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Restoring Balance. Renewing Life.

Phase 2b HARMONY Study Results

September 13, 2022

Safe Harbor

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Evaluating EFRUXIFERMIN (EFX), An Fc-FGF21 Fusion Protein

HARMONY

Statistically Significant Effects after 24 Weeks

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

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Key Inclusion Criteria

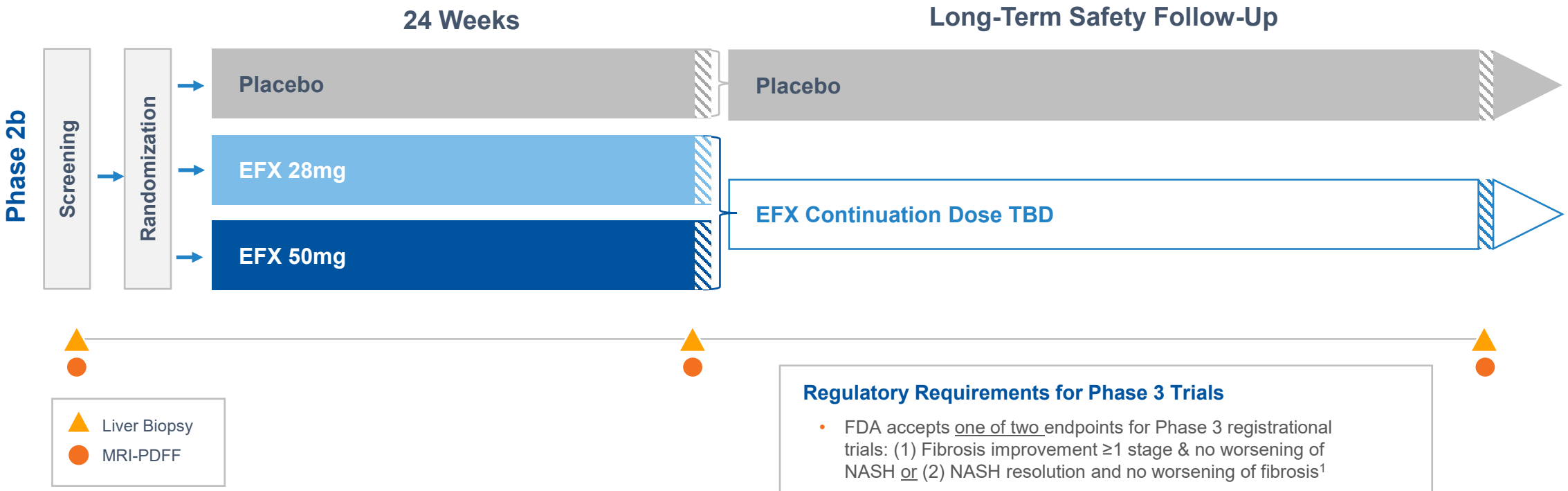
- F2-F3 NASH
- NAS ≥4
- Liver Fat (MRI-PDFF) ≥8%

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



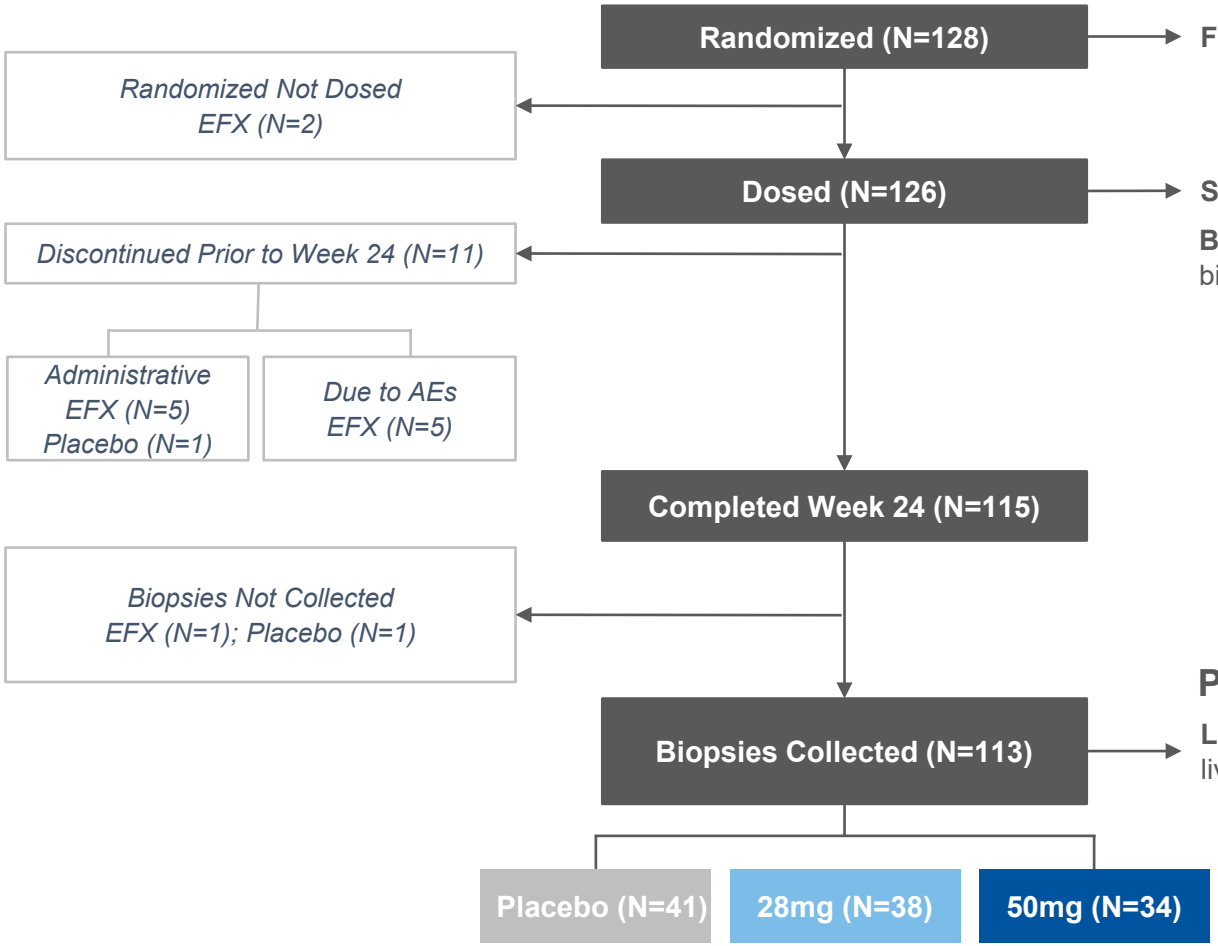
Regulatory Requirements for Phase 3 Trials

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[1] FDA Draft Guidance, Noncirrhotic Nonalcoholic Steatohepatitis With Liver Fibrosis: Developing Drugs for Treatment (2018)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



Key Analysis Sets

Full Analysis Set – All subjects who were randomized

Safety Set – All subjects who received at least one dose of study drug

Biomarker Analysis Set – All subjects who have baseline and on-study biomarker measurement at given timepoint

Primary Endpoint

Liver Biopsy Analysis Set – All subjects who have Baseline and Week 24 liver biopsy results

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

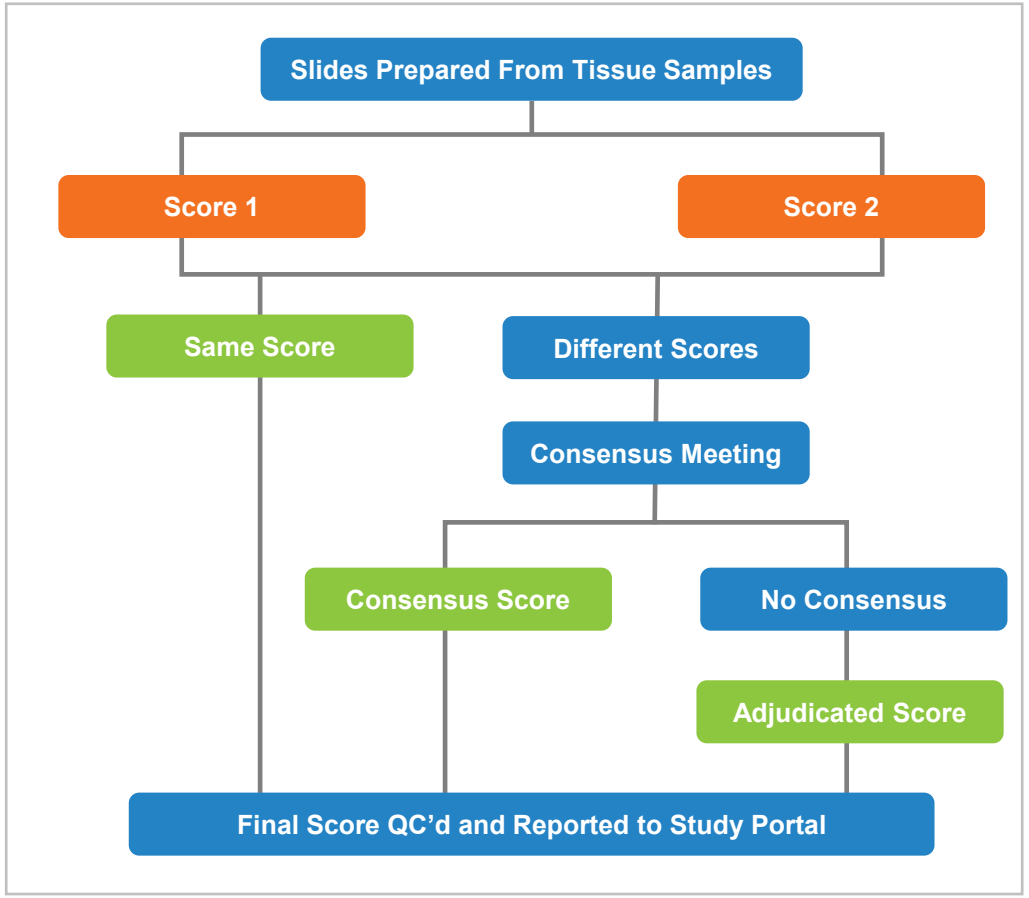
[1] All patients either fibrosis stage 2 (F2) or stage 3 (F3); [2] Procollagen 3 N-Terminal Propeptide; [3] Vibration-controlled transient elastography; [4] Magnetic Resonance Imaging Proton Density Fat Fraction

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

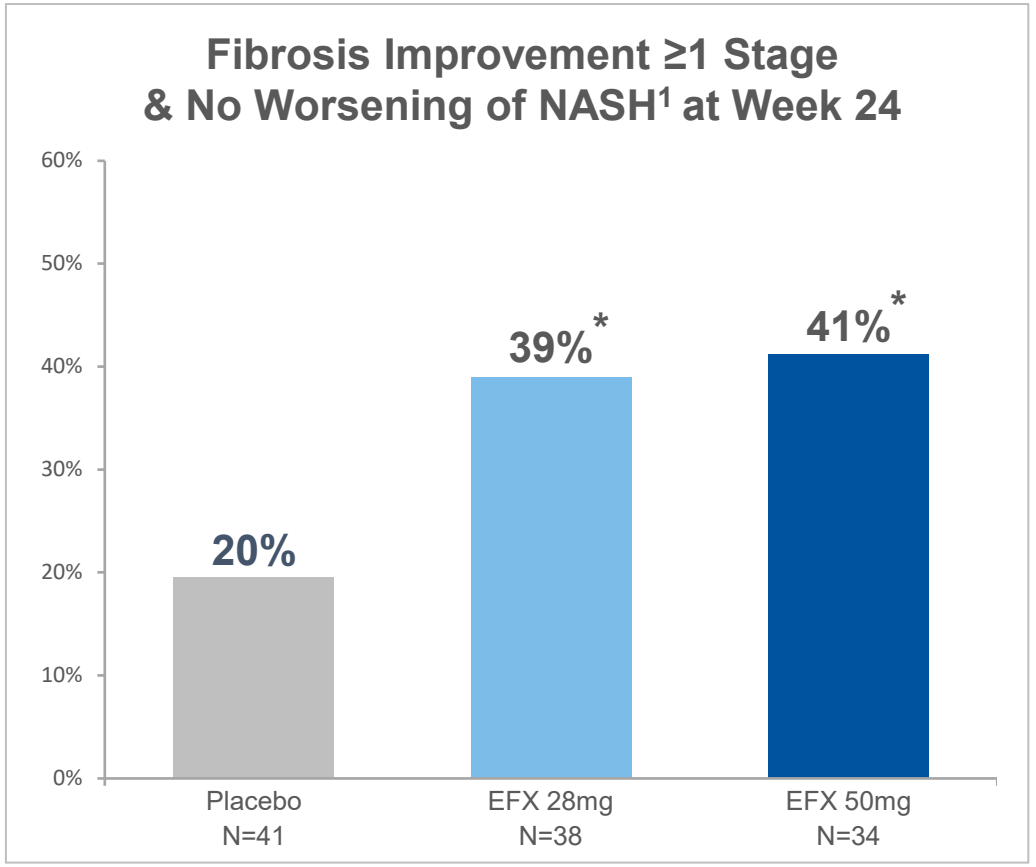
Key Features of EFX Biopsy Analysis Plan

- 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)



[1] Improvement in liver fibrosis greater than or equal to one stage and no worsening of NASH (defined as no increase in NAS for ballooning, inflammation, or steatosis)

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

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

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

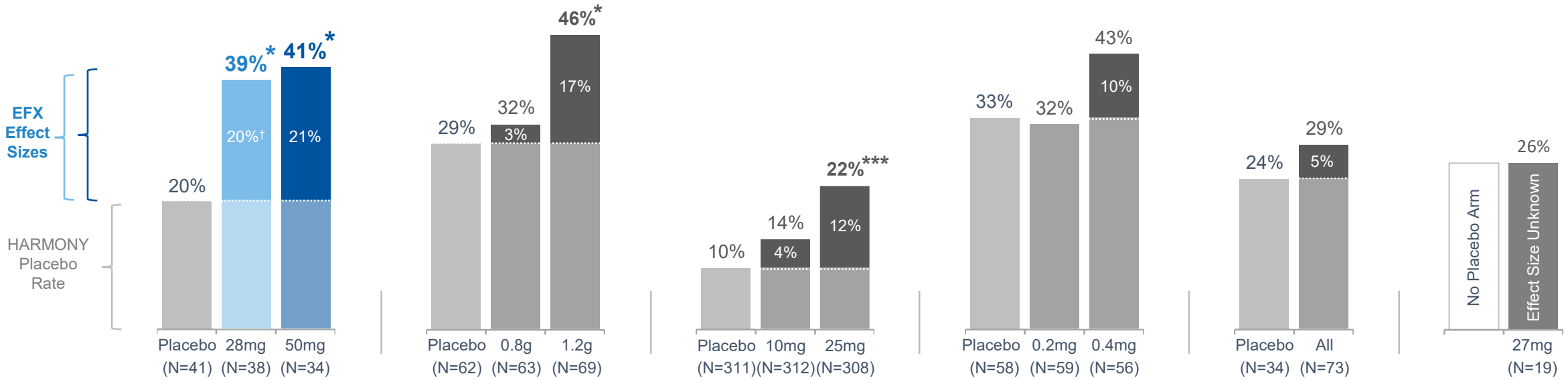
Obeticholic Acid
Phase 3 (F2-F3)
54% F3
72 Wks / ITT[3]
Consensus Readers

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

Resmetirom
Phase 2 (F1-F3)
20% F3
36 Wks / Completers[4]
Single Reader

Pegozafermin
Phase 1b/2a (F2-F3)
65% F3
20 Wks / Completers[5]
Single Reader

By Reported Effect Size (Treatment Minus Placebo)



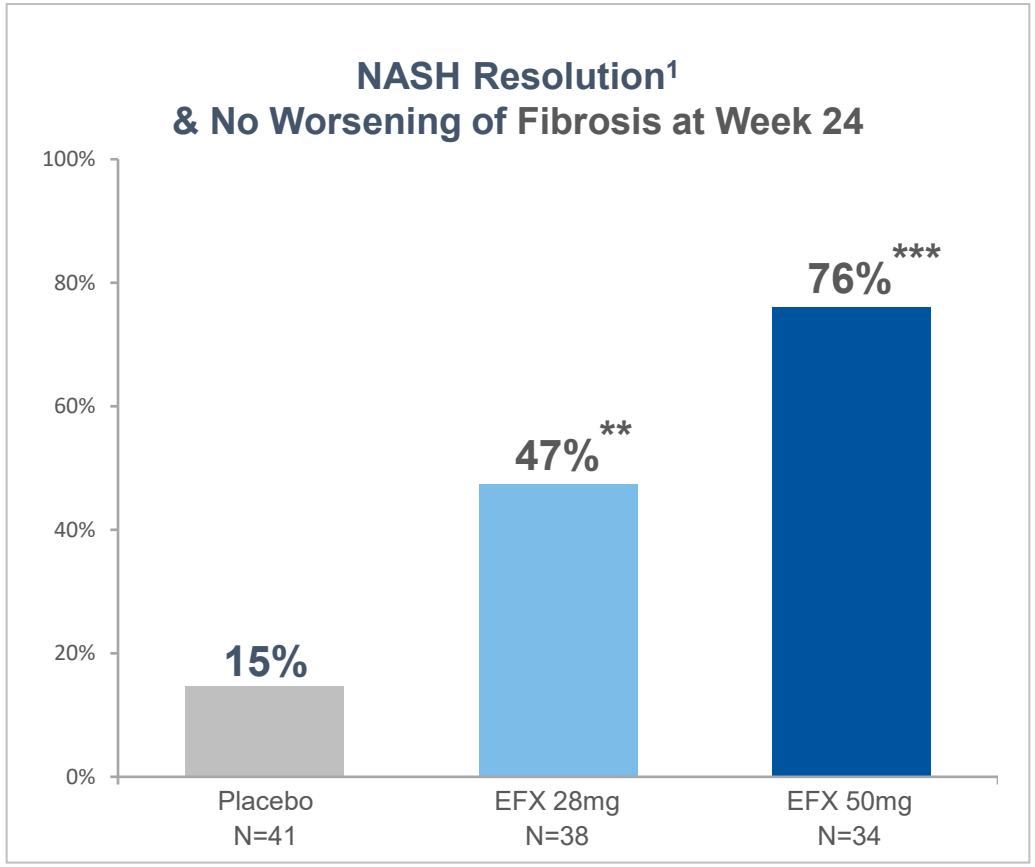
Note: These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.

[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] Completed 36 weeks of treatment and had end-of-study biopsy; [5] End-of-study biopsy available.

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, 1113–1124; Resmetirom - Harrison, S et al. (2019) Lancet 394(10213):2012-24; Pegozafermin - 89Bio (2022) August 1 Corporate Presentation. 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)



[1] NAS score of 0 or 1 for lobular inflammation and a score of 0 for ballooning

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

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

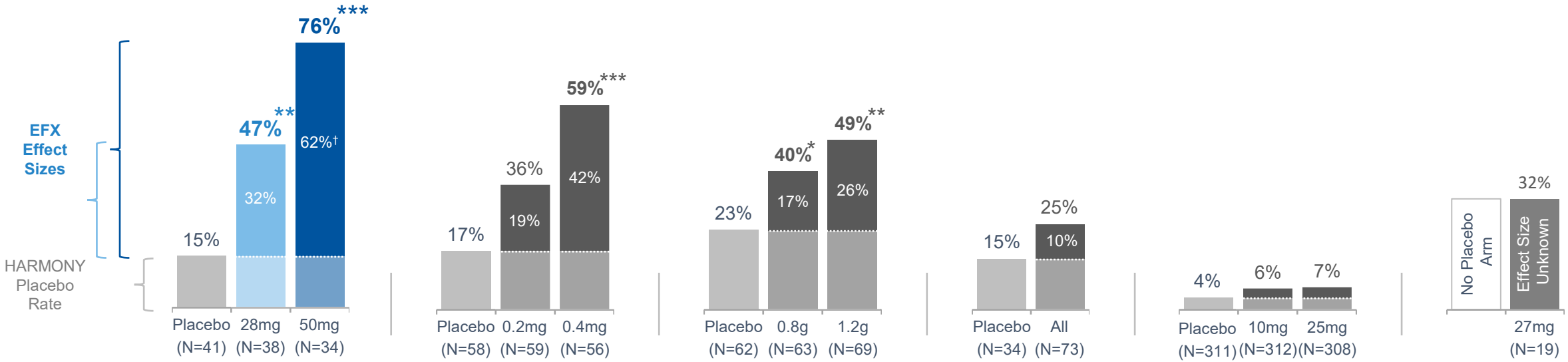
Lanifibranor
Phase 2b (F1-F3)
% F3 Not Reported
24 Wks / Completers[3]
Single Reader

Resmetirom
Phase 2 (F1-F3)
20% F3
36 Wks / Completers[4]
Single Reader

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

Pegozafermin
Phase 1b/2a (F2-F3)
65% F3
20 Wks / Completers[5]
Single Reader

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.

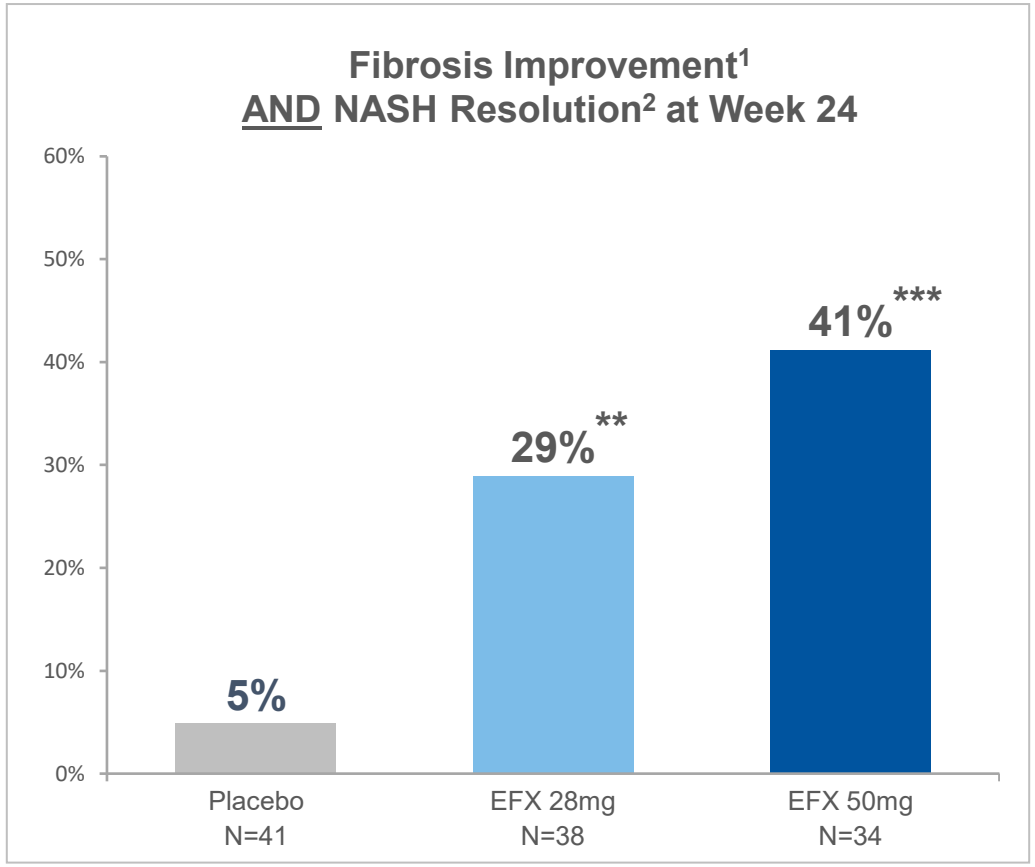
[1] Baseline and Week 24 biopsies available; [2] Missing biopsies were imputed as non-responders; [3] End-of-study biopsy available with no major protocol deviations; [4] Completed 36 weeks of treatment and had end-of-study biopsy; [5] End-of-study biopsy available.

Semaglutide - Newsome et al. (2020) New Engl J Med 384, 1113–1124; Lanifibranor - Francque et al. (2021) New Engl J Med 385, 1547–1558; Resmetirom - Harrison, S et al. (2019) Lancet 394(10213):2012-24; Obeticholic acid - Intercept (2022) July 7 Press Release; Pegozafermin - 89Bio (2022) August 1 Corporate Presentation. 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)



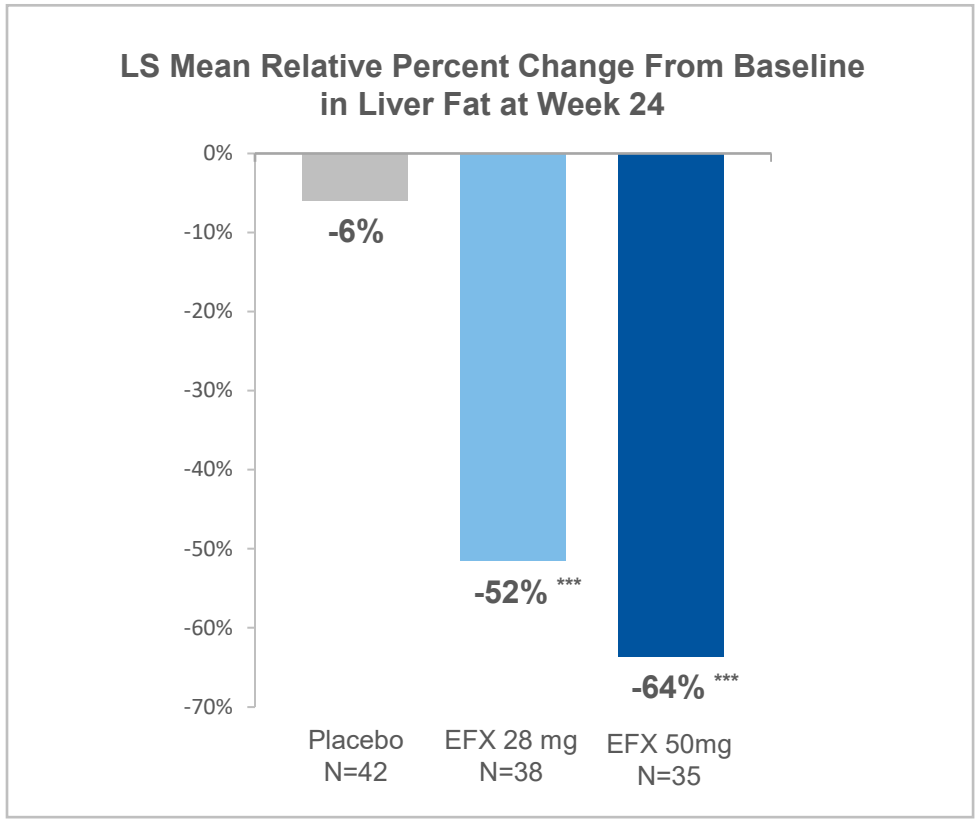
[1] Improvement in liver fibrosis greater than or equal to one stage
[2] NAS score of 0 or 1 for lobular inflammation and a score of 0 for ballooning
** p<0.01, *** p<0.001, versus placebo (CMH)

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%

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

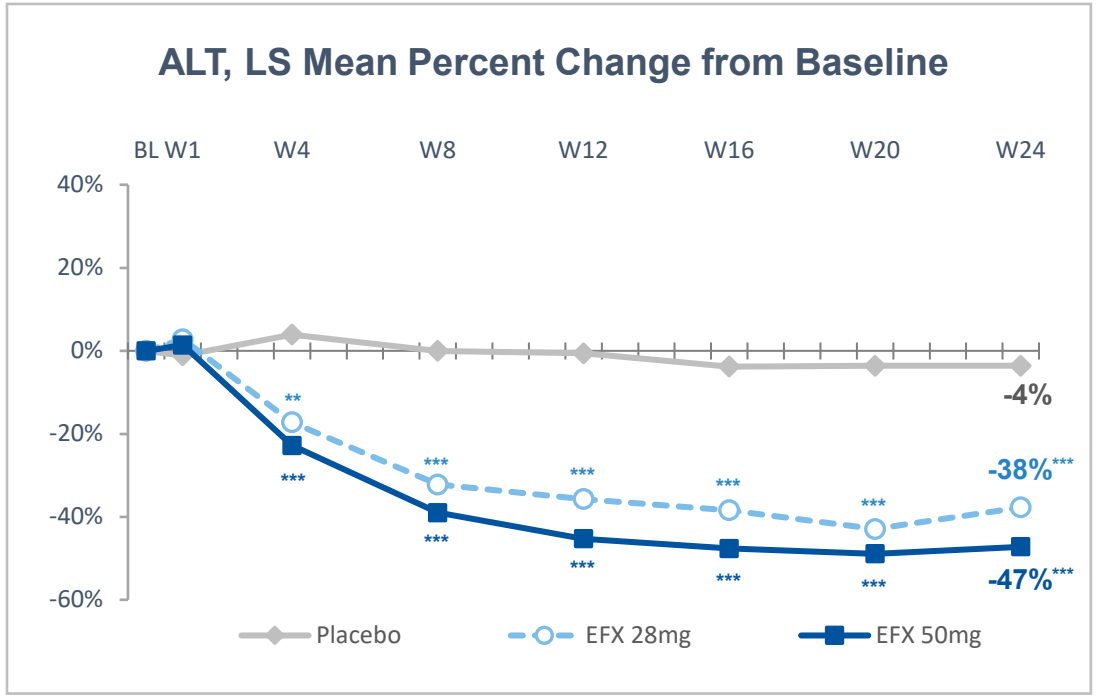
Endpoint	Placebo (N=42)	EFX 28mg (N=38)	EFX 50mg (N=35)
Relative Reduction in Liver Fat			
≥50%	2%	63% ***	77% ***
Normalization of Liver Fat Content			
≤5%	2%	34% ***	51% ***

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

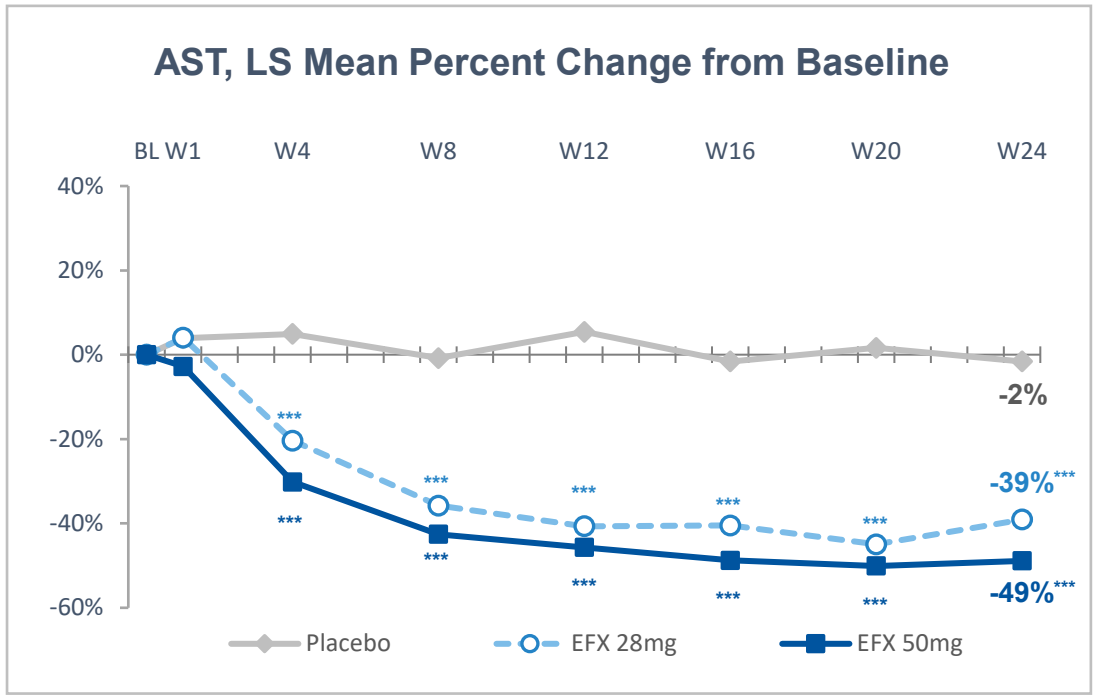
[1] The Phase 2a BALANCED study was a 12-week randomized clinical trial in patients with F1-F3 NASH

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



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



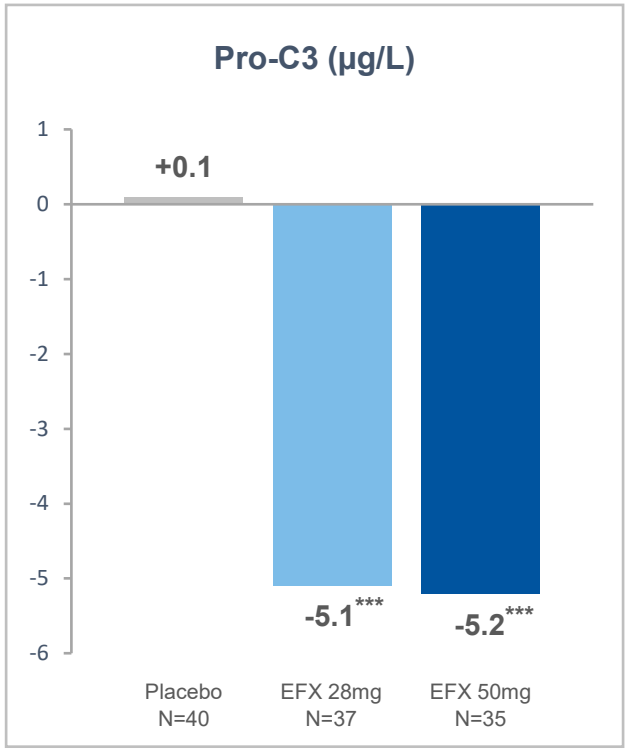
*** p<0.001, versus placebo (MMRM[1])

[1] Mixed Model Repeated Measures

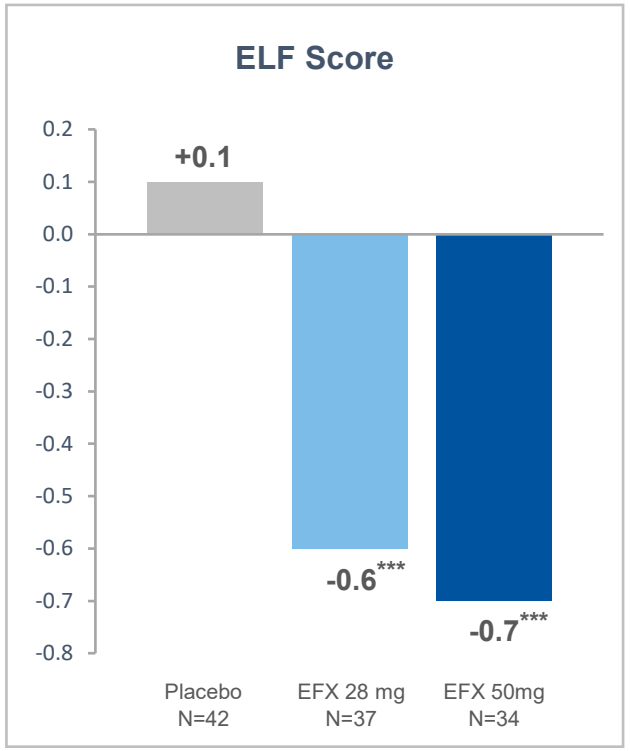
Source Data: Full Analysis Set

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

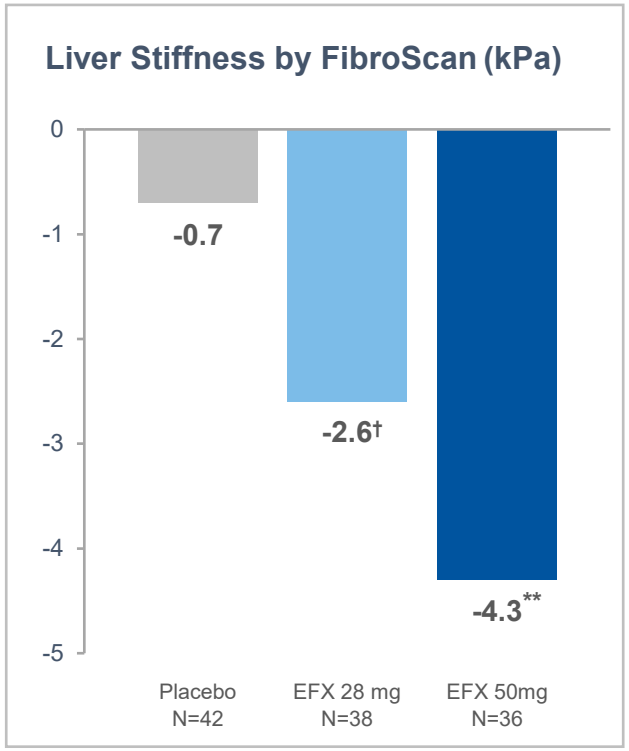
LS Mean Change From Baseline to Week 24



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



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



** p<0.01, versus placebo (ANCOVA[1])
† p<0.01, versus baseline (ANCOVA)

[1] 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)

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]
TEAE Leading to Discontinuation	0 (0%)	2 (5%)[c]	3 (7%)[d]
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%)

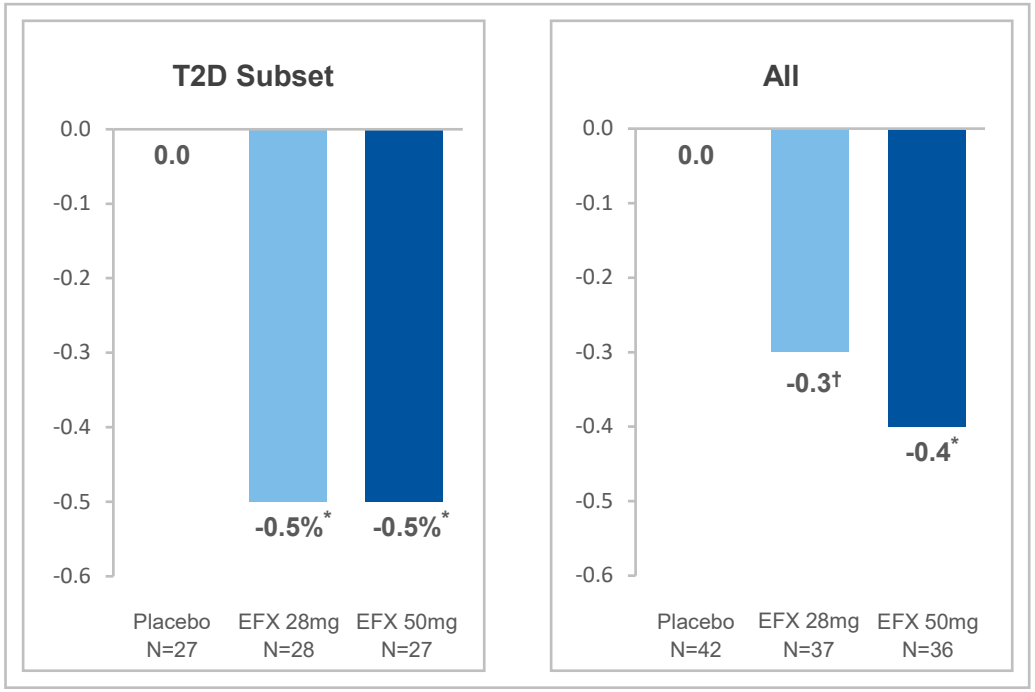
[a] (1) Esophagitis
[b] There were three additional non-drug-related SAEs: (1) Edema; (2) Covid-19; (3) Pancreatitis
[c] (1) Increased appetite & weight gain; (2) diarrhea
[d] (1) Esophagitis & vomiting; (2) Nausea; (3) Lymphadenopathy (not drug-related)

Source Data: Safety Set

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

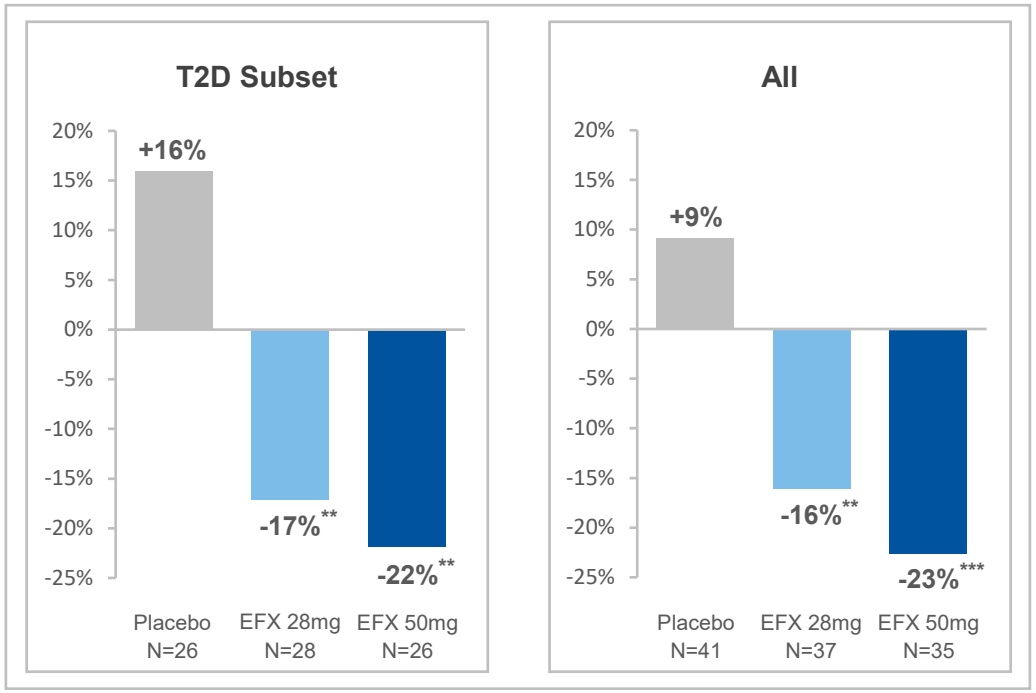
LS Mean Change From Baseline to Week 24[2]

HbA1c(%)[1]



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

C-Peptide[3]



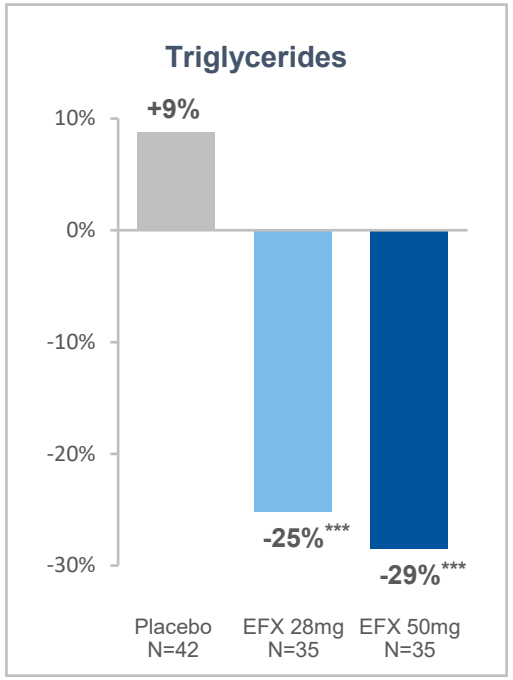
** p<0.01, *** p<0.001, versus placebo (MMRM)

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

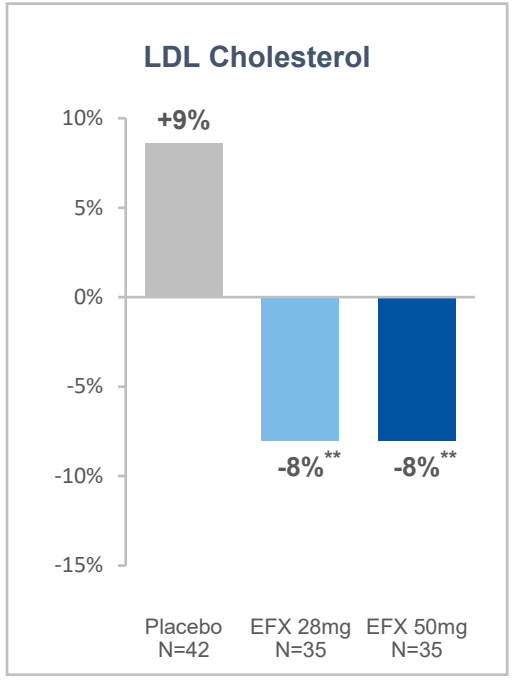
Source Data: Biomarker Analysis Set

Significant Improvements Observed in Lipoprotein Profile

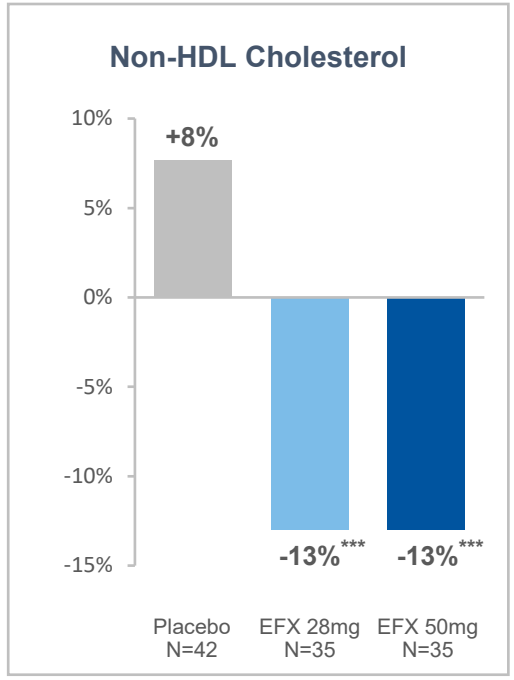
LS Mean Change From Baseline to Week 24 (%)



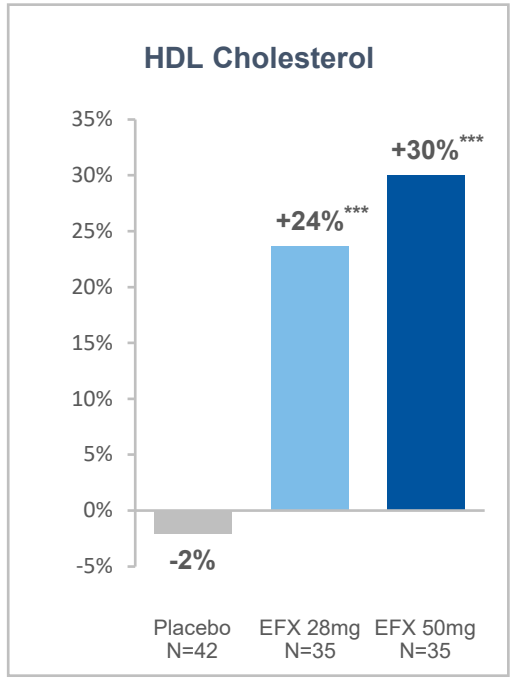
*** p<0.001, versus placebo (MMRM)



** p<0.01, versus placebo (MMRM)



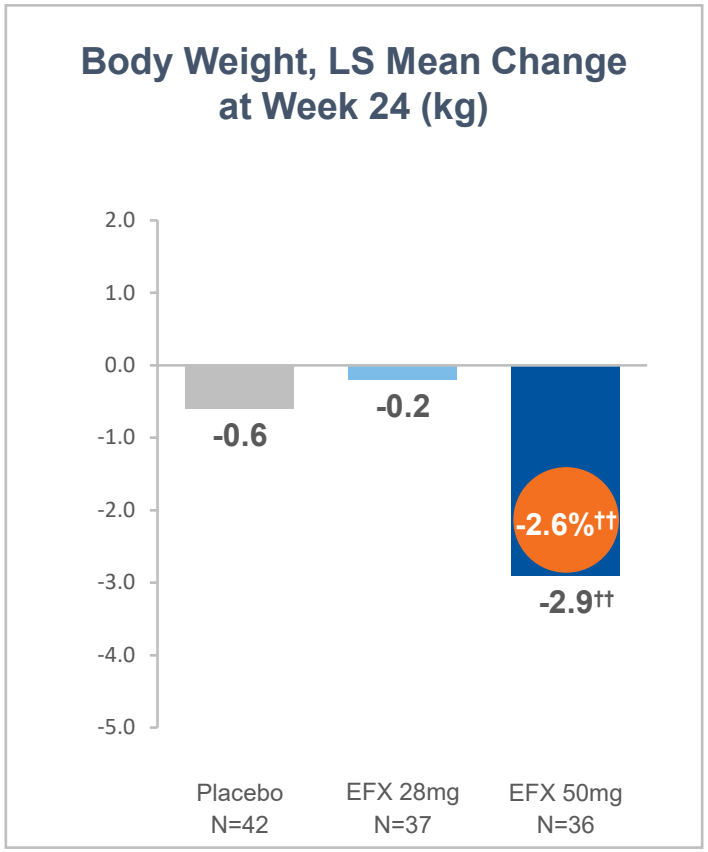
*** p<0.001, versus placebo (MMRM)



*** 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

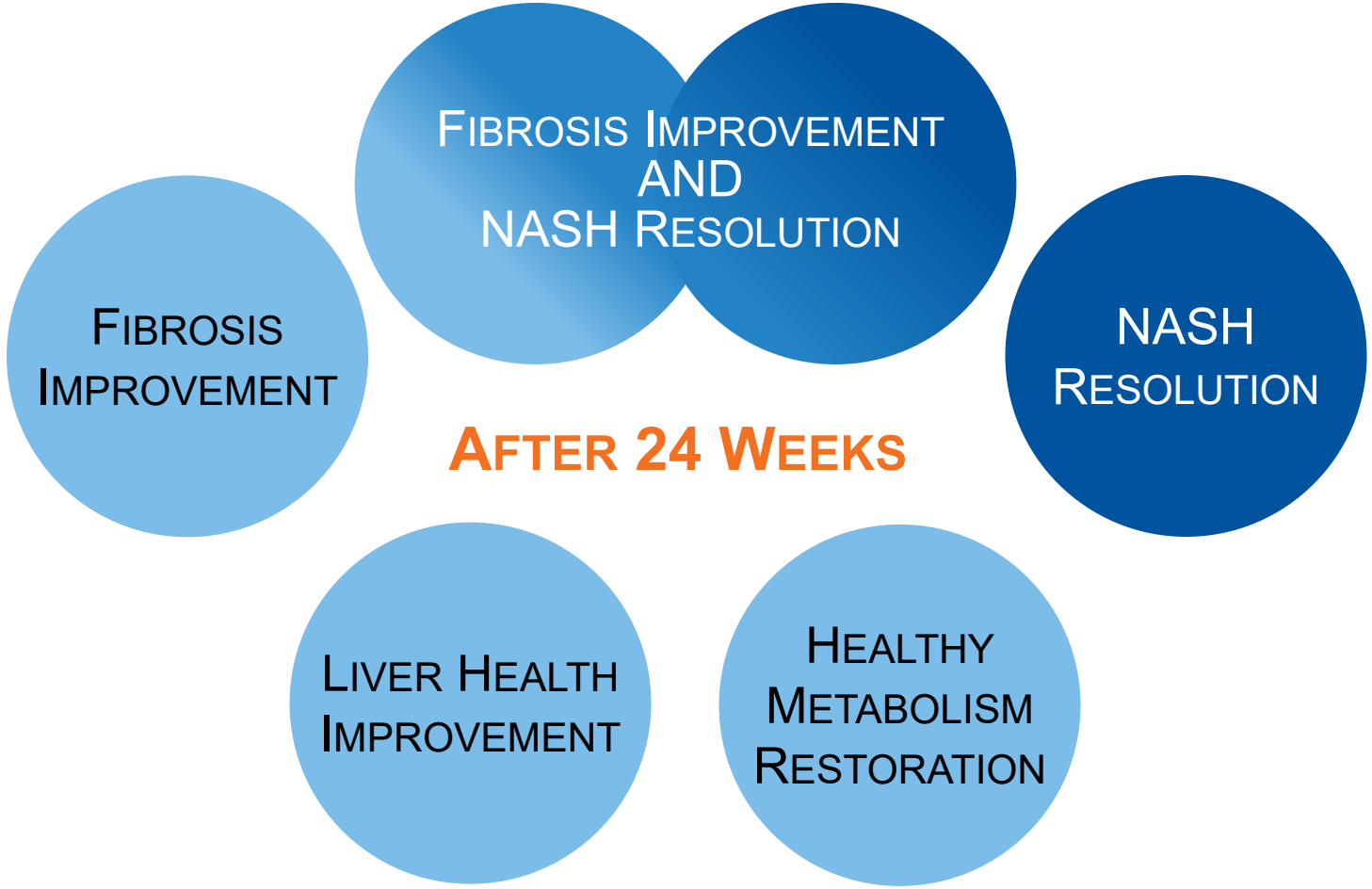


†† p<0.01, versus baseline (MMRM)

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

EFX: A Potentially Foundational NASH Therapy

ADDRESSING ALL CORE ASPECTS OF NASH PATHOGENESIS IN A SINGLE TREATMENT



NASDAQ: AKRO

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