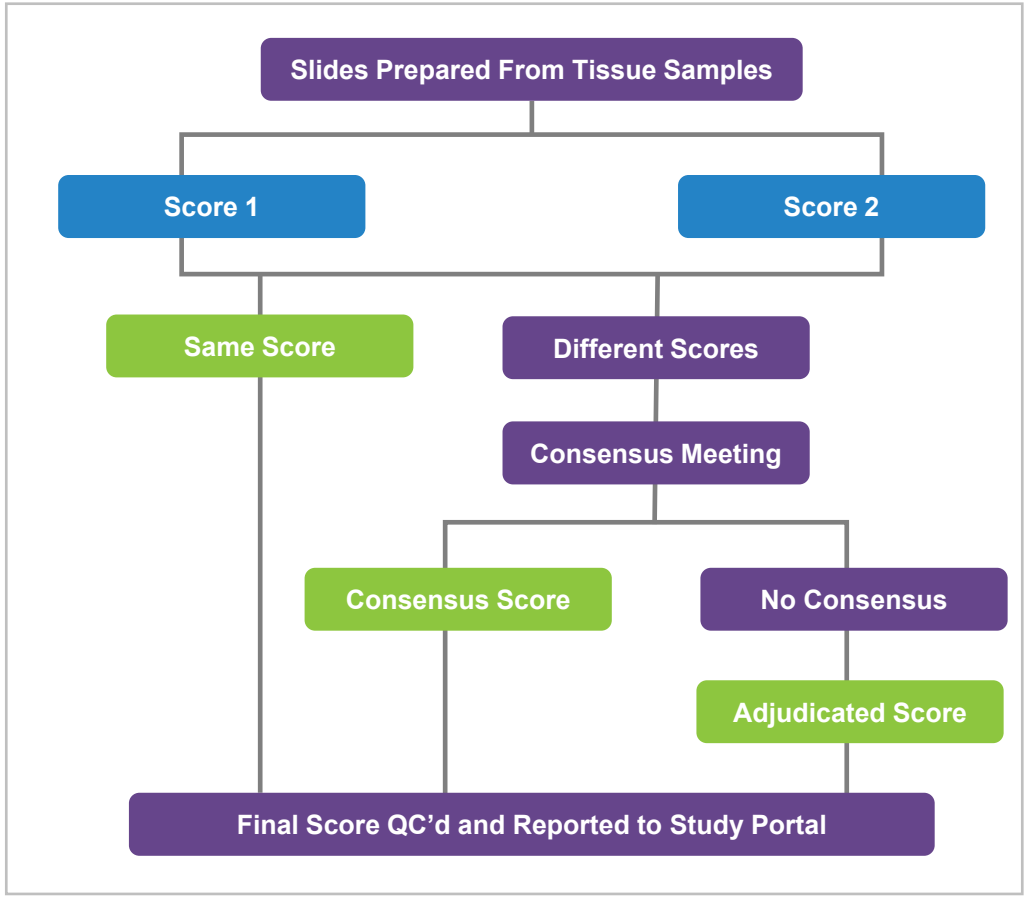
Parameter (Mean)	Placebo (N=61)	EFX 28mg (N=57)	EFX 50mg (N=63)
Age (Years)	61	62	59
Sex (% Female)	62	68	70
Definitive NASH (%) / Cryptogenic Cirrhosis (%)	74 / 26	79 / 21	83 / 17
Enhanced Liver Fibrosis (ELF) Score	10.4	10.6	10.5
Pro-C3 (µg/L) (Generation 2 ELISA)	132	142	147
Liver Stiffness by VCTE (FibroScan) (kPa)	24.7	24.1	24.5
FAST Score	0.60	0.60	0.62
Alanine Aminotransferase (ALT) (U/L)	40.3	40.1	38.4
Aspartate Aminotransferase (AST) (U/L)	35.5	37.1	37.5
Type 2 Diabetes (%)	82	81	78
HbA1c (%)	6.8	6.8	6.6
Baseline Use of GLP-1 (%) / Sulfonylurea / (%) Insulin (%)	28 / 20 / 16	21 / 21 / 11	32 / 30 / 21
Triglycerides (mg/dL)	143	148	159
Statin Use (%)	52	46	43
Weight (kg)	102	99	95

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

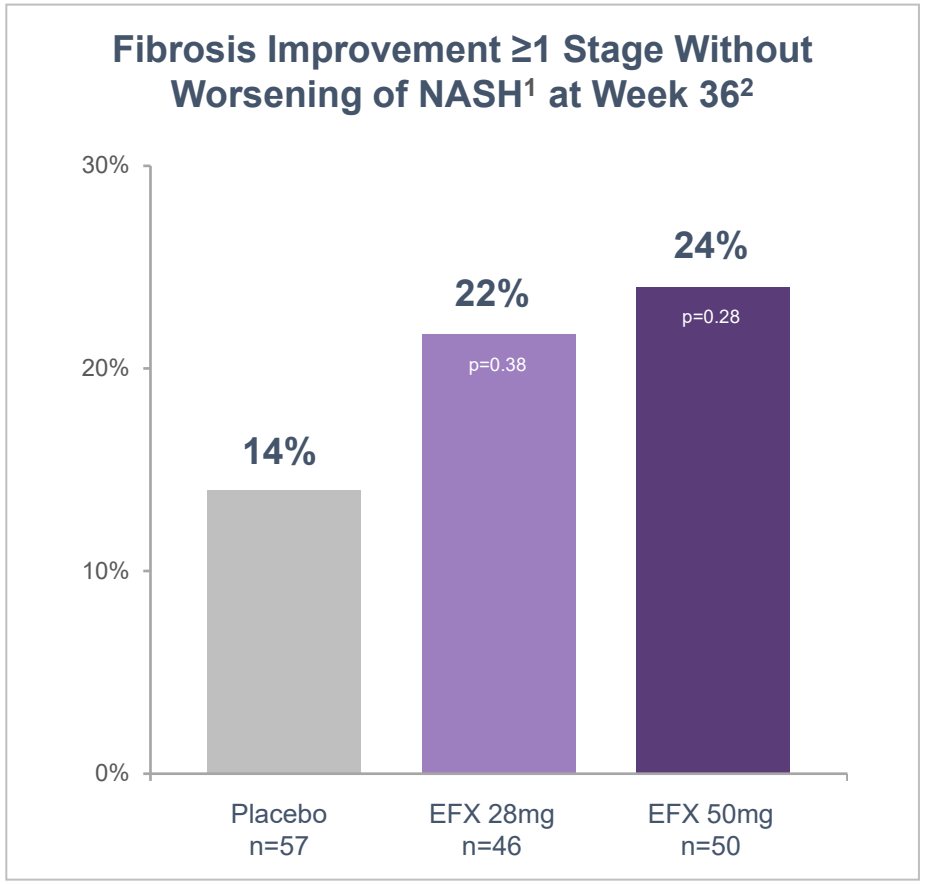
Key Features of EFX Biopsy Analysis Plan

- 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
- Pathologists did not review Week 36 biopsy slides with the corresponding patient's baseline biopsy slides as a comparison
- Previously interpreted baseline biopsy slides were randomly presented to pathologists throughout the study duration to minimize the potential for sequence bias

Consensus Biopsy Analysis Flow Chart



Trend to Improvement for Primary Endpoint
(≥1 Stage Improvement in Fibrosis and No Worsening of NASH)



Four Patients Experienced Three- or Two-Stage Fibrosis Improvement Without Worsening of NASH at Week 36

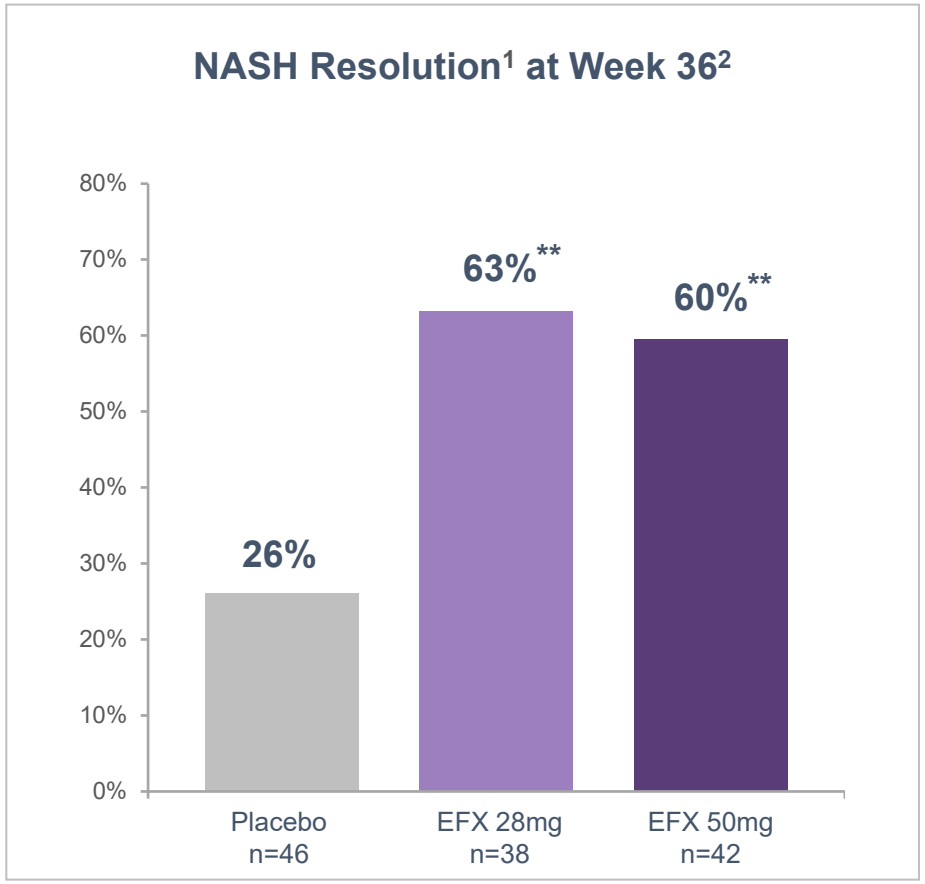
	Dose Group	Baseline Fibrosis Stage	Week 36 Fibrosis Stage
Subject A	EFX 28mg	F4	F1
Subject B	EFX 50mg	F4	F1
Subject C	EFX 28mg	F4	F2
Subject D	EFX 50mg	F4	F2

[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*

[2] Results for ITT Analysis: Placebo, 13%; 28mg, 18%; EFX 50mg, 19%

Source Data: Liver Biopsy Analysis Set; Topline preliminary data

Statistically Significant Improvement on NASH Resolution for Both Doses



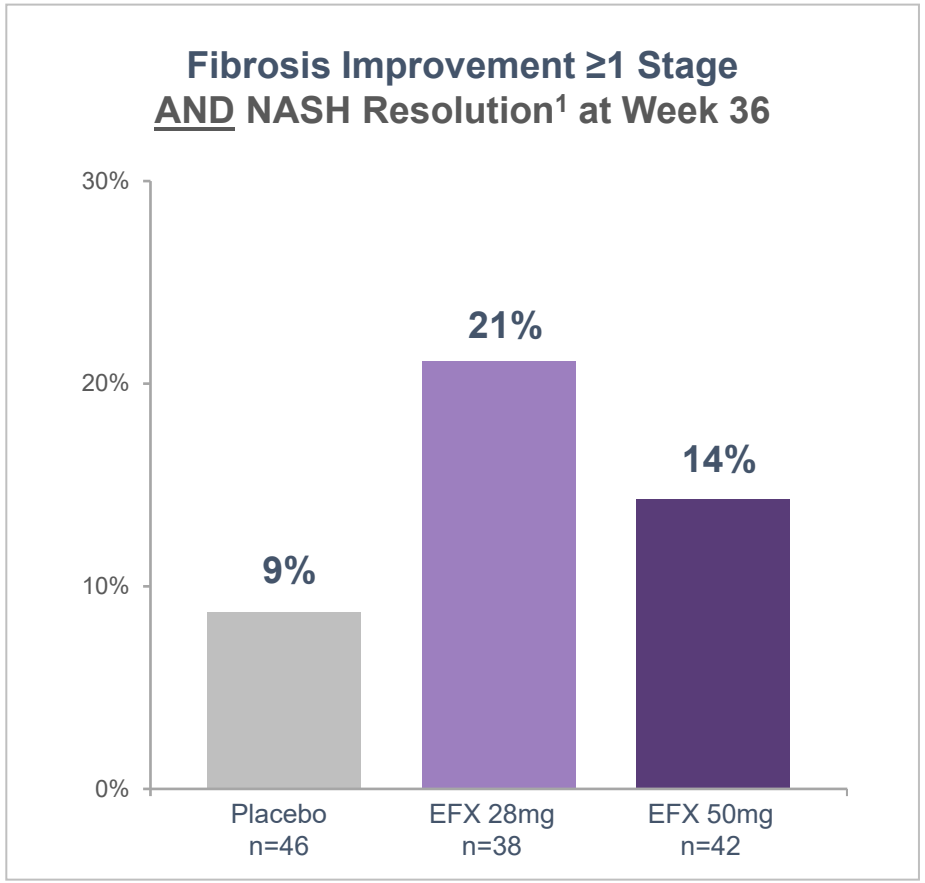
** p<0.01, versus placebo (Cochran–Mantel–Haenszel test [CMH])

[1] Per FDA guidance, 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

[2] Results for ITT Analysis: Placebo, 24%; 28mg, 51% (p<0.05, versus placebo [CMH]); EFX 50mg, 47% (p<0.05, versus placebo [CMH])

Source Data: Liver Biopsy Analysis Set (definitive NASH only); Topline preliminary data

Combined Histological Endpoint



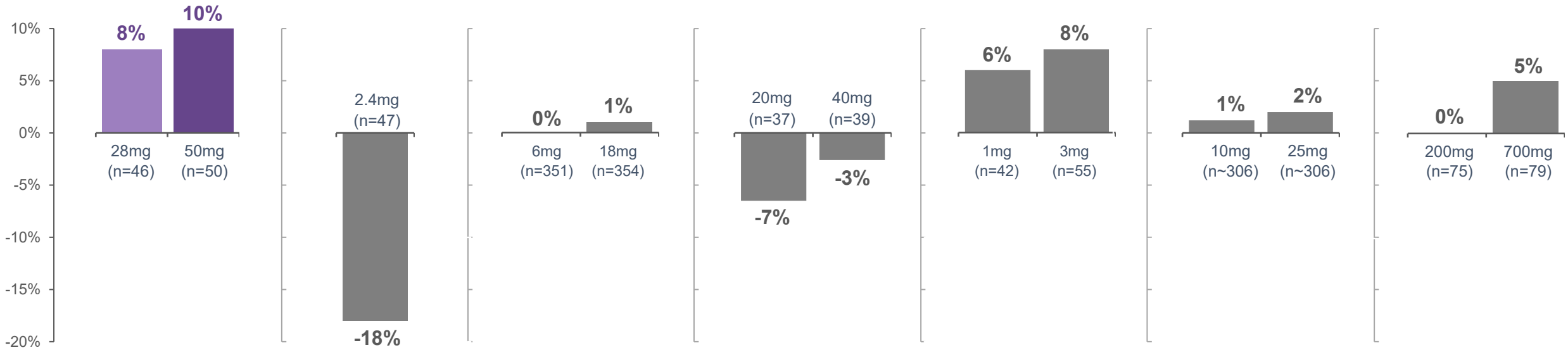
[1] Per FDA guidance, this endpoint is defined as: "Both resolution of steatohepatitis and improvement in fibrosis…. Resolution of steatohepatitis is defined as absent fatty liver disease or isolated or simple steatosis without steatohepatitis and a NAS score of 0–1 for inflammation, 0 for ballooning, 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 (definitive NASH only); Topline preliminary data

Landscape for Cirrhosis Due to NASH:
Placebo-Corrected Fibrosis Improvement With No Worsening of NASH

	Fc-FGF21	GLP-1	ASK-1	Peg-FGF21	FGF19	FXR	LOXL-2
	Efruxifermin	Semaglutide	Selonsertib	Pegbelfermin	Aldafermin	Obeticholic acid	Simtuzumab
	36 Wks / Ph2b	48 Wks / Ph2b	48 Wks / Ph3	48 Wks / Ph2b	48 Wks / Ph2b	78 Wks / Ph3	96 Wks / Ph2b
	Active	Active	Discontinued	Discontinued	Discontinued	Discontinued	Discontinued
Placebo Rate	14%	29%	13%	31%	15%	10%	8%

By Treatment Duration



Includes results from publicly reported placebo-controlled studies in patients with compensated cirrhosis due to NASH reporting either ≥ 1-stage fibrosis improvement and no worsening of NASH (EFX, semaglutide, selonsertib, pegbelfermin, obeticholic acid) or only ≥ 1-stage fibrosis improvement (aldafermin, simtuzumab); numerical values represent percent responders

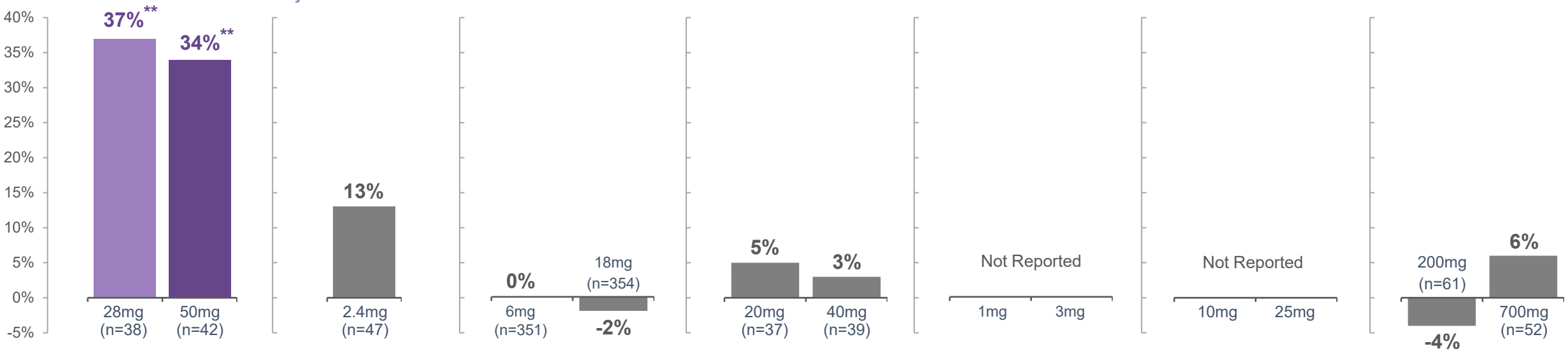
Semaglutide – Loomba, R et al. (2023) Lancet Gastro Hep 8:511-22; Selonsertib – Harrison, SH et al. (2020) J Hepatol 73(1):26-39; Pegbelfermin – Abdelmalek, MF et al. (2023) Clinical Gastro Hep 23:S1542-3565; Aldafermin – NGM Bio (2023) September Corporate Overview; Obeticholic acid - Intercept (2022) September 30 Press Release; Simtuzumab – Harrison, SA et al. (2018) Gastroenterology 155:1140–1153

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.

Landscape for Cirrhosis Due to NASH:
Placebo-Corrected NASH Resolution

	Fc-FGF21	GLP-1	ASK-1	Peg-FGF21	FGF19	FXR	LOXL-2
	Efruxifermin	Semaglutide	Selonsertib	Pegbelfermin	Aldafermin	Obeticholic acid	Simtuzumab
	36 Wks / Ph2b	48 Wks / Ph2b	48 Wks / Ph3	48 Wks / Ph2b	48 Wks / Ph2b	78 Wks / Ph3	96 Wks / Ph2b
	Active	Active	Discontinued	Discontinued	Discontinued	Discontinued	Discontinued
Placebo Rate	26%	21%	4%	0%	NA	NA	6%

By Treatment Duration



** p<0.01, versus placebo (CMH)

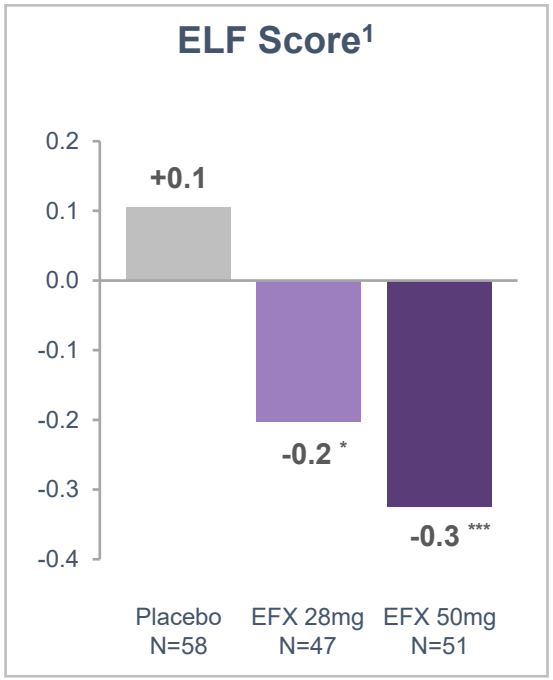
Includes results from publicly reported placebo-controlled studies in patients with compensated cirrhosis due to NASH reporting either ≥ 1-stage fibrosis improvement and no worsening of NASH (EFX, semaglutide, selonsertib, pegbelfermin, obeticholic acid) or only ≥ 1-stage fibrosis improvement (aldafermin, simtuzumab); numerical values represent percent responders

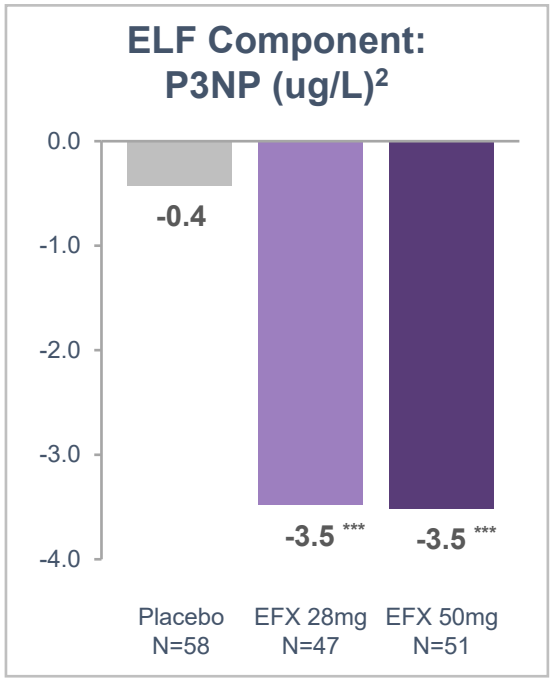
Semaglutide – Loomba, R et al. (2023) Lancet Gastro Hep 8:511-22; Selonsertib – Harrison, SH et al. (2020) J Hepatol 73(1):26-39; Pegbelfermin – Abdelmalek, MF et al. (2023) Clinical Gastro Hep 23:S1542-3565; Aldafermin – NGM Bio (2023) September Corporate Overview; Obeticholic acid - Intercept (2022) September 30 Press Release; Simtuzumab – Harrison, SA et al. (2018) Gastroenterology 155:1140–1153

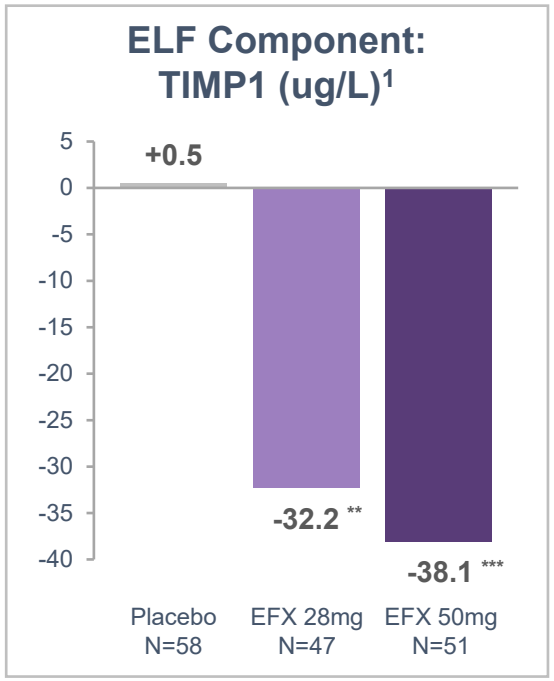
Note: These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. No head-to-head clinical trials have been conducted.

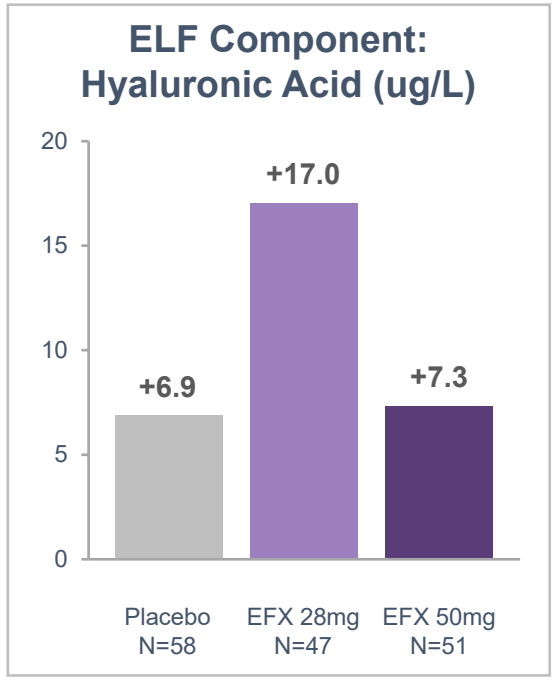
Evidence of Anti-Fibrotic Activity:
Analysis of ELF Score and its Components

LS Mean Change From Baseline to Week 36









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

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

[2] Procollagen 3 N-Terminal Peptide

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

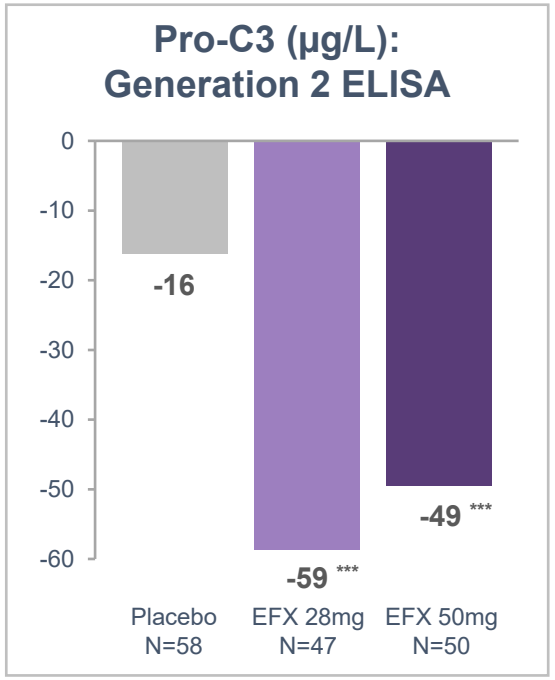
[1] Tissue Inhibitor of Metalloproteinase 1

Source Data: Full Analysis Set (non-missing values only, no imputation); Topline preliminary data

Additional Non-Invasive Fibrosis Markers

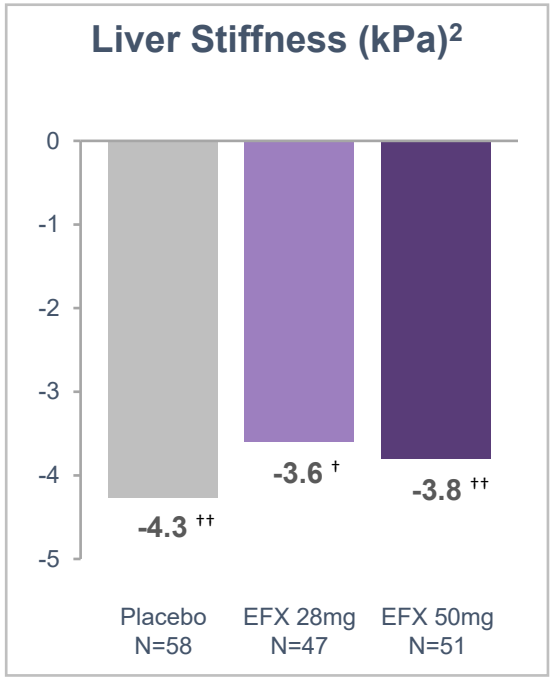
LS Mean Change From Baseline to Week 36

Pro-C3 (µg/L): Generation 2 ELISA



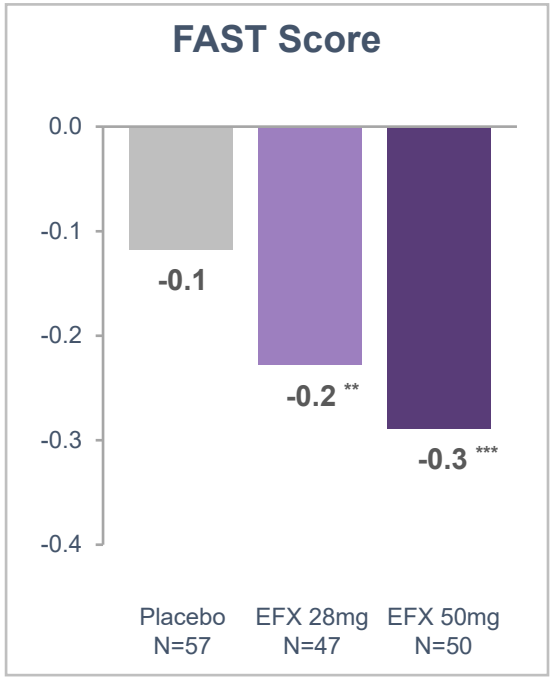
*** p<0.001, versus placebo (MMRM[1])

Liver Stiffness (kPa)[2]



† p<0.05, †† p<0.01, versus baseline (MMRM)

FAST Score



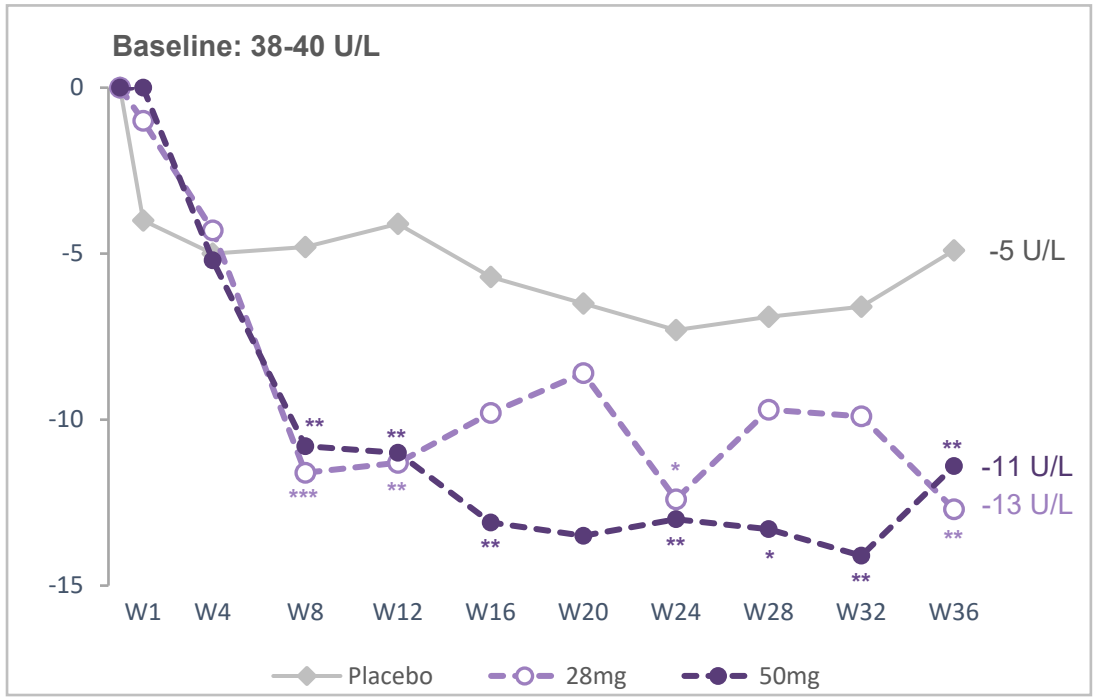
** p<0.01, *** p<0.001, versus placebo (MMRM[1])

[1] Mixed Model Repeated Measures; [2] Measured by FibroScan

Source Data: Full Analysis Set (non-missing values only, no imputation); Topline preliminary data

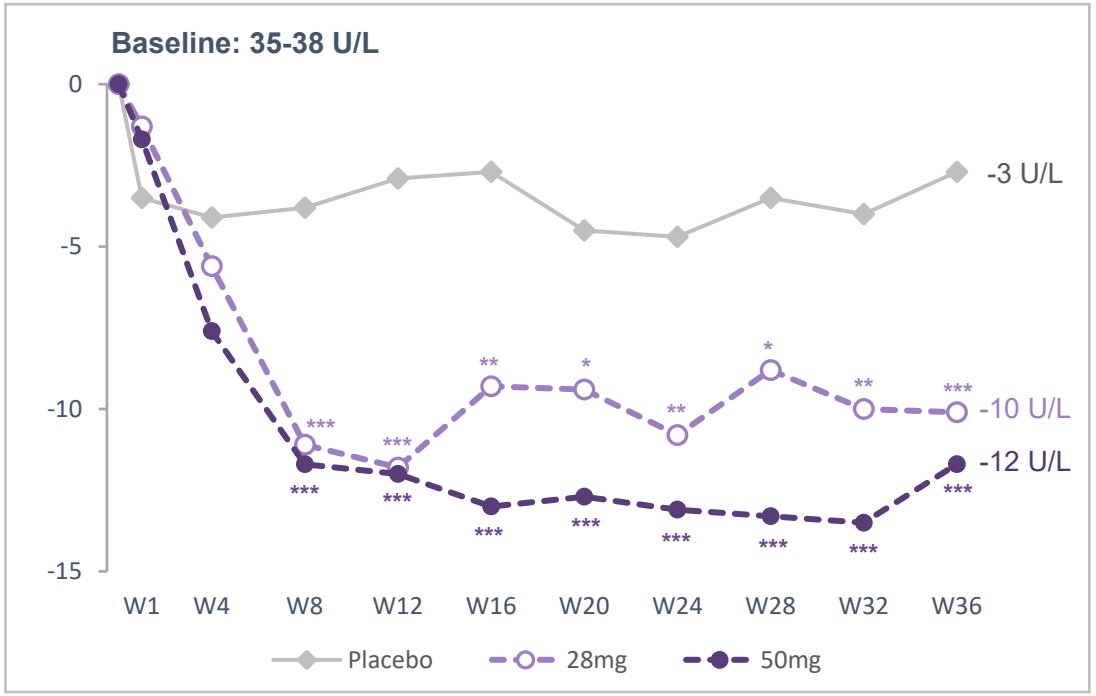
Early and Sustained Statistically Significant Improvements in Markers of Liver Injury

ALT
LS Mean Change from Baseline (U/L)



* p<0.05, ** p<0.01, *** p<0.001, versus placebo (MMRM[1])

AST
LS Mean Change from Baseline (U/L)



* p<0.05, ** p<0.01, *** p<0.001, versus placebo (MMRM[1])

Statistically significant improvements from baseline observed for platelet counts for both EFX groups

[1] Mixed Model Repeated Measures

Source Data: Full Analysis Set; Topline preliminary data

Safety & Tolerability Summary

TEAE Overview	Placebo (N=61)	EFX 28mg (N=57)	EFX 50mg (N=63)
TEAE Leading to Death	1 (2%) [a]	0 (0%)	0 (0%)
Treatment-Emergent Serious Adverse Event (SAE) [b]	6 (10%)	9 (16%)	6 (10%)
Drug-related TEAE Leading to Discontinuation	1 (2%)	3 (5%)	8 (13%)
Diarrhea (Grades 1-3)	1	1	5
Other	0	2[c]	3[d]

[a] Pneumonia

[b] None of the SAEs were deemed by the investigator to be drug-related

[c] Retching/vomiting; palpitation/feeling jittery

[d] Soft feces/nausea; hypersensitivity (rash); injection site rash

Source Data: Safety Set; Topline preliminary data

Safety & Tolerability (continued)

Most Frequent (≥15%) Drug-Related TEAEs	Placebo (N=61)	EFX 28mg (N=57)	EFX 50mg (N=63)
Diarrhea	9 (15%)	10 (18%)	19 (30%)
Nausea	7 (12%)	11 (19%)	18 (29%)
Increased Appetite	3 (5%)	7 (12%)	17 (27%)
Injection Site Erythema	5 (8%)	8 (14%)	13 (21%)

Vital Signs and Bone Mineral Density

No clinically meaningful changes were observed for heart rate or diastolic blood pressure. At Week 36, increases of 4-7mmHg in systolic blood pressure were observed in the EFX dose groups.

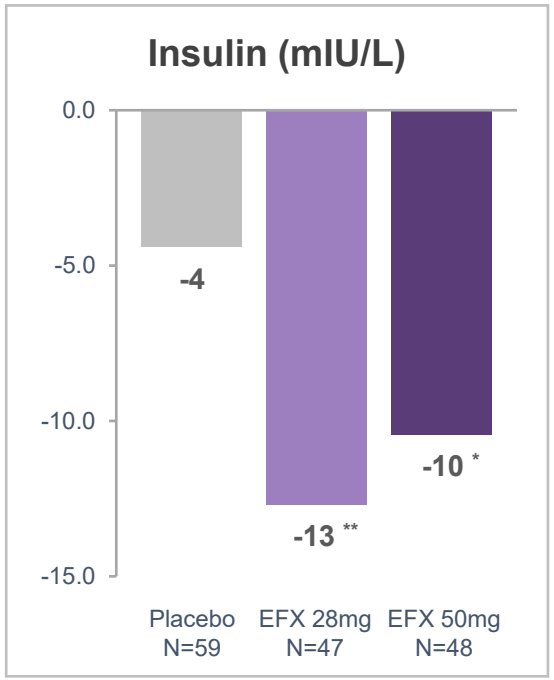
At Week 36, small reductions in bone mineral density were observed for the EFX dose groups in the lumbar spine region (≤1%) and the femoral neck region (2-3%).

Source Data: Safety Set; Topline preliminary data

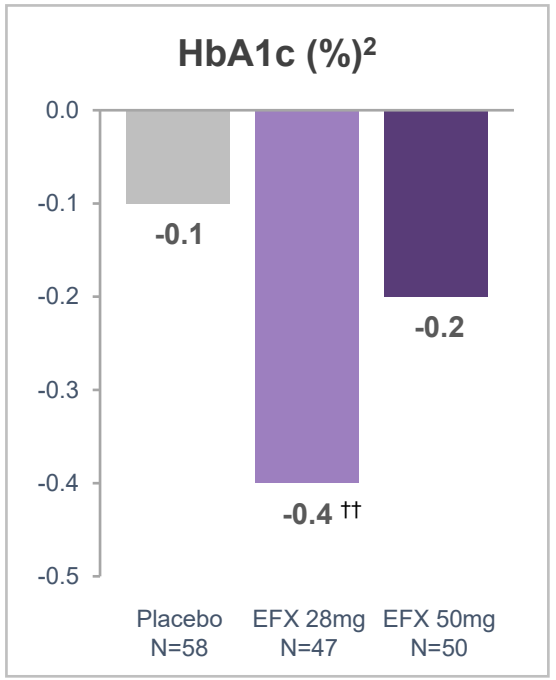
Statistically Significant Improvements Observed in Insulin Sensitivity

LS Mean Change From Baseline to Week 36

[1] Relative percent change from baseline
* p<0.05, ** p<0.01, versus placebo (MMRM)



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

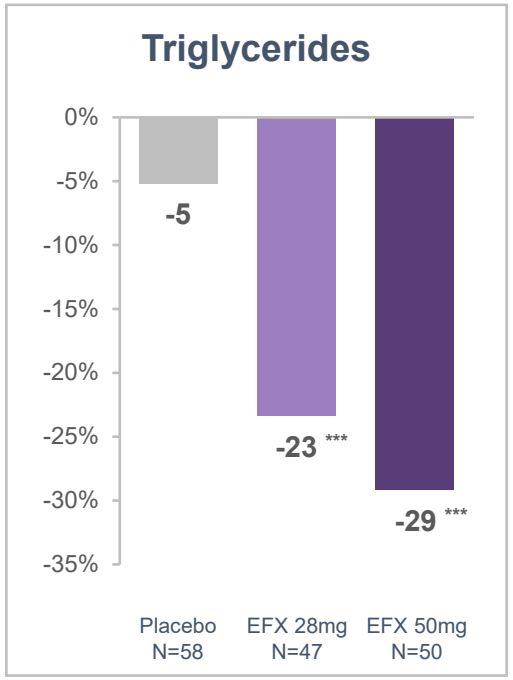


[2] Absolute change from baseline, %
†† p<0.01, versus baseline (MMRM)

Source Data: Full Analysis Set; Topline preliminary data

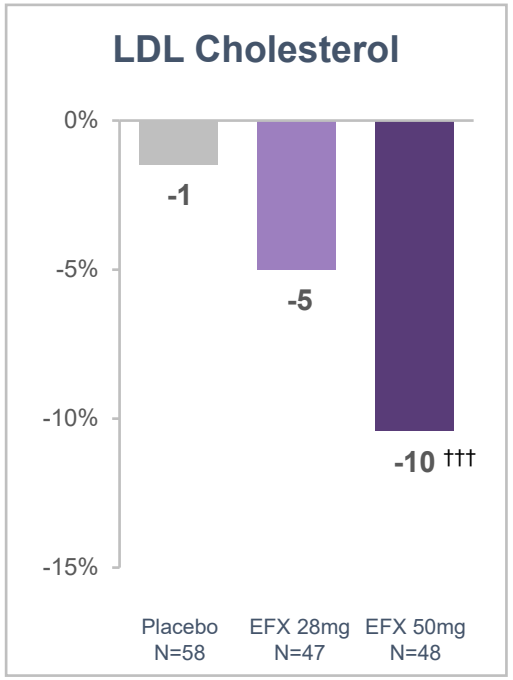
Statistically Significant Improvements Observed in Lipoprotein Profile

LS Mean Percent Change From Baseline to Week 36

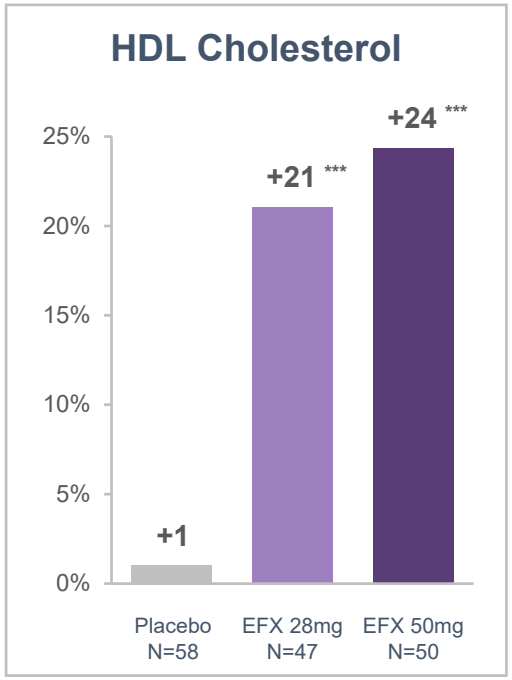


*** p<0.001, versus placebo (MMRM)

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



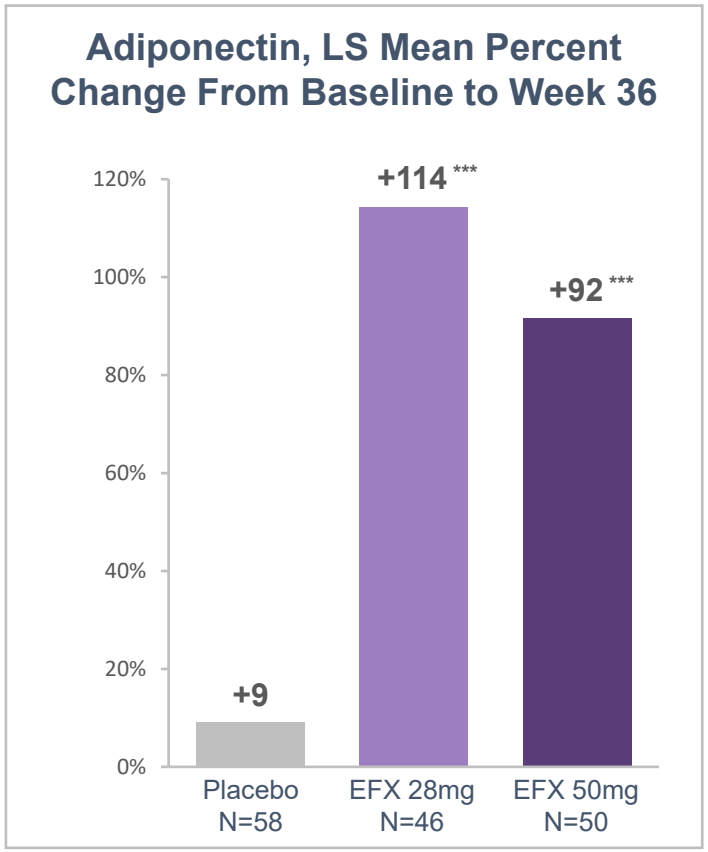
††† p<0.001, versus baseline (MMRM)



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

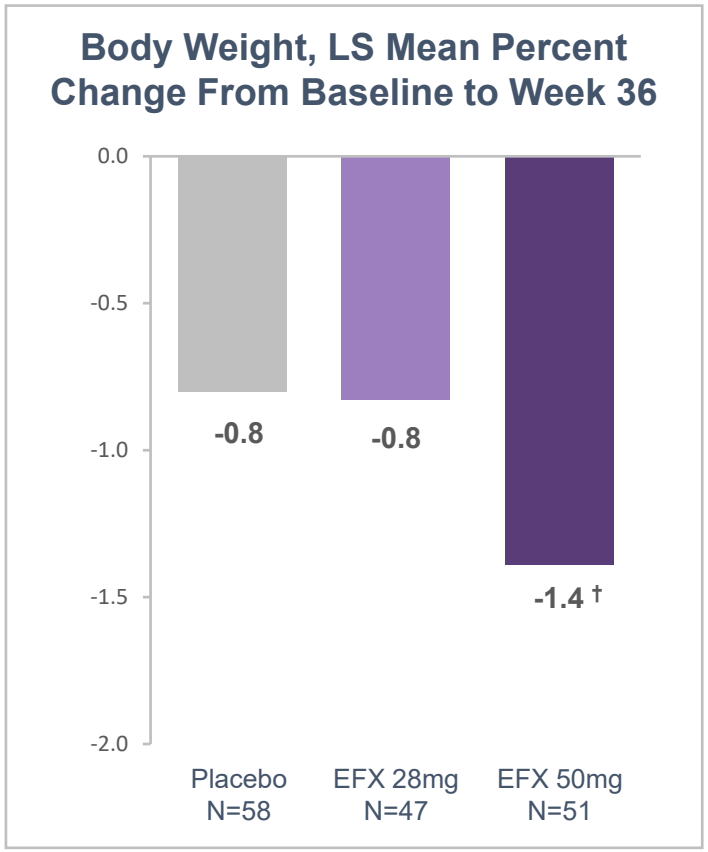
Source Data: Full Analysis Set; Topline preliminary data

Statistically Significant Increases Observed in Adiponectin:
PD Marker for EFX's Action on Adipose Tissue



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

Trend Toward Weight Loss for 50mg EFX Dose Group



† p<0.05 versus baseline (MMRM)

Source Data: Full Analysis Set; Topline preliminary data

Looking Ahead

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 discussion with FDA

Screening for SYNCHRONY Histology and SYNCHRONY Real-World has begun
First patient enrollments expected by December 2023

NASDAQ: AKRO

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