



Restoring Balance. Renewing Life.

Corporate Presentation



November 2025



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1

Potential to Treat Pre-Cirrhotic MASH (F2-F3)

- HARMONY: 96-wk Ph2b study
- Week 96 data provided strongest reported efficacy data to date across MASH field:
 - ≥1 stage fibrosis improvement
 - 2 stage fibrosis improvement
 - MASH resolution
 - Fibrosis improvement and MASH resolution

Unprecedented Fibrosis Improvement
After 96 Weeks of Treatment

2

Potential to Treat MASH Due to Cirrhosis (F4, compensated)

- SYMMETRY: 96-wk Ph2b study
- Week 96 data provided first-ever report of statistically significant reversal of cirrhosis
- 50mg EFX versus placebo
 - Completer Analysis: 39% vs. 15%
 - ITT Analysis: 29% vs. 12%
- Favorable tolerability profile

Unprecedented Reversal of Cirrhosis
After 96 Weeks of Treatment

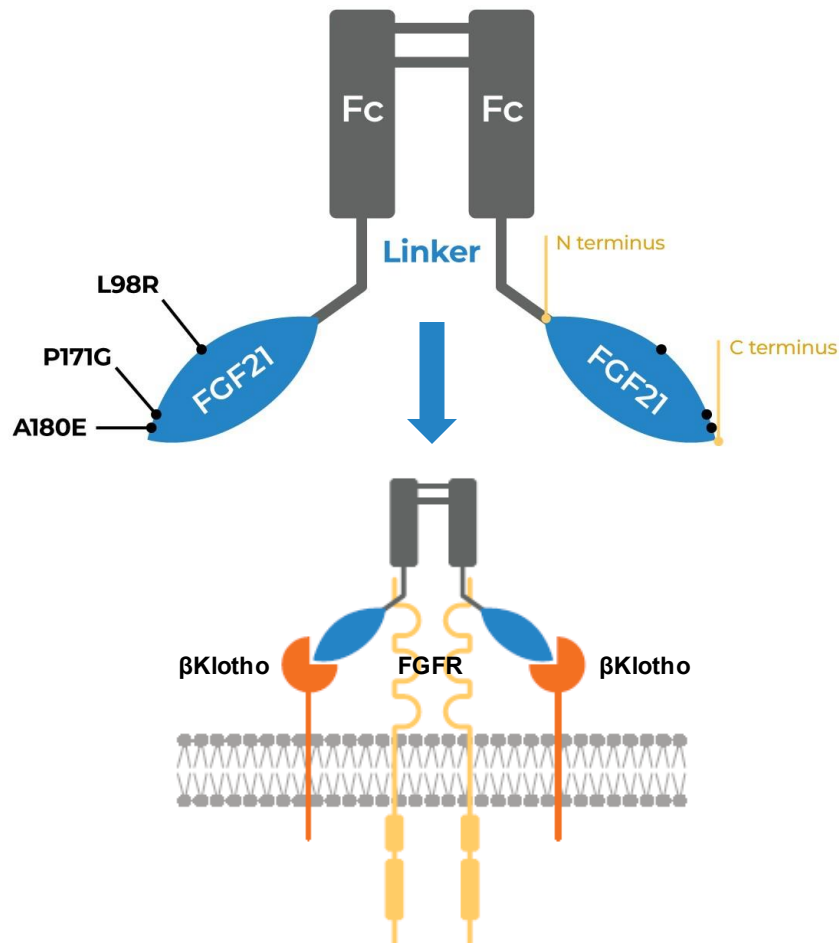
3

Global Phase 3 SYNCHRONY Program Underway (F1-F4, compensated)

- Phase 3 SYNCHRONY program comprised of three clinical trials
 - *Histology* (F2-F3), readout with histology expected 1H'27
 - *Real-World* (F1-F3), non-invasive tests only, readout expected 1H'26
 - *Outcomes* (F4, compensated)

All three SYNCHRONY studies are
actively enrolling patients

EFX Bivalent Structure Potentially Optimal for MASH Efficacy, With Convenient Once-weekly Dosing



Bivalent FGF21 Analog Brings:



High β -Klotho affinity



High systemic exposure

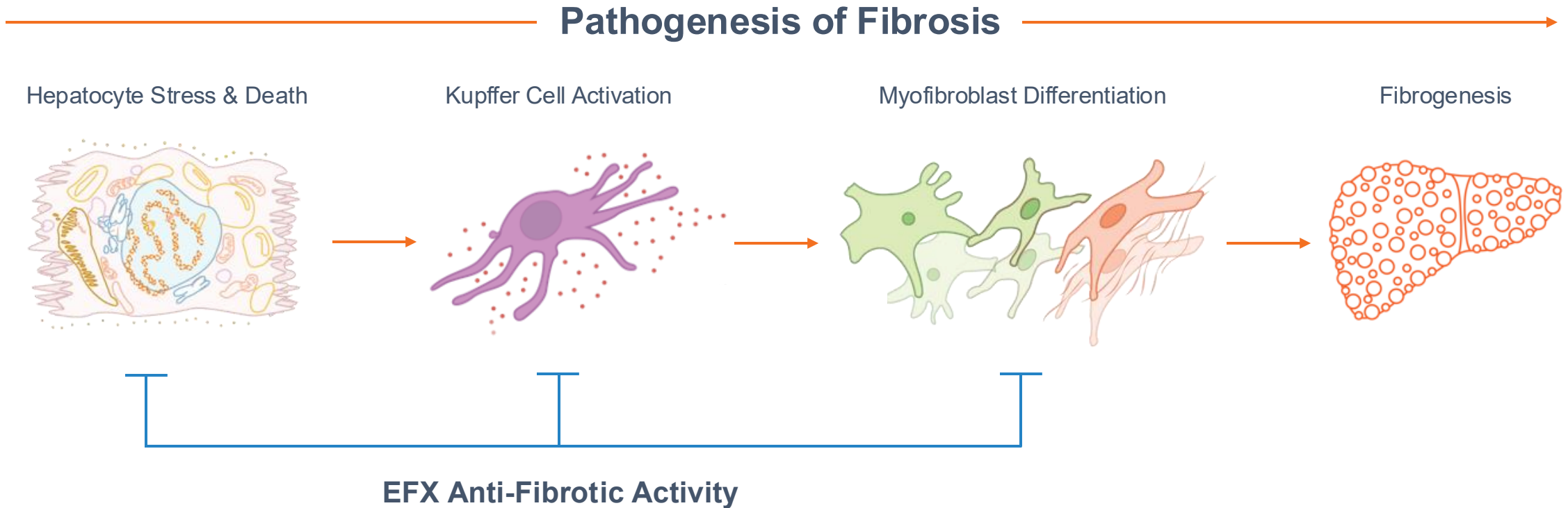


Maintained agonism of FGFRs throughout weekly dosing interval



Sustained pharmacodynamic effect through week 24 (F2-F3) and week 36 (F4, compensated)

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



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*

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 MASH drug to receive all three designations

Comprehensive Phase 3 SYNCHRONY Program Builds on Data from Two Biopsy-based Phase 2b Studies

Comprehensive Phase 3 SYNCHRONY program (N ~3500) builds on two biopsy-based Phase 2b studies (N ~300) in corresponding patient populations

HARMONY¹



symmetry²
FOR CIRRHOTIC NASH



Fibrosis Stage	F2-F3	F2-F3	F4, Compensated	F4, Compensated
Phase	2b	3	2b	3
N	128	1650	182	1150
Weeks	96	240	96	~260



Phase 3 study evaluating safety & tolerability in ~700 clinically-diagnosed patients (F1 to F4, compensated) for 52 weeks

¹ HARMONY Phase 2b 24-Week Results published in Lancet Gastro Hepatol 2023; 8(12):1080–1093

² SYMMETRY Phase 2b 36-Week Results presented at AASLD 2023, LB-5005 Hepatology 2024; 79:E33-E85

» Phase 3 SYNCHRONY Trial Designs: *Histology (F2-F3) and Real-World (F1-F3)*

Phase 3 SYNCHRONY program (N ~3500) is comprised of two efficacy studies with both histology and long-term clinical outcomes endpoints and a third one-year study evaluating safety and tolerability

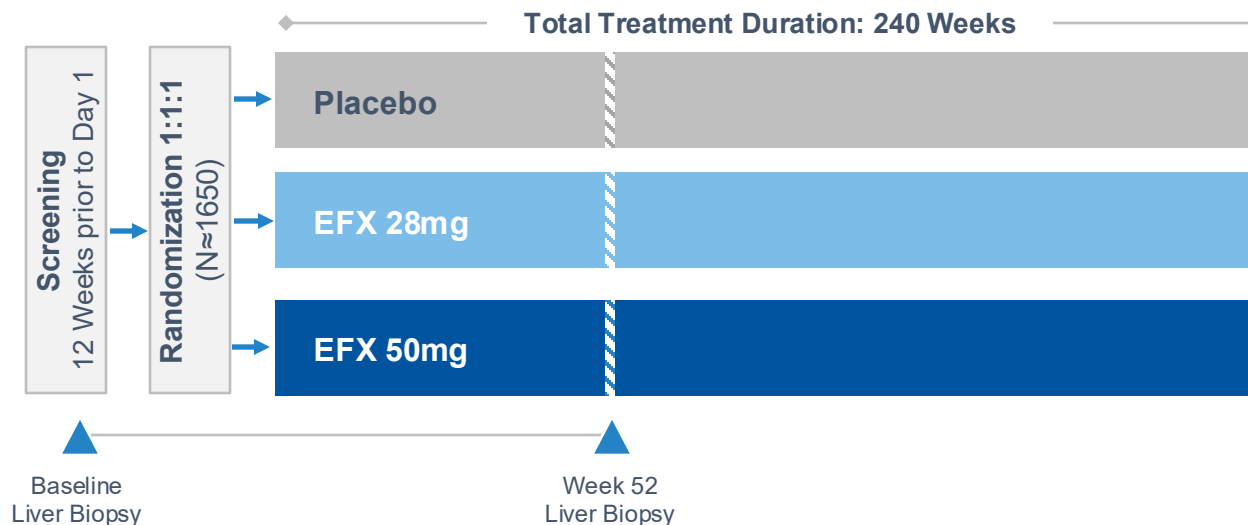


Primary Histology Endpoint
≥ 1-stage fibrosis improvement and
MASH resolution at Week 52

Patient Population
Biopsy-confirmed F2-F3 MASH

Readout Expected
1H 2027

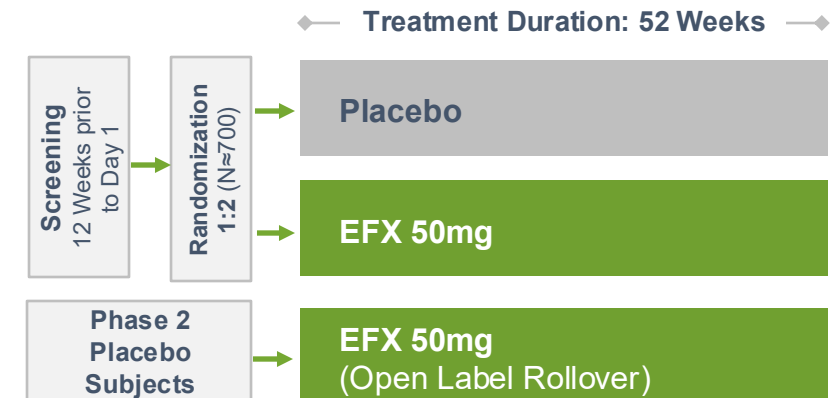
Primary Outcomes Endpoint
Evaluated at 240 Weeks



Primary Endpoint
Safety & Tolerability

Patient Population
MASH/MASLD

Readout Expected
1H 2026



Double-Blind Enrollment Completed



Phase 3 SYNCHRONY Trial Design: *Outcomes (F4, Compensated)*

Patient Population

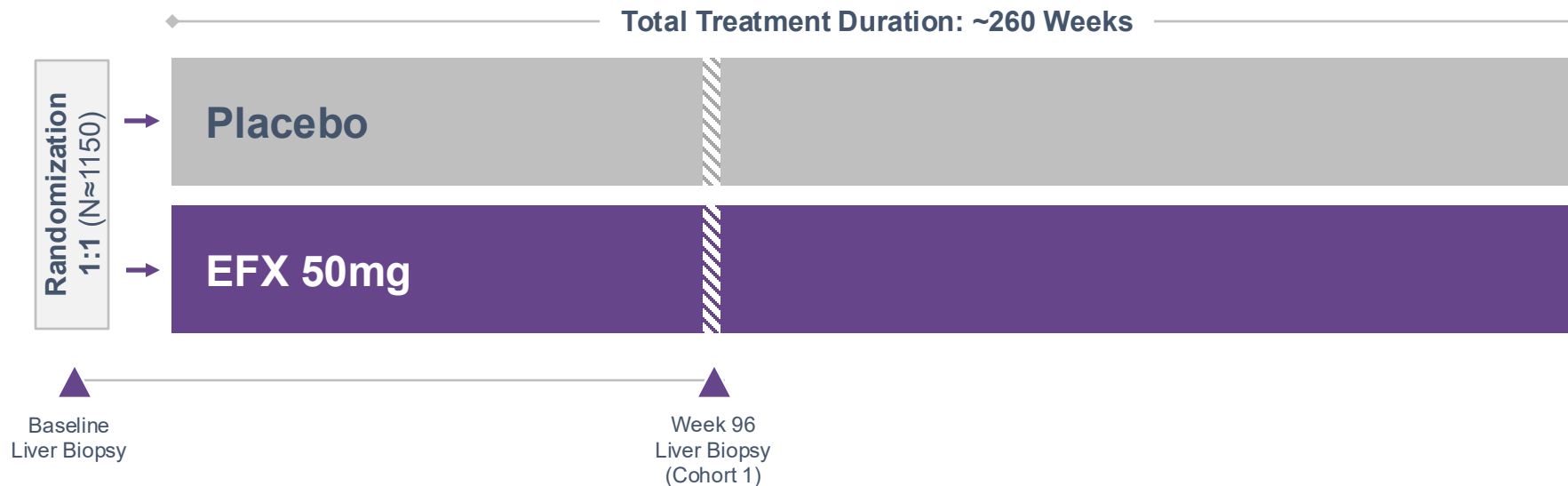
Cirrhosis Due to MASH
(F4, Compensated)

Primary Histology Endpoint

≥ 1-stage fibrosis improvement and
no worsening of MASH at Week 96

Primary Outcomes Endpoint

Time to first occurrence of
protocol-specified clinical events



Key Secondary Efficacy Endpoints for All Phase 3 Studies

- Fibrosis Markers
- Lipoproteins
- Glycemic Control
- Weight Change
- Liver Injury Markers

Commercial Supply Chain of API and Drug Product/Device: Supply Authorized Globally for Initiated Phase 3 Studies

Drug Substance (API)



- ✓ Commercial scale
- ✓ High Titer E. Coli Expression
- ✓ Process validation complete

Drug Product/Device Combination

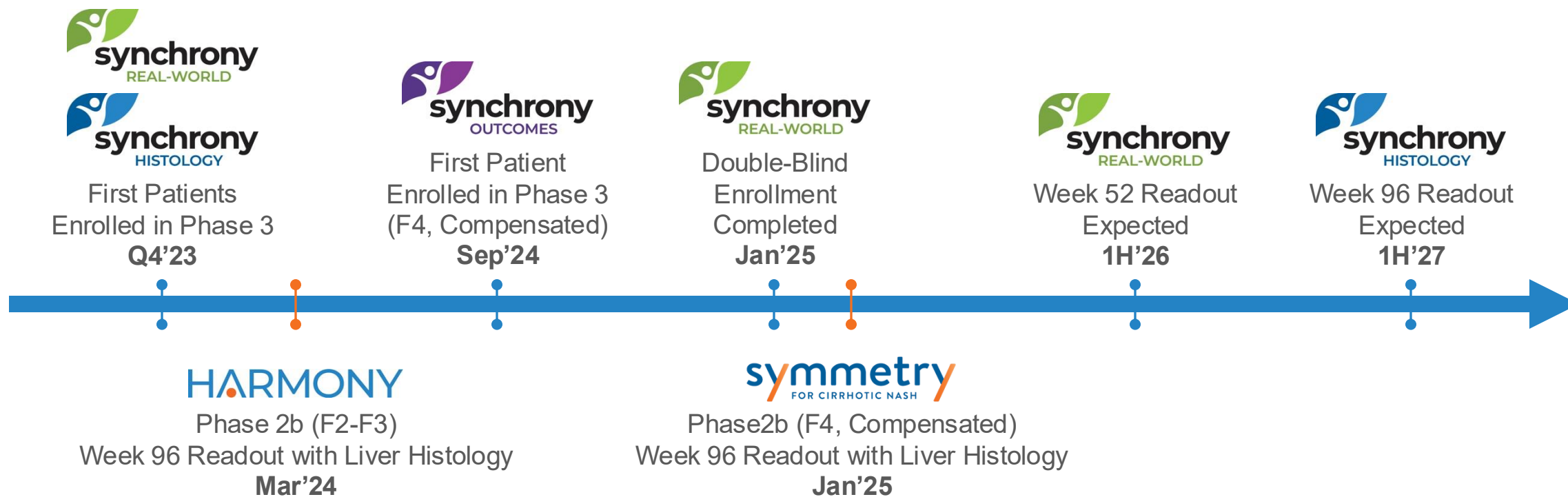


- ✓ Commercially precedented
- ✓ 1 mL Iyo/liquid Dual Chamber Syringe
- ✓ Self-administered, stable at 2-25°C

China / U.S. Tariffs

- No current or expected manufacturing in China
- DS/DP manufactured in Europe for clinical trials currently exempt from U.S. tariffs
- Given timeline to commercial launch, flexibility to adapt to changing tariff regime

» Recent Progress, Near-Term Milestones, and Cash on Hand

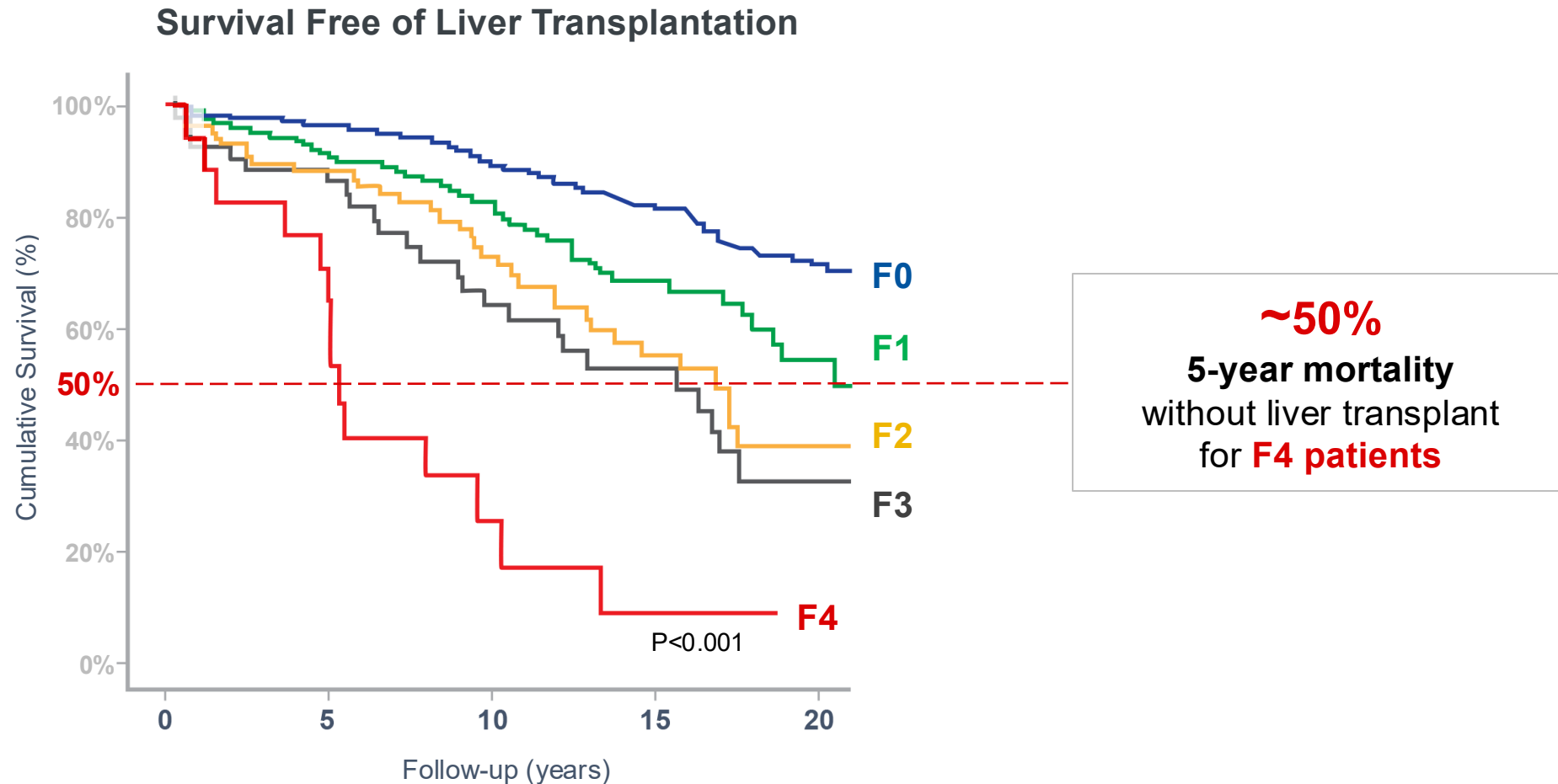


~\$988M cash on hand¹ at September 30, 2025



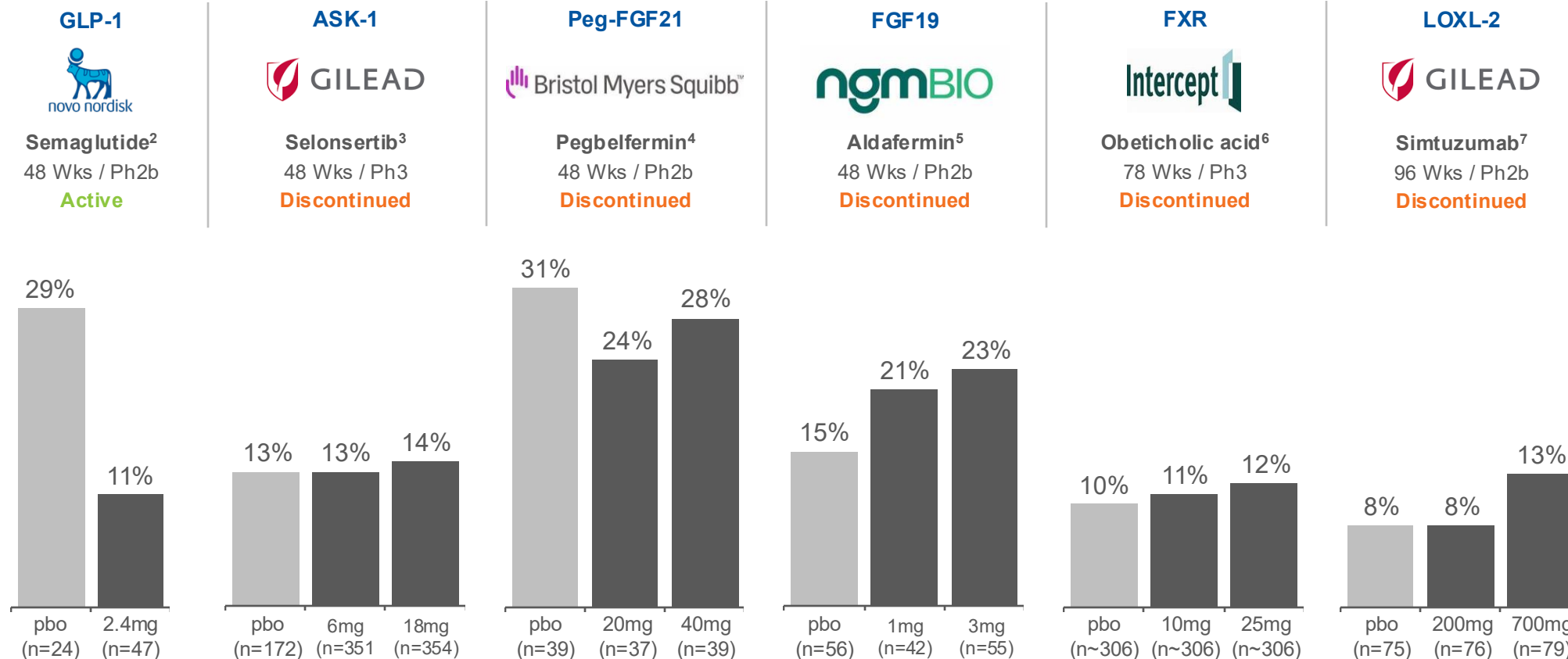
**STATISTICALLY SIGNIFICANT
REVERSAL OF CIRRHOSIS
AFTER 96 WEEKS**

» High Risk of Mortality Associated with Cirrhosis Due to MASH



No Compound To Date Has Shown Statistically Significant Reversal of Cirrhosis Due to MASH in Clinical Trials

Fibrosis Improvement ≥ 1 Stage¹



¹ Includes results from publicly reported placebo-controlled studies in patients with compensated cirrhosis due to MASH reporting either ≥ 1 -stage fibrosis improvement and no worsening of MASH (semaglutide, selonsertib, pegbelfermin, obeticholic acid) or only ≥ 1 -stage fibrosis improvement (aldafermin, simtuzumab); numerical values represent percent responders. ² Loomba, R et al. (2023) Lancet Gastro Hep 8:511-22; ³ Harrison, SH et al. (2020) J Hepatol 73(1):26-39; ⁴ Abdelmalek, MF et al. (2023) Clinical Gastro Hep 23:S1542-3565; ⁵ NGM Bio (2023) September Corporate Overview; ⁶ Intercept (2022) September 30 Press Release; ⁷ 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. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.



Phase 2b SYMMETRY Trial Design: Compensated Cirrhosis (F4) Due to MASH with Liver Histology at 36 and 96 weeks

Key Inclusion Criteria¹

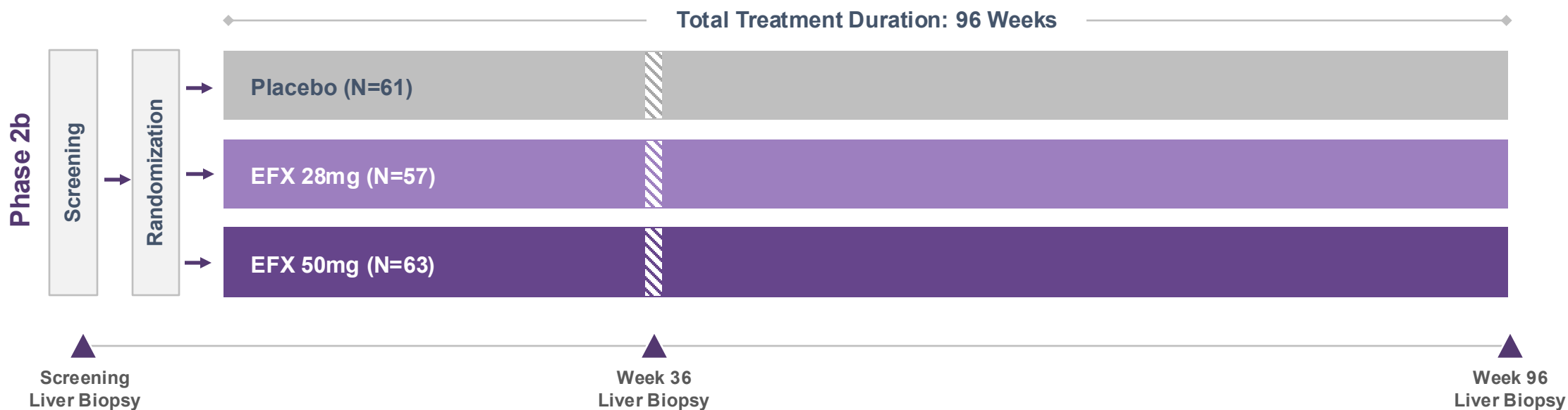
- F4 MASH, Child-Pugh A
- T2D or 2 of 4 components of metabolic syndrome²

Phase 2b Primary Endpoint

- ≥1 Stage Fibrosis Improvement with no Worsening of MASH at Week 36

Key Secondary Efficacy Endpoints

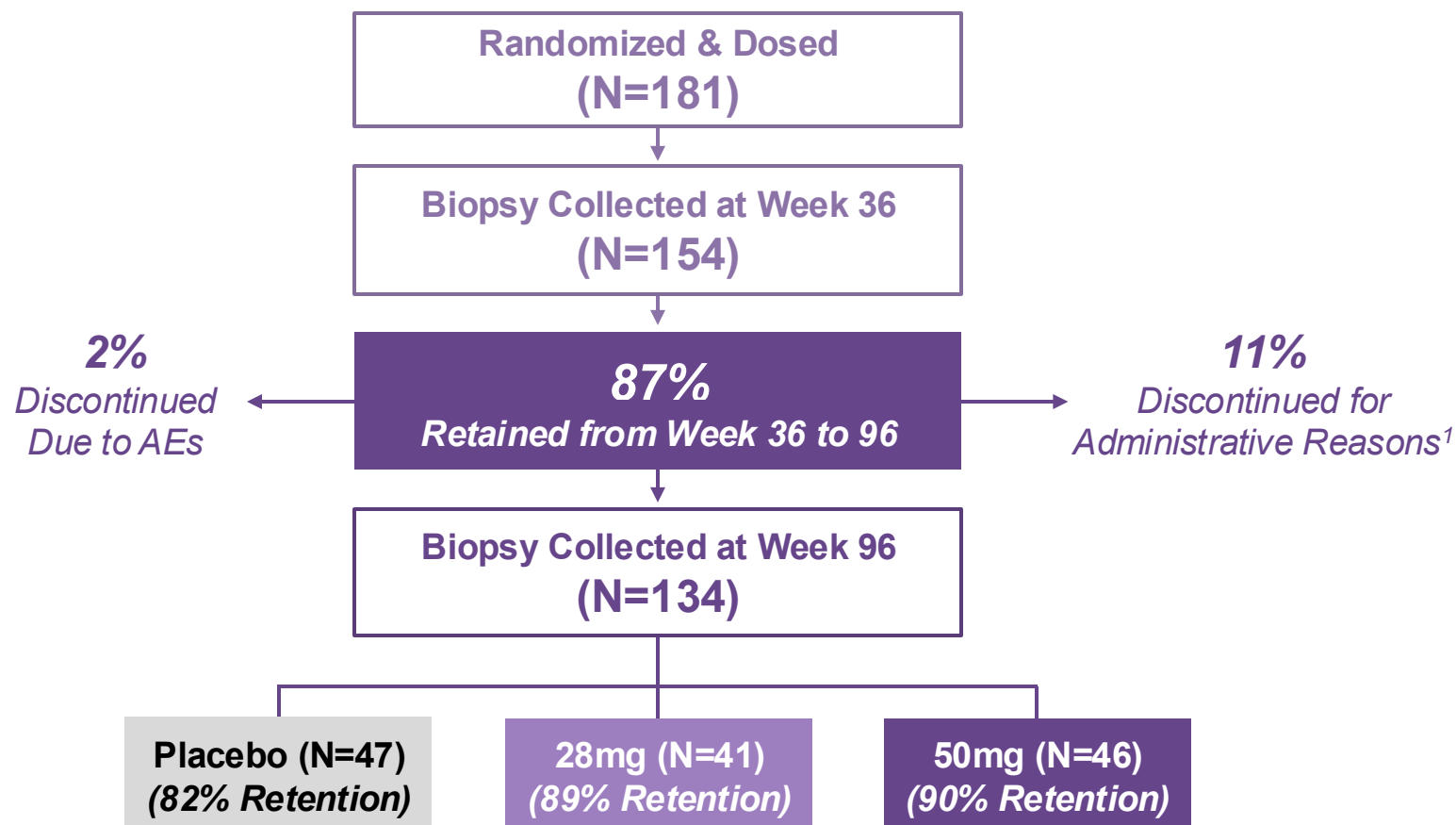
- MASH Resolution
- Glycemic Control
- Fibrosis Markers
- Weight Change
- Lipoproteins
- Liver Injury Markers



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

² Obesity, dyslipidemia, elevated blood pressure, and elevated fasting glucose

Parameter (Mean)	Placebo (N=61)	EFX 28mg (N=57)	EFX 50mg (N=63)
Age (Years)	61	62	59
Sex (% Female)	62	68	70
Enhanced Liver Fibrosis (ELF) Score	10.4	10.6	10.5
Liver Stiffness by VCTE (FibroScan) (kPa)	24.7	24.1	24.5
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
HOMA-IR	11.8	11.7	11.5
Baseline Use of GLP-1 Receptor Agonists (%)	26	19	33
Triglycerides (mg/dL)	143	148	159
Statin Use (%)	53	46	43
Weight (kg)	102	99	95



Analysis Set ¹	N	Description
Week 96 Liver Biopsy Analysis Set (LBAS) Placebo (N=47) 28mg (N=41) 50mg (N=46)	134	All patients with baseline and Week 96 biopsy results
Safety Set / Full Analysis Set (FAS)² Placebo (N=61) 28mg (N=57) 50mg (N=63)	181	All randomized patients who received at least one dose of study drug

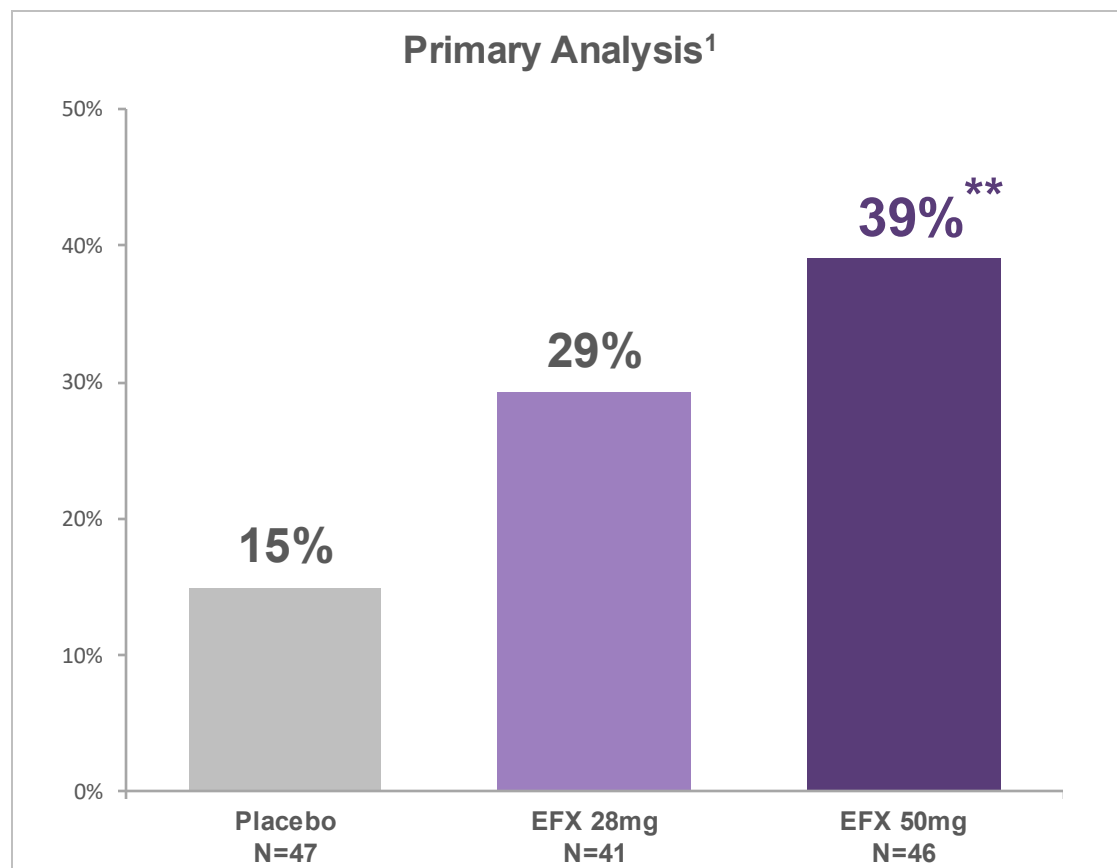
¹ P-values, where presented, are nominal

² ITT Analyses are based on FAS where missing biopsy = failure



Unprecedented **Reversal of Cirrhosis** Observed in SYMMETRY with 50mg EFX

Fibrosis Improvement ≥ 1 Stage & No Worsening of MASH at Week 96



¹ All patients with baseline and Week 96 biopsies

** p<0.01, versus placebo (CMH test³)

³ Cochran-Mantel-Haenszel test

ITT Analysis²

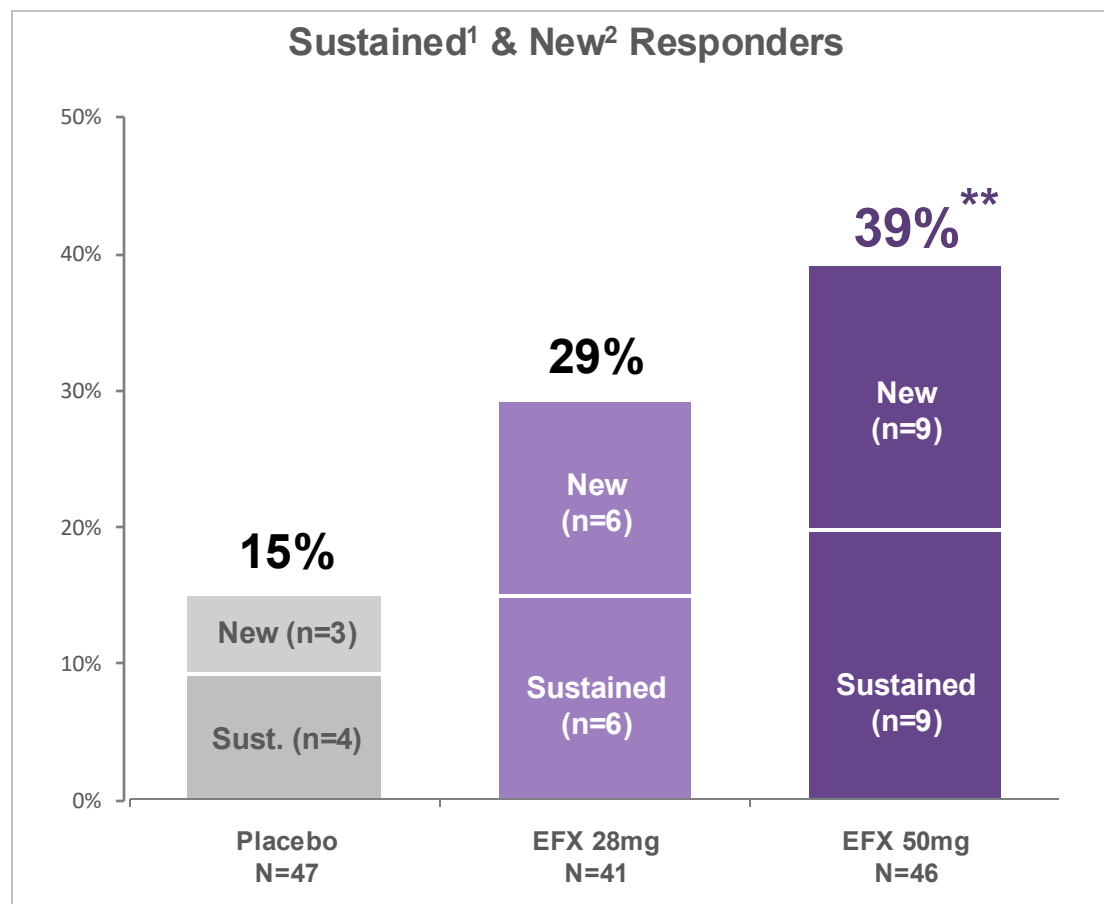
Placebo (N=61)	EFX 28mg (N=57)	EFX 50mg (N=63)
12%	21%	29%*

² Missing biopsy = failure

* p<0.05, versus placebo (CMH test)

» Improved and Durable Response Observed with Longer Treatment

Fibrosis Improvement ≥ 1 Stage & No Worsening of MASH at Week 96



¹ Responder at Weeks 36 & 96; ² Responder at Week 96

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

Proportion of Week 36 Responders with Sustained Response at Week 96^{3,5}

Placebo (N=8)	EFX 28mg (N=9)	EFX 50mg (N=12)
4 (50%)	6 (67%)	9 (75%)

Proportion of Week 36 Non-Responders with New Response at Week 96^{4,5}

Placebo (N=39)	EFX 28mg (N=32)	EFX 50mg (N=34)
3 (8%)	6 (19%)	9 (26%)

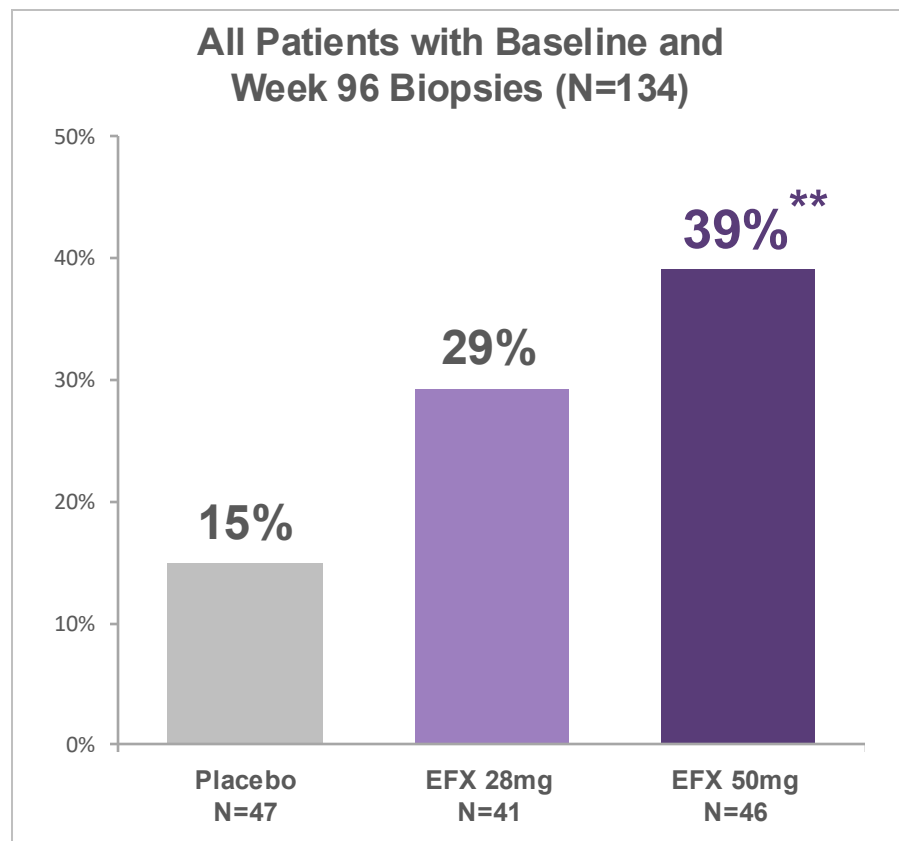
³ Among Week 36 responders with Week 96 biopsies

⁴ Among Week 36 non-responders with Week 96 biopsies

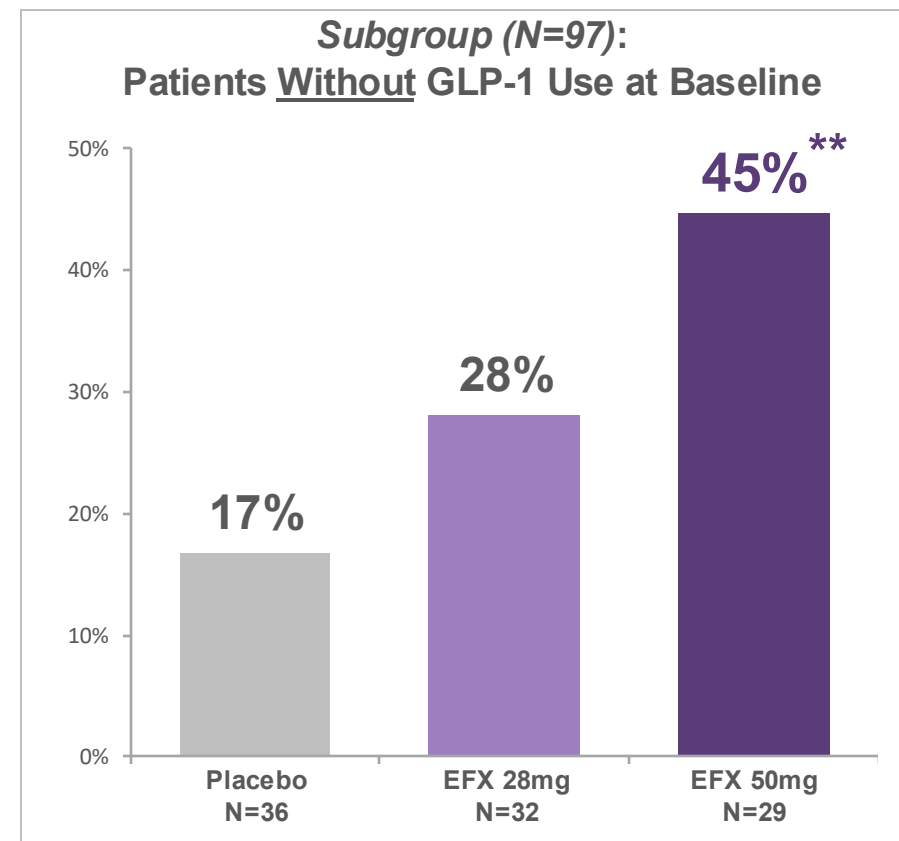
⁵ Not analyzed for statistical significance

» Baseline GLP-1 Therapy Did Not Impact Reversal of Cirrhosis

Fibrosis Improvement ≥ 1 Stage & No Worsening of MASH at Week 96



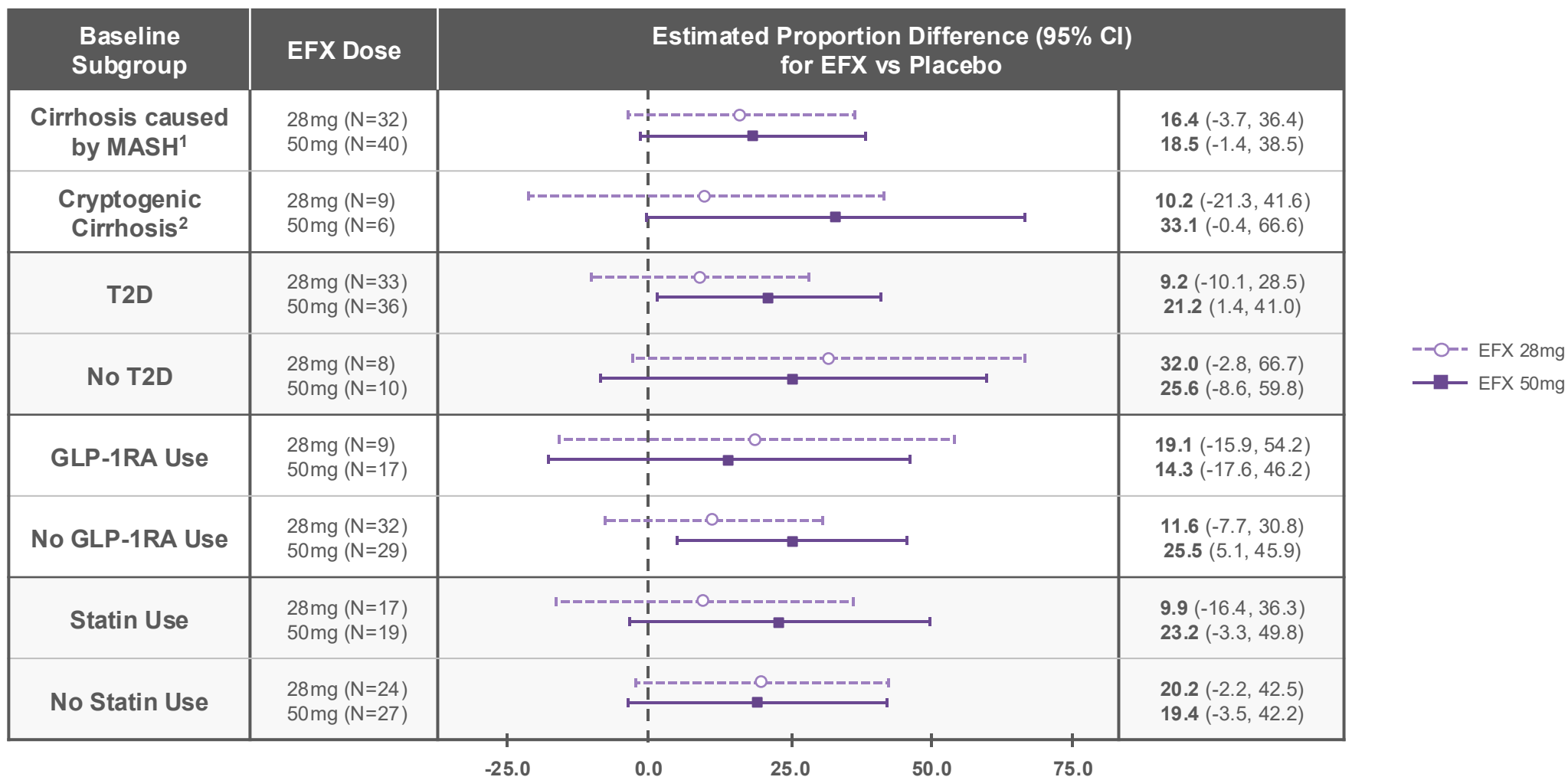
** p<0.01, versus placebo (CMH test)



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



Consistent Response Across Multiple Baseline Subgroups for Primary Histological Endpoint at Week 96

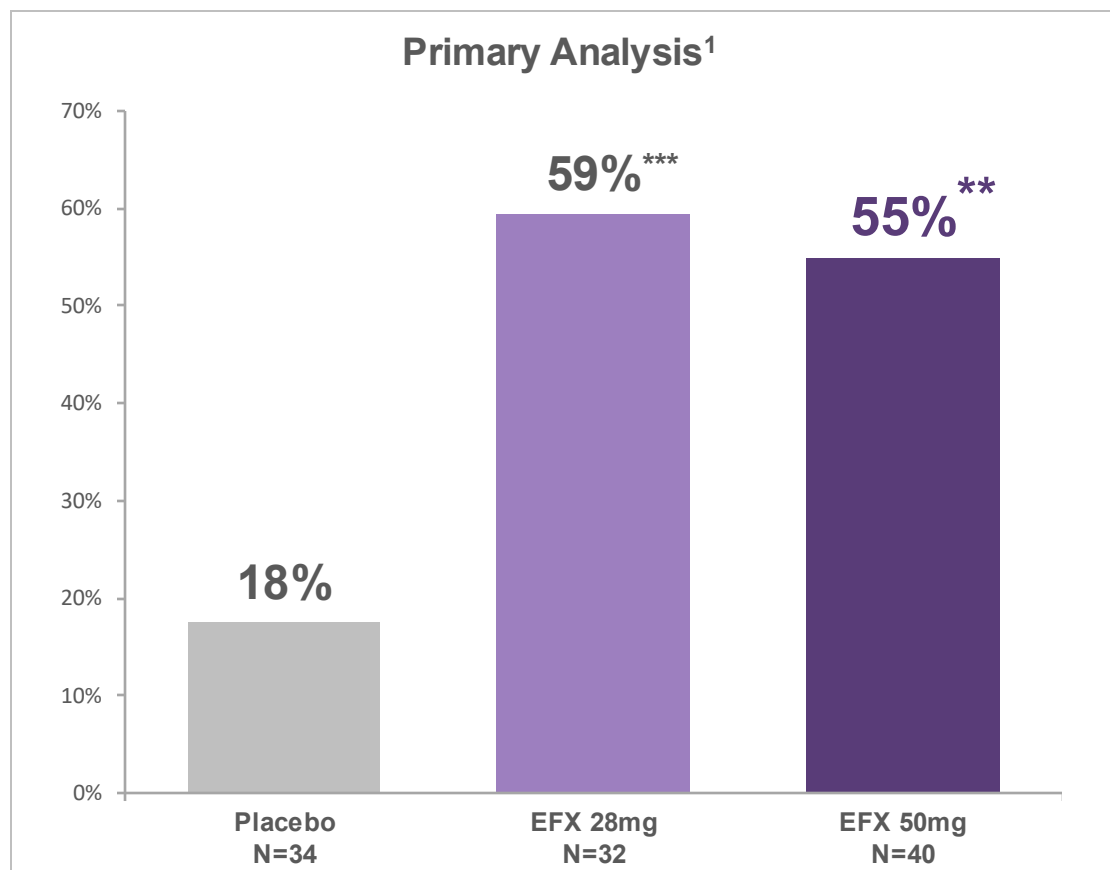


¹ Biopsy-confirmed compensated cirrhosis caused by MASH ("definitive MASH") ² Biopsy-confirmed cryptogenic cirrhosis attributed to MASH

» MASH Resolution Observed at Week 96

MASH Resolution

Primary Analysis¹



¹ All patients with baseline and Week 96 biopsies who had definitive MASH at baseline

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

ITT Analysis²

Placebo (N=45)	EFX 28mg (N=45)	EFX 50mg (N=52)
13%	42%**	42%**

² Missing biopsy = failure

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



Treatment-Emergent Adverse Events (TEAEs): Cumulative from Baseline through Week 96

TEAE Overview	Placebo (N=61)	EFX 28mg (N=57)	EFX 50mg (N=63)
TEAEs Leading to Death	1 (2%) ^a	0 (0%)	0 (0%)
Treatment-Emergent Serious Adverse Events (SAEs)	11 (18%)	15 (26%)	15 (24%)
Drug-Related SAEs	0	0	0
TEAEs Leading to Discontinuation of Treatment	2 (3%)	6 (11%)	11 (18%)
Weeks 37-96: Cirrhosis-Related Clinical Events	0	1 ^b	1 ^c
Weeks 37-96: Other Adverse Events	0	0	1 ^d
Most Frequent (≥15%) Drug-Related TEAEs	Placebo (N=61)	EFX 28mg (N=57)	EFX 50mg (N=63)
Diarrhea, n (%)	10 (16%)	11 (19%)	19 (30%)
Nausea, n (%)	8 (13%)	11 (19%)	18 (29%)
Increased Appetite, n (%)	3 (5%)	7 (12%)	18 (29%)
Injection Site Erythema, n (%)	5 (8%)	10 (18%)	14 (22%)

^a Pneumonia (prior to week 36); ^b Ascites; ^c Hepatic encephalopathy; ^d Diarrhea

Additional Safety Observations for 50mg EFX (Phase 3 Dose) Versus Placebo at Week 96

Bone Mineral Density

- 43% of 50mg EFX and 41% of placebo patients had osteopenia¹ at baseline, but only 3% of 50mg EFX and 7% of placebo patients were treated with bisphosphonates
- Placebo-adjusted, significant relative reductions in bone mineral density (5%) for spine and hip were observed for 50mg EFX, or about 2-3% per year
- For context, treatment with a diabetic dose of GLP-1 was recently reported to be associated with about a 2% reduction in bone mineral density over one year.²
- Equal number of fractures (4 each) observed for 50mg EFX and placebo

¹ T-score < -1.0 by DXA

² M. S. Hansen *et al.*, *eClinicalMedicine*. 72, 102624 (2024)

Electrocardiograms (ECGs), Vital Signs & Body Weight

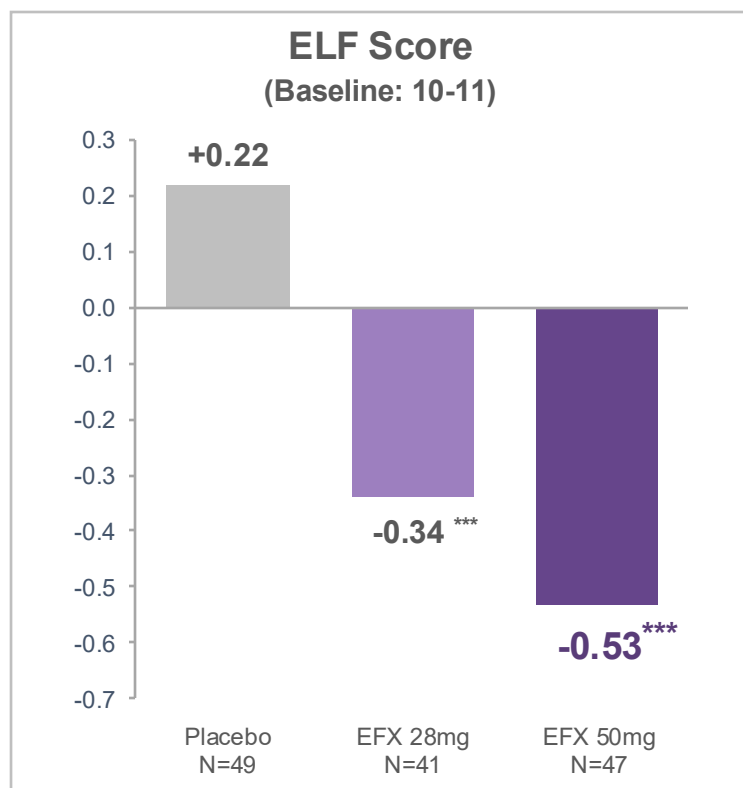
- No statistically significant changes in ECGs, heart rate, or blood pressure were observed for 50mg EFX versus placebo
- Weight reduction of ~2% was observed for 50mg EFX and placebo

Markers of Hemostasis and Liver Function

- Markers of hemostasis and liver function, including bilirubin, MELD score, INR, platelet count, albumin and Child-Pugh score, remained stable or trended toward improvement for 50mg EFX

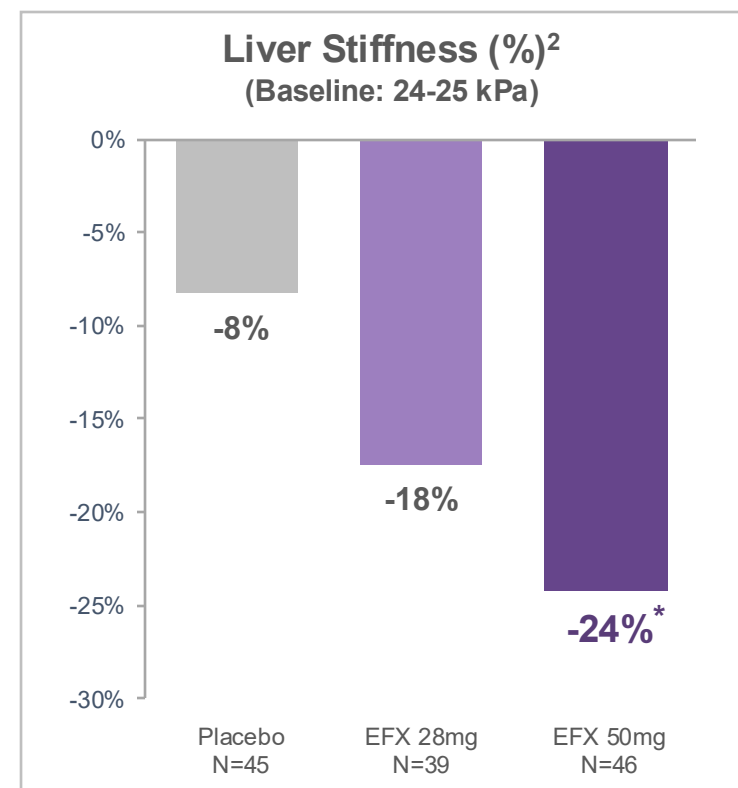
Pattern of Reductions in Imaging and Circulating Biomarkers of Fibrosis **Corroborate** Histological Improvement in Cirrhosis

LS Mean Change From Baseline to Week 96



*** p<0.001, versus placebo (MMRM¹)

¹ Mixed Model Repeated Measures



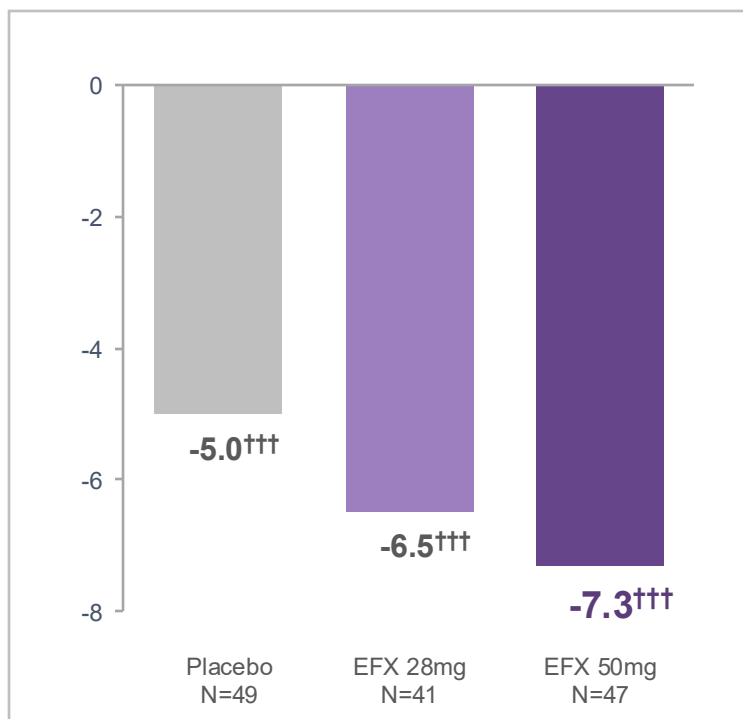
* p<0.05, versus placebo (MMRM¹)

² Measured by FibroScan



Absolute Reduction in **Liver Stiffness** Observed for 50mg EFX is **Largest Reported** to Date

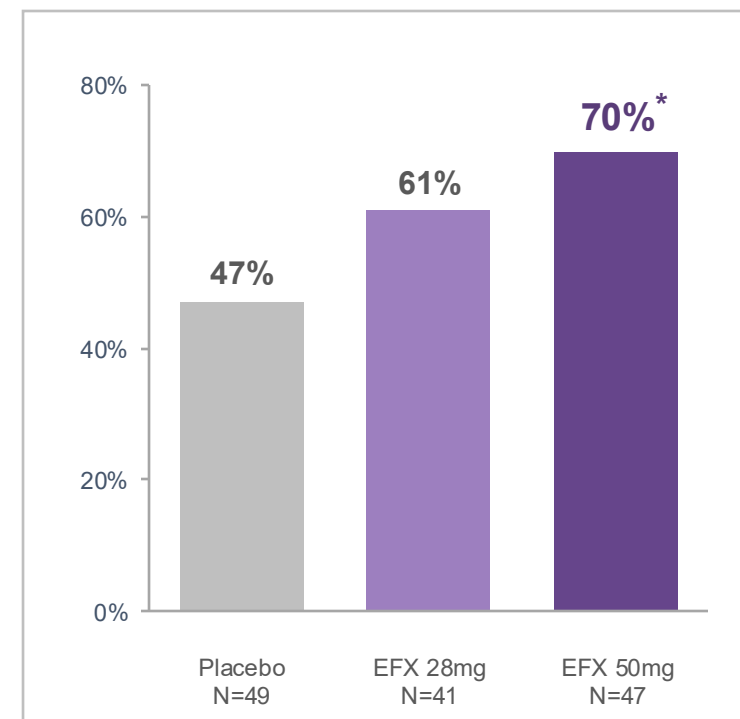
**LS Mean Absolute Change
from Baseline in Liver Stiffness (kPa)¹**



^{†††} p<0.001, versus baseline (MMRM)

¹ Measured by VCTE (FibroScan)

**Proportion of Patients with ≥25% Relative
Reduction in Liver Stiffness¹**



* p<0.05, versus placebo (CMH test)

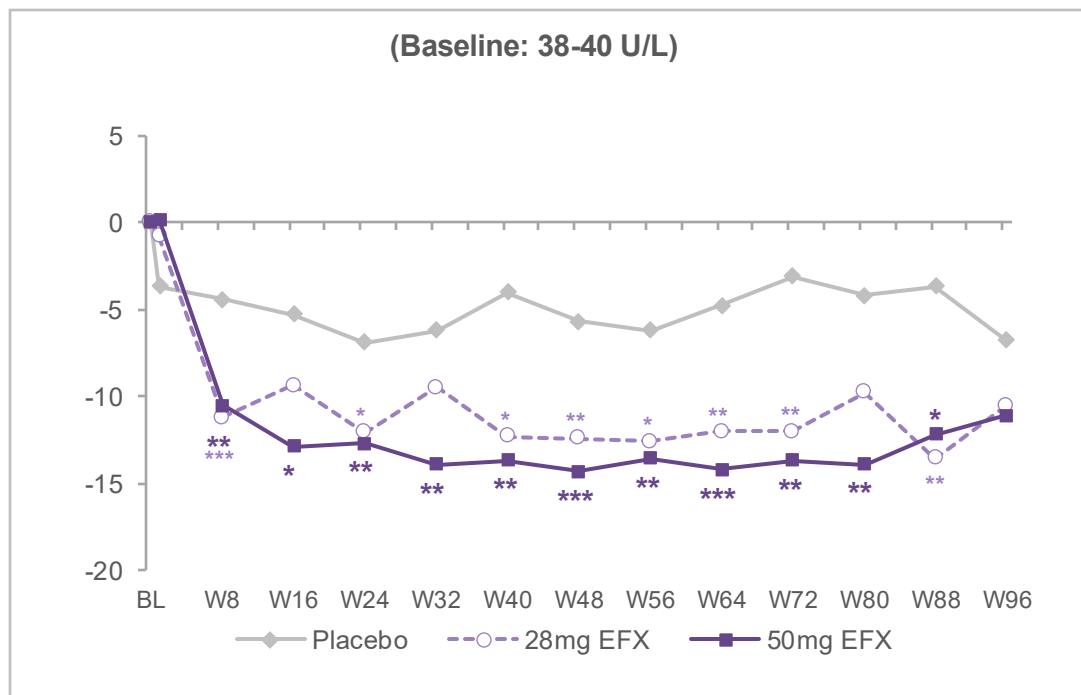
¹ Measured by VCTE (FibroScan)



Statistically Significant Reductions in **Markers of Liver Injury** Sustained Through Week 96 with 50mg EFX

ALT (U/L)
LS Mean Change from Baseline

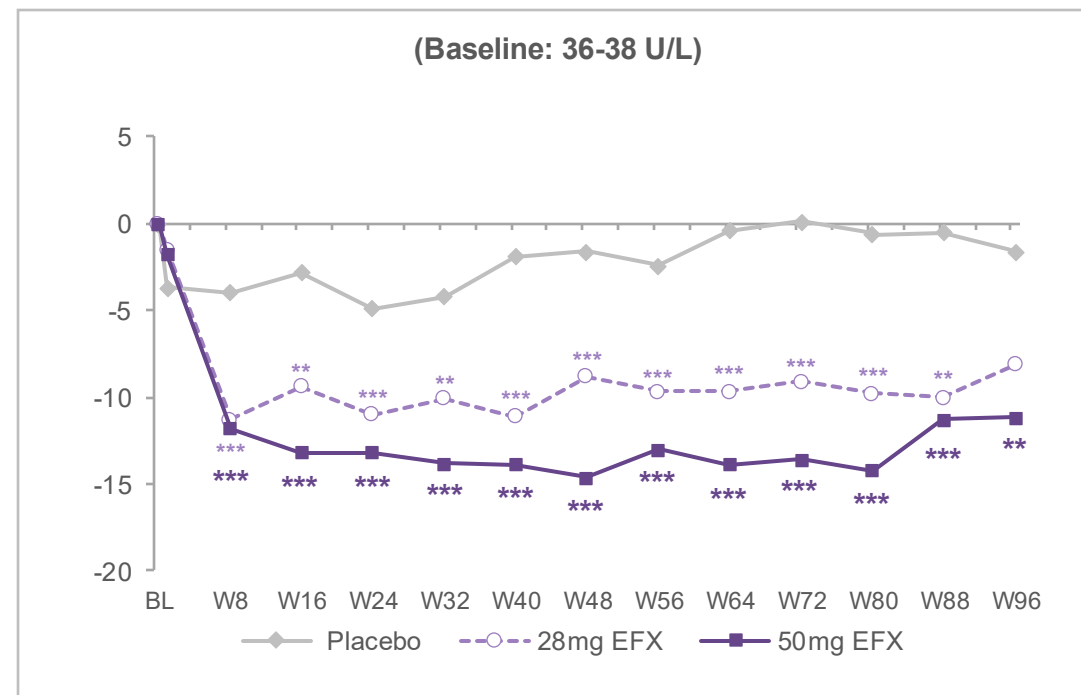
(Baseline: 38-40 U/L)



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

AST (U/L)
LS Mean Change from Baseline

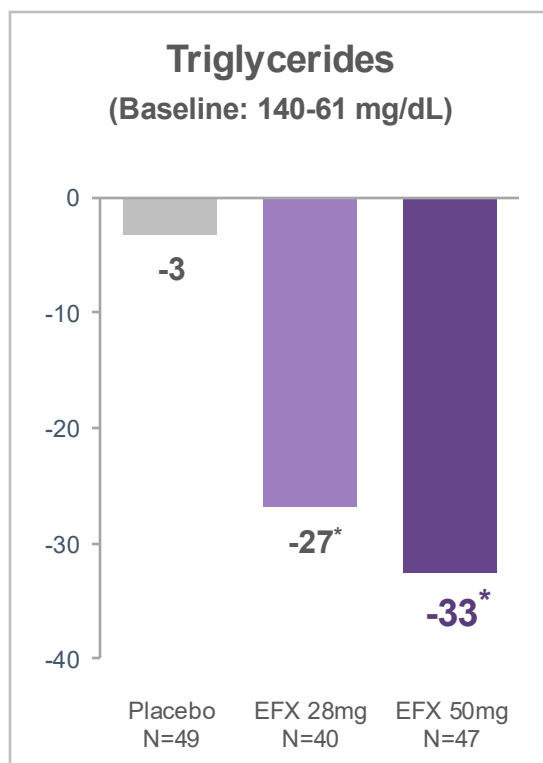
(Baseline: 36-38 U/L)



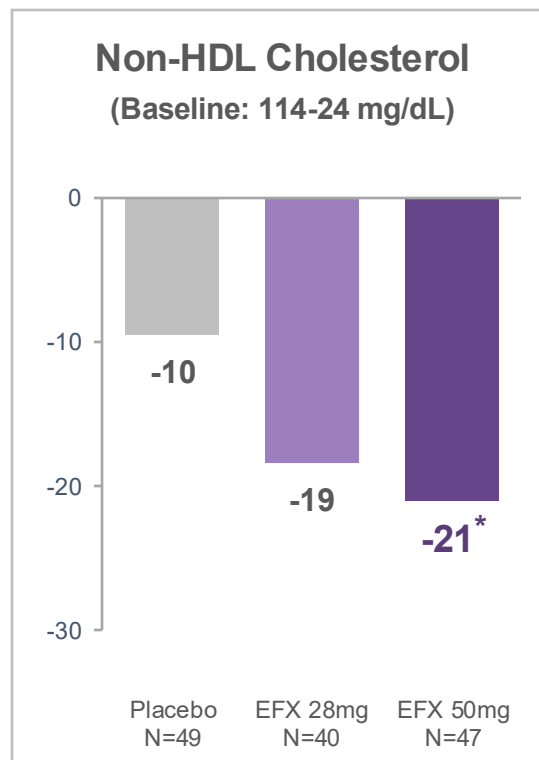
* p<0.05, ** p<0.01, *** p<0.001, versus placebo (MMRM)

» Significantly Improved Lipoprotein Profile Observed at Week 96

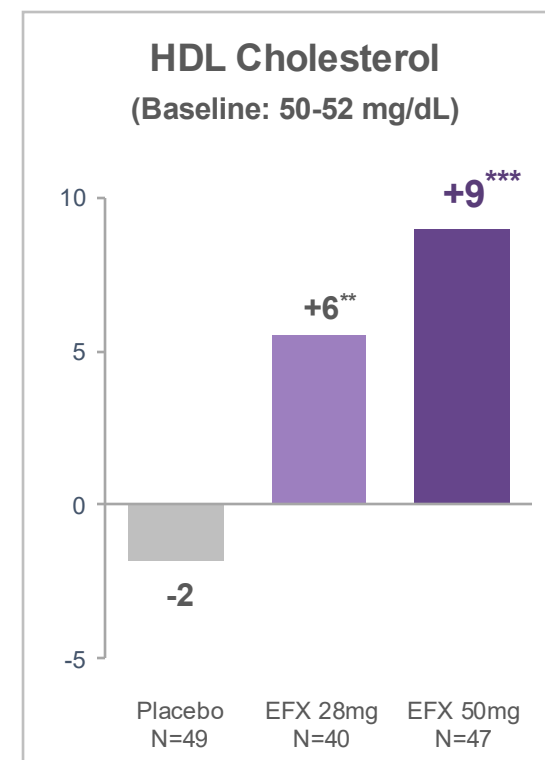
LS Mean Change From Baseline to Week 96 (mg/dL)



* p<0.05, *versus placebo (MMRM)



* p<0.05 versus placebo (MMRM)



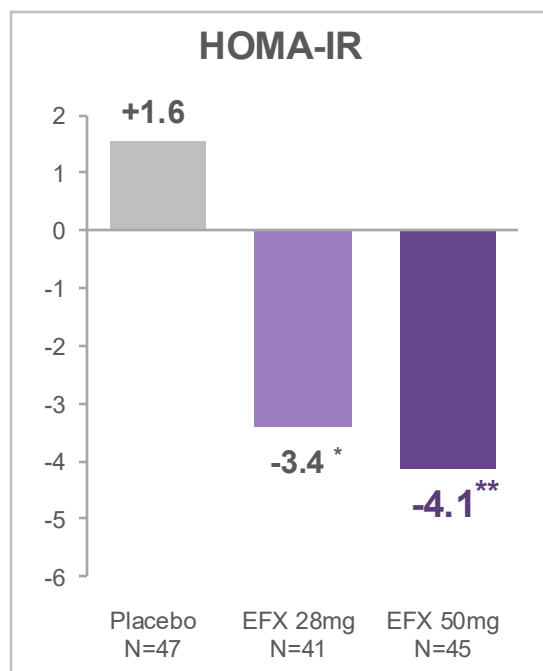
** p<0.01, *** p<0.001, versus placebo (MMRM)

LDL cholesterol was reduced by 11% and 9%, respectively, in the 50mg EFX and placebo groups

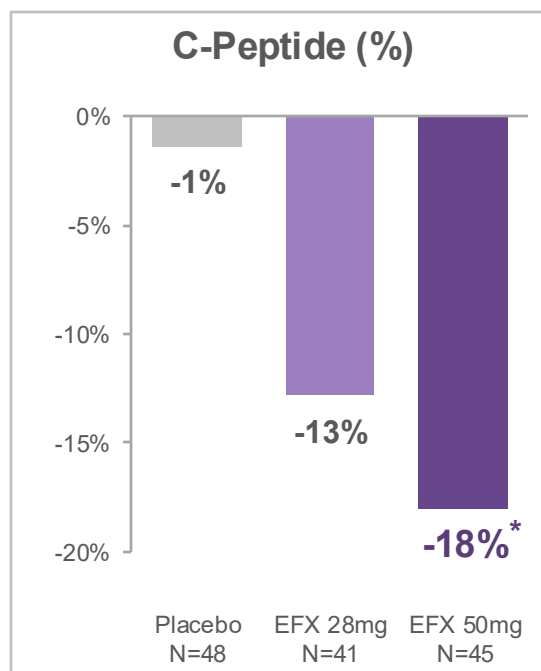


Significantly Improved **Insulin Sensitivity** Observed at Week 96 with 50mg EFX

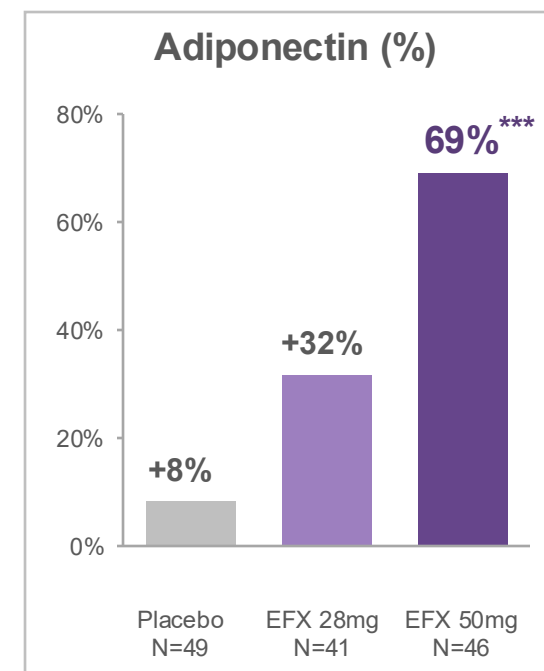
LS Mean Change From Baseline to Week 96



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



* p<0.05, versus placebo (MMRM)

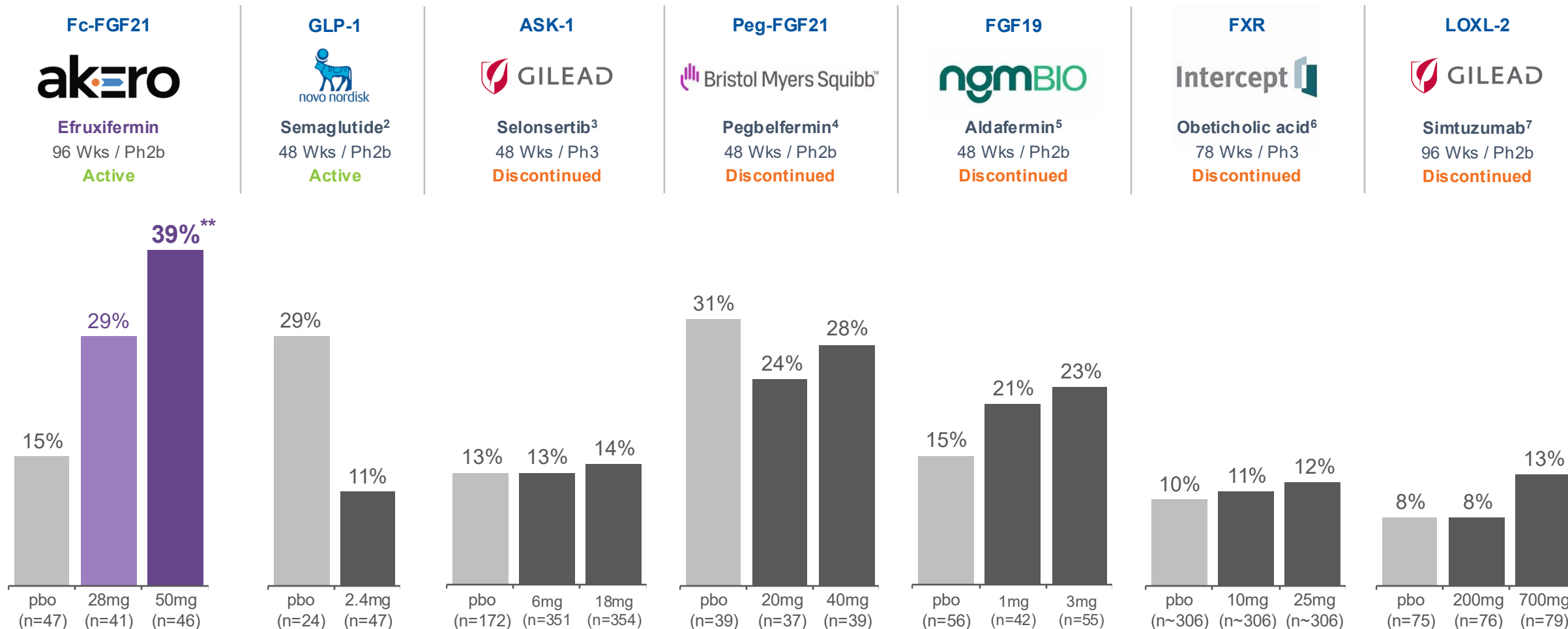


*** p<0.001, versus placebo (MMRM)

At Week 96, HbA1c remained unchanged from baseline for 50mg EFX, compared to a slight increase to 7.0 for placebo.



EFX is the **First Compound** that Has Been Reported to Statistically Significantly Reverse Cirrhosis Due to MASH¹



¹ Includes results from publicly reported placebo-controlled studies in patients with compensated cirrhosis due to MASH reporting either $\geq$ 1-stage fibrosis improvement and no worsening of MASH (EFX, semaglutide, selonsertib, pegbelfermin, obeticholic acid) or only $\geq$ 1-stage fibrosis improvement (aldafermin, simtuzumab); numerical values represent percent responders. ² Loomba, R et al. (2023) Lancet Gastro Hep 8:511-22; ³ Harrison, SH et al. (2020) J Hepatol 73(1):26-39; ⁴ Abdelmalek, MF et al. (2023) Clinical Gastro Hep 23:S1542-3565; ⁵ NGM Bio (2023) September Corporate Overview; ⁶ Intercept (2022) September 30 Press Release; ⁷ 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. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.

Completers

39% vs. 15%
(24% Effect Size)

p=0.009

**Reversal of
Cirrhosis in
<2 Years**

ITT

29% vs. 12%
(17% Effect Size)

p=0.031

With Favorable Tolerability Profile

ORIGINAL ARTICLE

Efruxifermin in Compensated Liver Cirrhosis Caused by MASH

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Mark Burch, Ph.D.,¹⁰ Doreen C. Chan, Ph.D.,¹⁰ Erik J. Tillman, Ph.D.,¹⁰
Arian Zari, B.S.,¹⁰ Brittany de Temple, B.S.,¹⁰ Reshma Shringarpure, Ph.D.,¹⁰
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HARMONY

STATISTICALLY SIGNIFICANT EFFECTS AFTER 96 WEEKS

1-STAGE
FIBROSIS
IMPROVEMENT

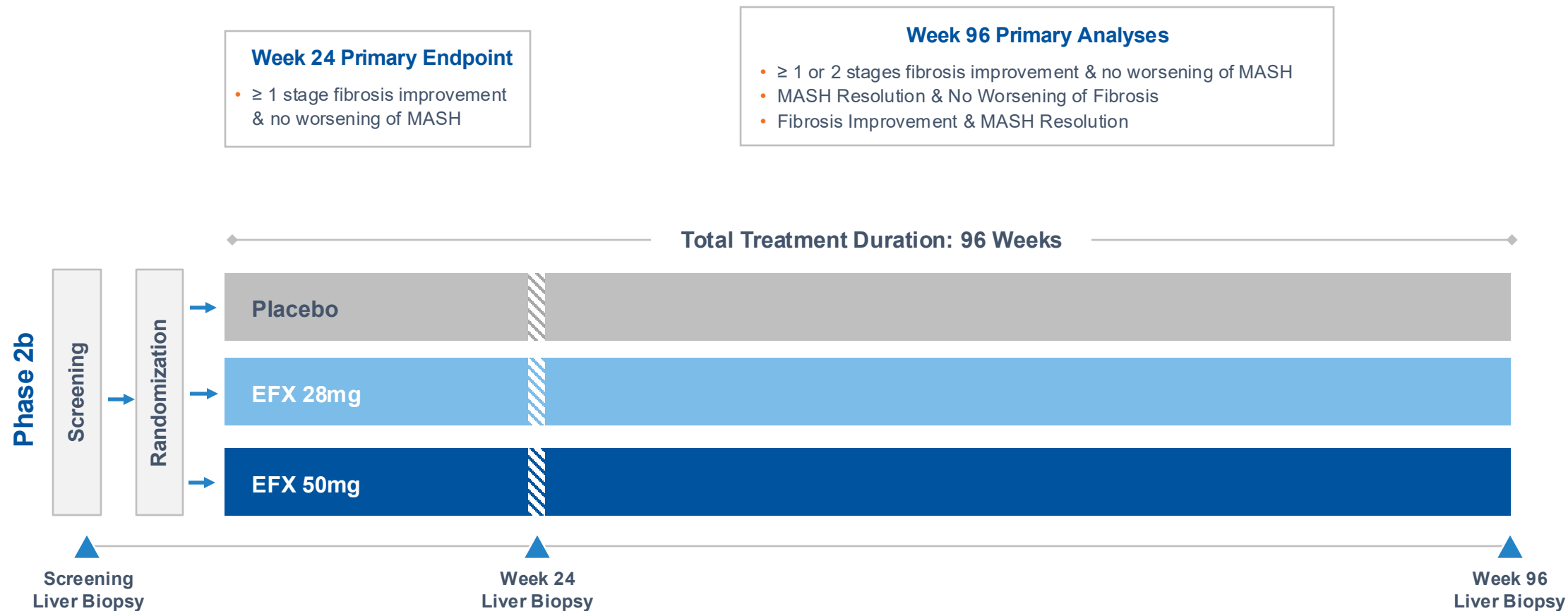
2-STAGE
FIBROSIS
IMPROVEMENT

FIBROSIS IMPROVEMENT
AND
MASH RESOLUTION

MASH
RESOLUTION



HARMONY Trial Design: Pre-Cirrhotic (F2-F3) MASH with Liver Histology at 24 and 96 weeks



Analysis Set	N	Description
Full Analysis Set	128	All randomized subjects
Safety Set / Modified Full Analysis Set (ITT) Placebo (N=43) 28mg (N=40) 50mg (N=43)	126	All randomized and dosed subjects ¹
Week 24 Liver Biopsy Analysis Set Placebo (N=41) 28mg (N=38) 50mg (N=34)	113	All subjects with baseline and Week 24 biopsy results
Week 96 Liver Biopsy Analysis Set Placebo (N=34) 28mg (N=26) 50mg (N=28)	88	All subjects with completed second on-study biopsy

¹ The Modified Full Analysis Set includes subjects that were randomized and received at least one dose of study drug per the Statistical Analysis Plan.

Parameter (Units)	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) (GEN 2 ELISA)	125	113	145
Liver Stiffness by VCTE ³ (FibroScan) (kPa)	15	14	16
Hepatic Fat Fraction by MRI-PDFF ⁴ (%)	17.1	18.5	17.5
MASLD Activity Score (MAS)	5.4	5.1	5.6
Alanine Aminotransferase (ALT) (U/L)	62	50	63
Aspartate Aminotransferase (AST) (U/L)	57	42	52

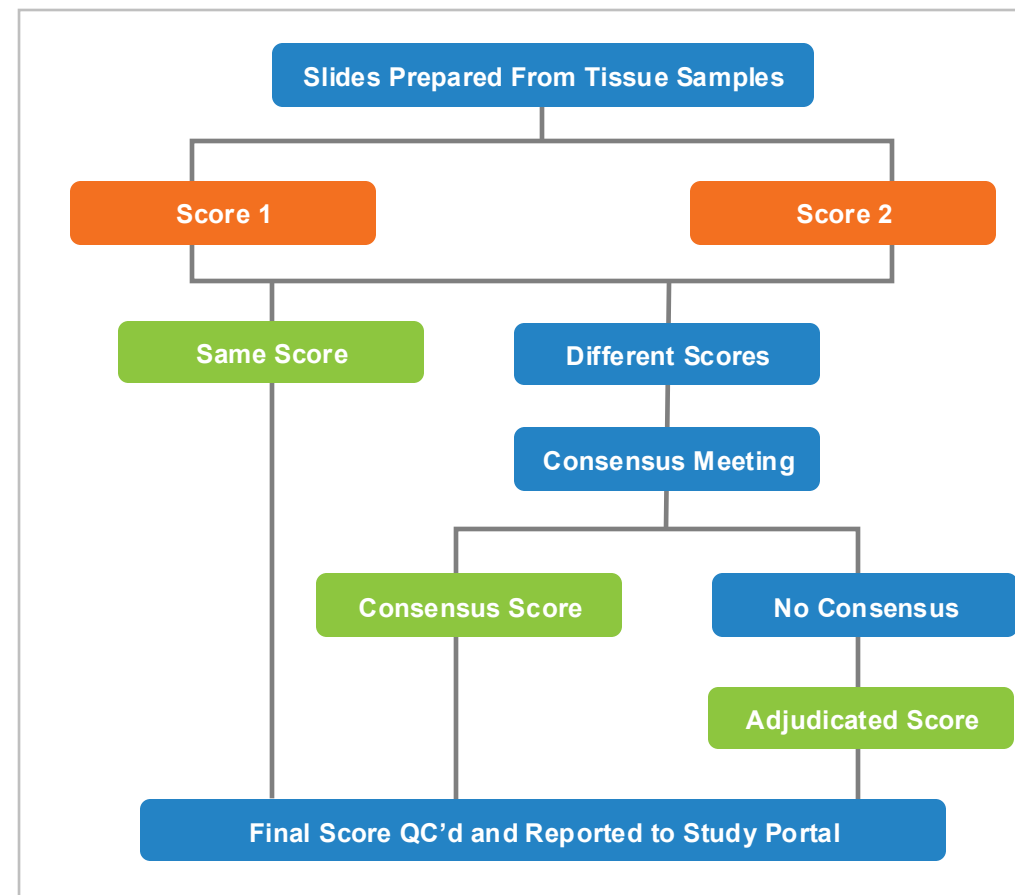
¹ All patients either fibrosis stage 2 (F2) or stage 3 (F3); ² Procollagen 3 N-Terminal Propeptide; ³ Vibration-controlled transient elastography; ⁴ Magnetic Resonance Imaging Proton Density Fat Fraction

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 MASH-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)

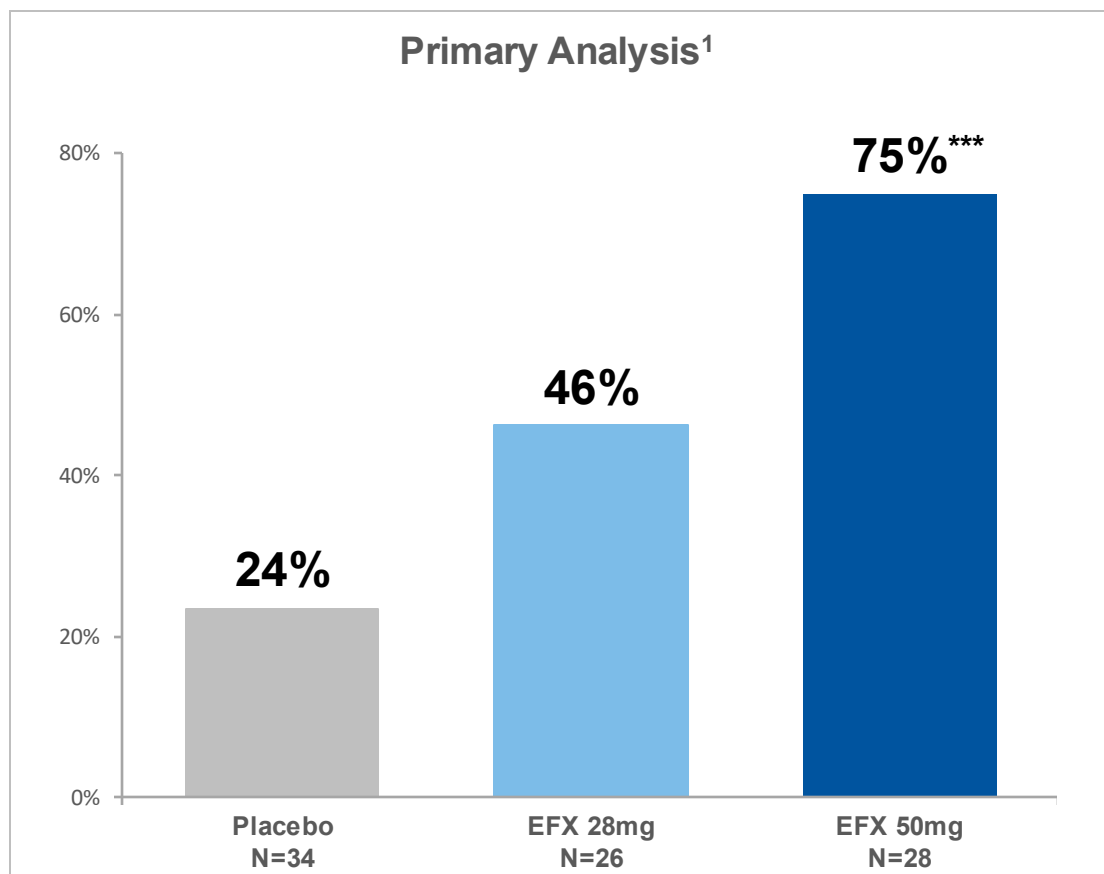
Consensus Biopsy Analysis Flow Chart





≥1 Stage Fibrosis Improvement & No Worsening of MASH: Statistically Significant Response Observed for 50mg EFX at Week 96

Fibrosis Improvement ≥1 Stage & No Worsening of MASH at Week 96



¹ All subjects with baseline and Week 96 biopsies

*** p<0.001, versus placebo
(Cochran-Mantel-Haenszel Test [CMH])

ITT Analysis²

Placebo (N=43)	EFX 28mg (N=40)	EFX 50mg (N=43)
19%	30%	49%**

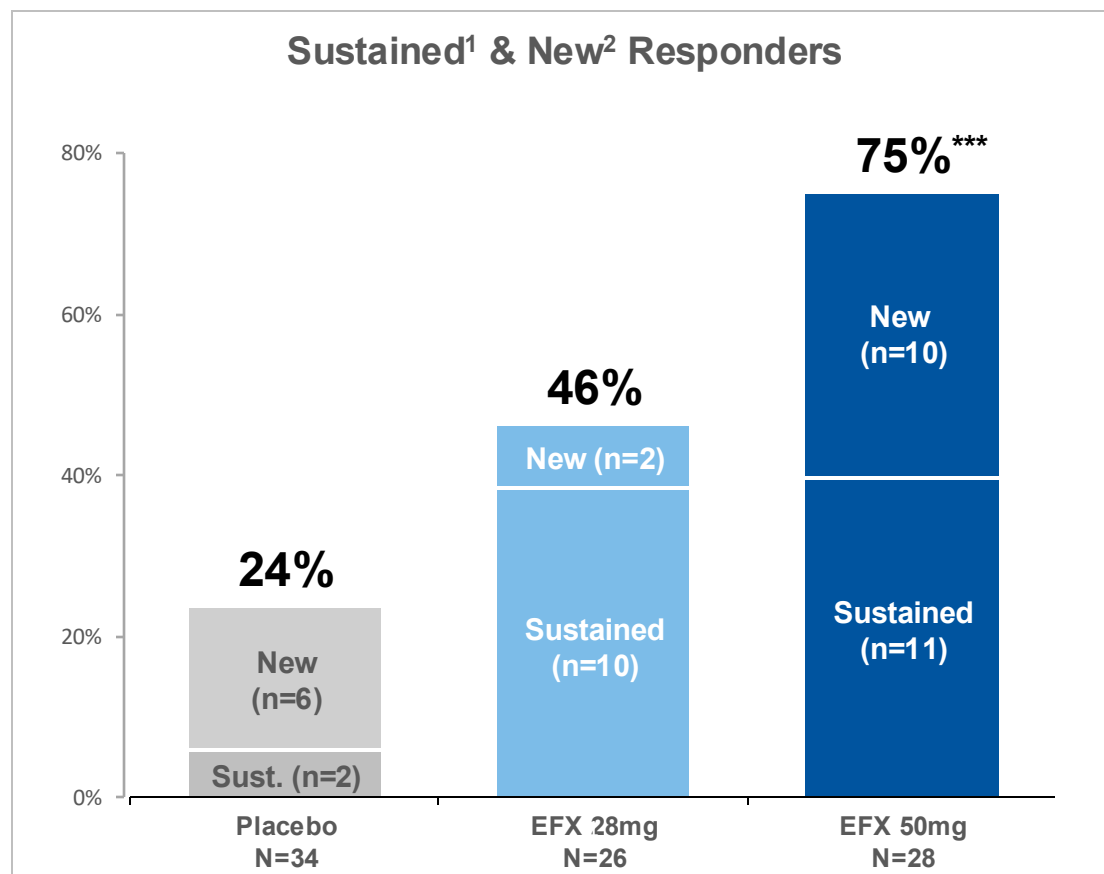
² All missing biopsies are imputed as a non-responder

** p<0.01, versus placebo (CMH)



≥1 Stage Fibrosis Improvement & No Worsening of MASH: Sustained, Broad and Durable Response

Fibrosis Improvement ≥1 Stage & No Worsening of MASH at Week 96



¹ Responder at Weeks 24 & 96; ² Responder at Week 96

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

Proportion of Week 24 Responders with Sustained Response at Week 96^{3,5}

Placebo (N=5)	EFX 28mg (N=12)	EFX 50mg (N=12)
2 (40%)	10 (83%)	11 (92%)

Proportion of Week 24 Non-Responders with New Response at Week 96^{4,5}

Placebo (N=29)	EFX 28mg (N=14)	EFX 50mg (N=16)
6 (21%)	2 (14%)	10 (63%)

³ Among Week 24 responders with Week 96 biopsies

⁴ Among Week 24 non-responders with Week 96 biopsies

⁵ Not analyzed for statistical significance

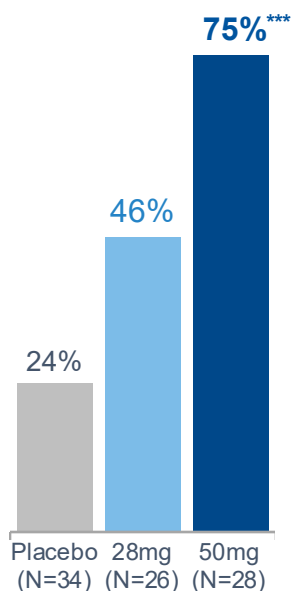


EFX Fibrosis Improvement in Context: Pre-Cirrhotic MASH: ≥1 Stage Improvement in Fibrosis & No Worsening of MASH



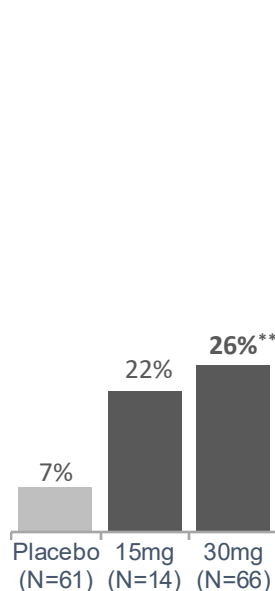
Efruxifermin

Phase 2b (F2-F3)
96 Wks / 66% F3
Consensus Reading
Completers⁷



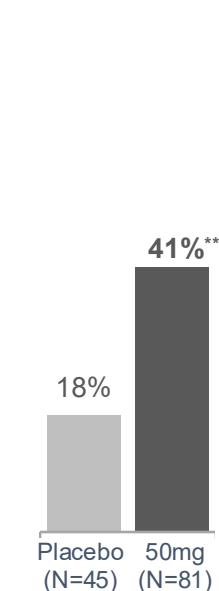
Pegozafermin¹

Phase 2b (F2-F3)
24 Wks / 65% F3
Algorithmic Scoring
Completers⁷



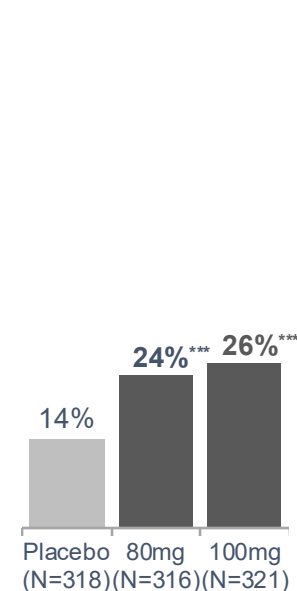
Denifanstat²

Phase 2b (F2-F3)
52 Wks / 58% F3
Single Pathologist
Completers⁷



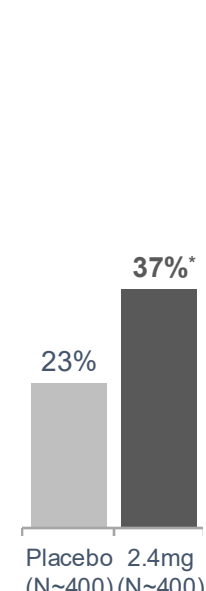
Rezdiffra³

Phase 3 (F1-F3)
52 Wks / 62% F3
Statistically Combined
ITT⁸



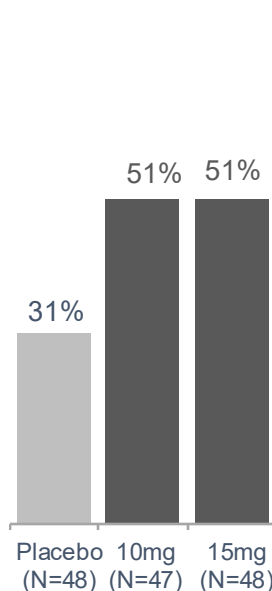
Semaglutide⁴

Phase 3 (F2-F3)
72 Wks / ?% F3
Consensus Reading
ITT¹⁰



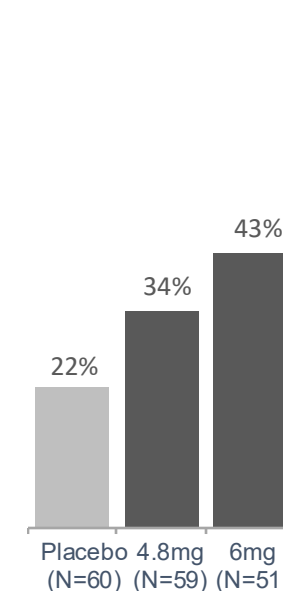
Tirzepatide⁵

Ph2b (F2-F3)
52 Wks / 57% F3
Consensus Reading
ITT¹¹



Survodutide⁶

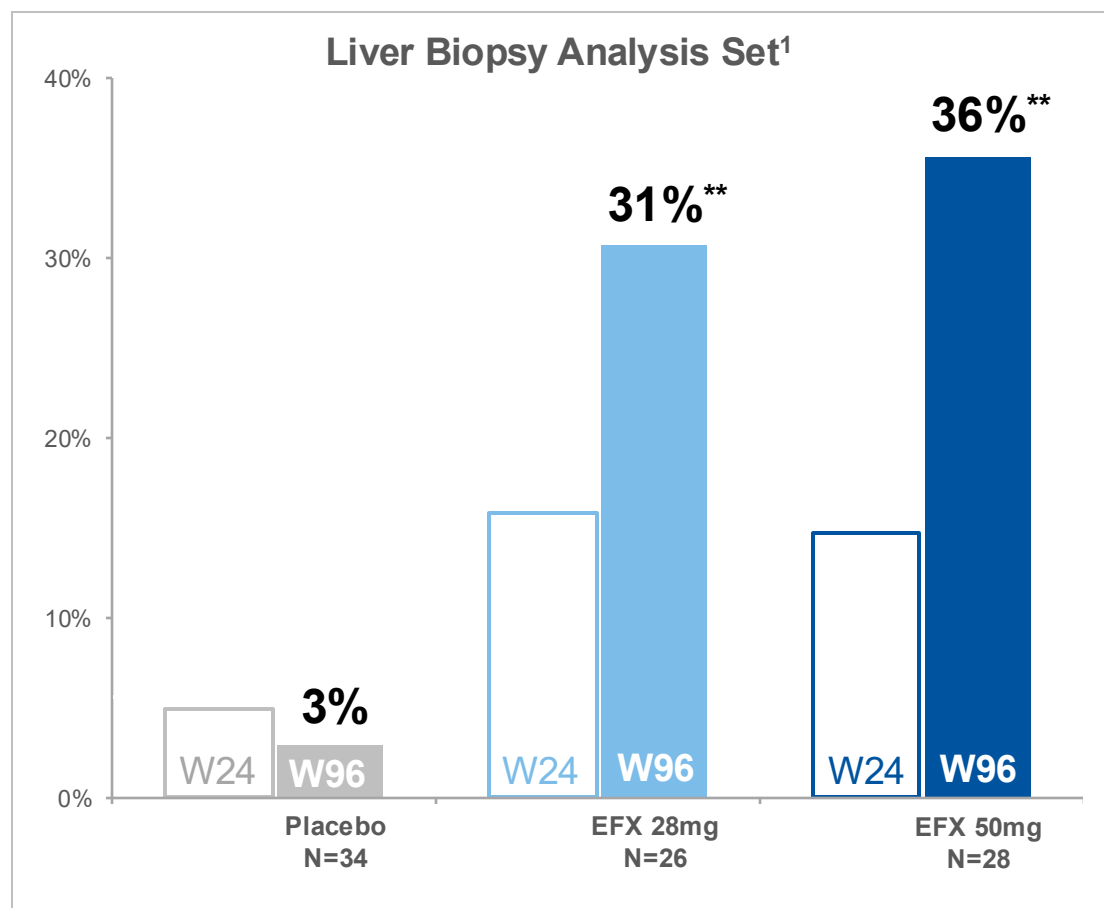
Ph 2b (F2-F3⁵)
48 Wks / 46% F3
Single Pathologist
ITT^{8,9}



¹ 89Bio (2023) Mar 22 Corp Pres; ² Sagimet (2024) Aug Corp Pres; ³ Madrigal (2022) Dec 19 Press Rel; ⁴ Novo Nordisk (2024) Nov 1 Press Rel; ⁵ Loomba et al. (2024) New Engl J Med 391, 299-310; ⁶ Sanyal et al. (2024) New Engl J Med 391, 311-9; ⁷ Baseline and end-of-study biopsies available; ⁸ Missing biopsies (or ⁹ failure to reach target dose) imputed as non-responders; ¹⁰ Based on treatment policy estimand: treatment effect regardless of treatment adherence; ¹¹ Missing biopsies imputed assuming they follow the pattern of the placebo group. All trademarks are the property of their respective owners. * p<0.05, ** p<0.01, *** p<0.001, versus placebo (CMH). 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.

» Rate of 2-Stage Fibrosis Improvement Doubled from Week 24 to 96

Fibrosis Improvement 2 Stages & No Worsening of MASH, Weeks 24 and 96



Week 96 ITT Analysis²

Placebo (N=43)	EFX 28mg (N=40)	EFX 50mg (N=43)
2%	20%**	23%**

² Subjects with missing biopsies are imputed as non-responders

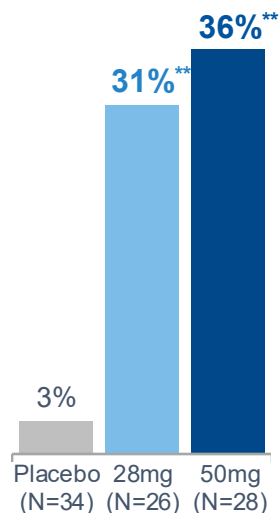
** p<0.01, versus placebo (CMH)



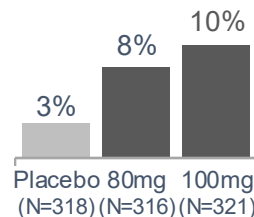
EFX Fibrosis Improvement in Context: Pre-Cirrhotic MASH: ≥2 Stage Improvement in Fibrosis & No Worsening of MASH



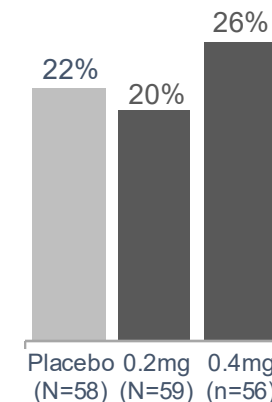
akero
Efruxifermin
Phase 2b (F2-F3)
96 Wks / 66% F3
Consensus Readers
Completers¹




Resmetirom
Phase 3 (F1-F3)
52 Wks / 62% F3
Two Readers
ITT²




Semaglutide
Phase 2b (F2-F3)
72 Wks / 69% F3
Consensus Readers
ITT²



Fibrosis Improvement Only
(Worsening of MASH Not
Reported)

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.

** p<0.01, versus placebo (CMH)

¹ Baseline and end-of-study biopsies available; ² Missing biopsies imputed as non-responders
Resmetirom – Madrigal (2022) December 19 Press Release; Semaglutide - Newsome et al. (2021) New Engl J Med 384, 1113-24

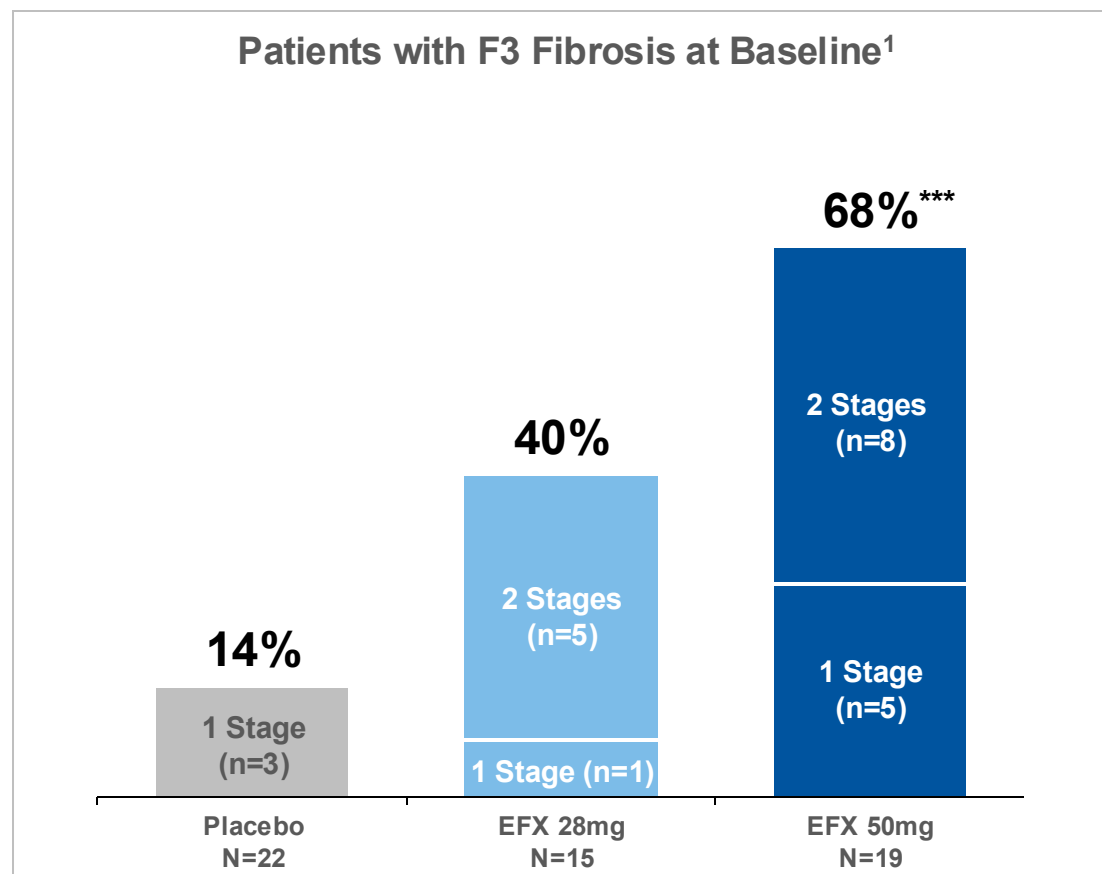
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≥1 Stage Fibrosis Improvement & No Worsening of MASH: Statistically Significant Response **Among F3 Patients** Observed for 50mg EFX

Fibrosis Improvement ≥1 Stage & No Worsening of MASH at Week 96

Patients with F3 Fibrosis at Baseline¹

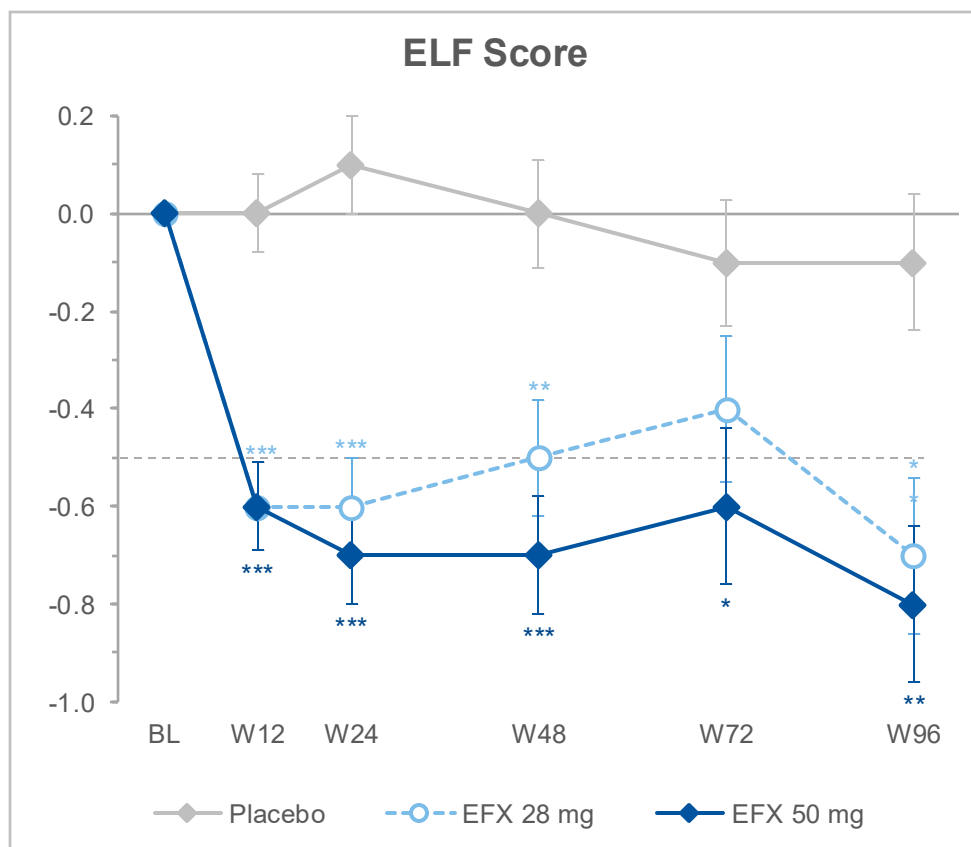


*** p<0.001, versus placebo (CMH)

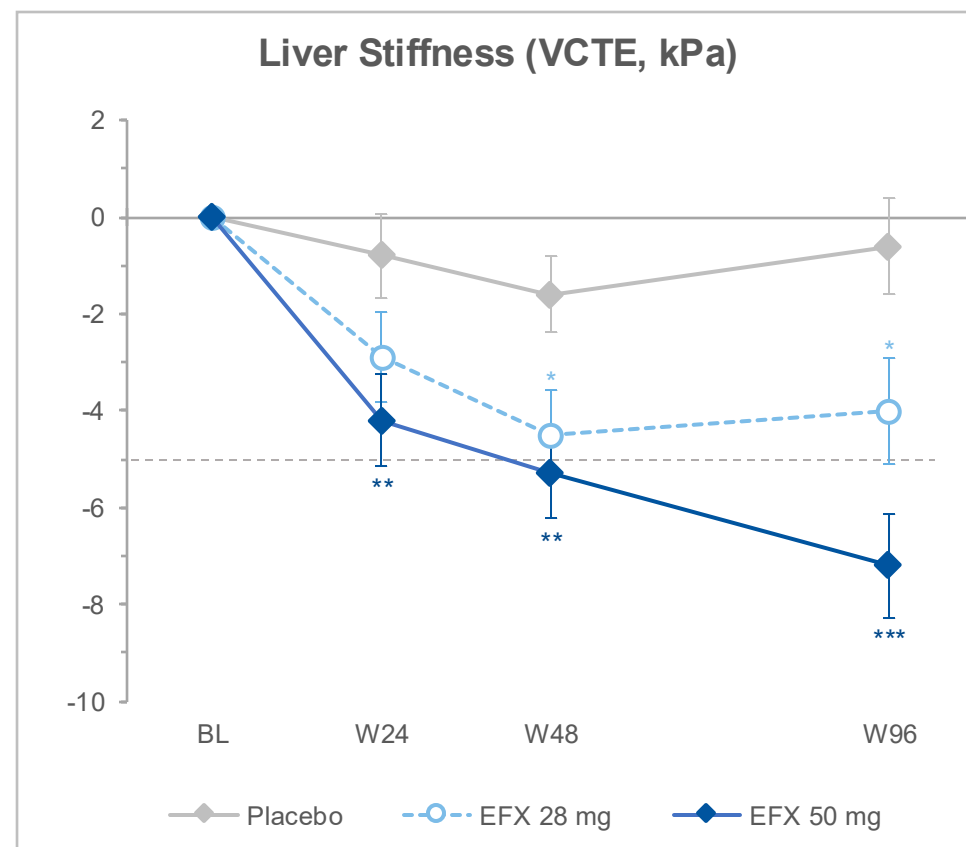


Pattern of Reductions in Imaging and Circulating Biomarkers of Fibrosis Corroborate Histological Improvement in Fibrosis

LS Mean (SE) Absolute Change From Baseline to Week 96



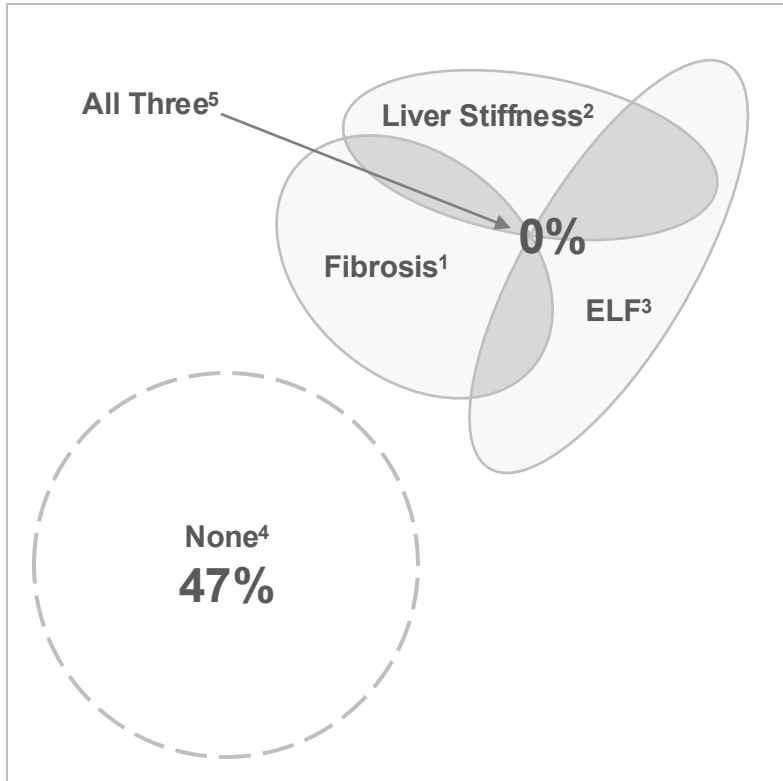
*p<0.05, **p<0.01, ***p<0.001 versus placebo (MMRM)



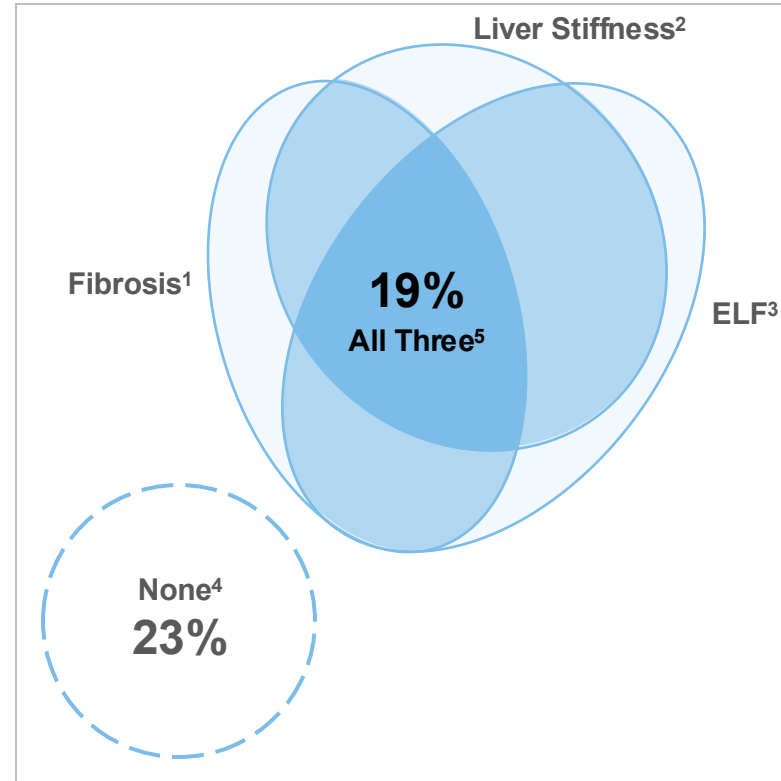
*p<0.05, **p<0.01, ***p<0.001 versus placebo (MMRM)

» Overlap of Imaging and Circulating Biomarkers of Fibrosis at 96 Weeks Corroborate Conventional Histopathology only in EFX-treated Individuals

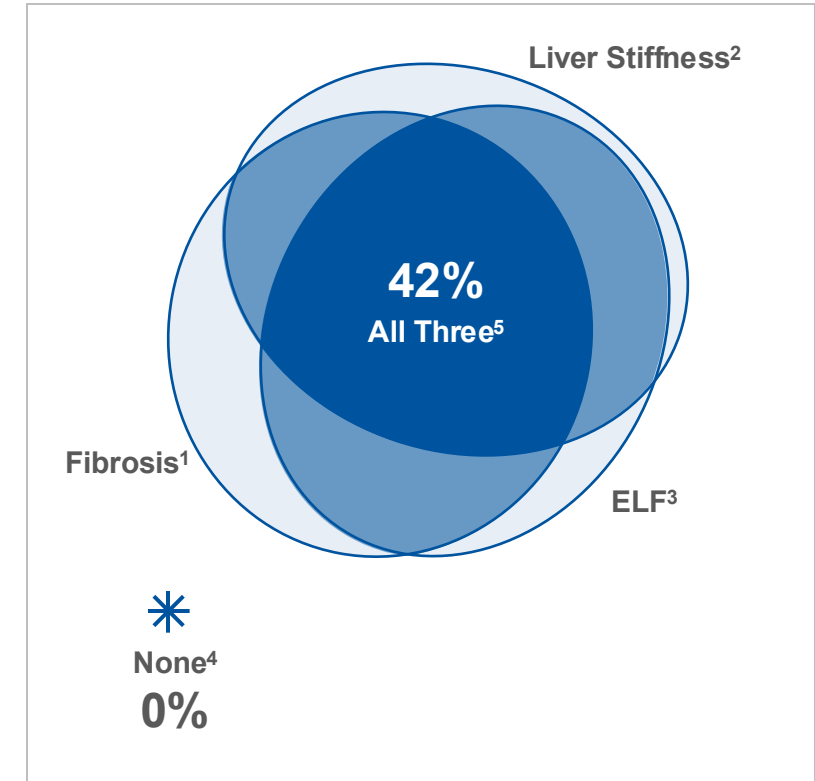
Placebo (N=32)



EFX 28 mg (N=26)



EFX 50 mg (N=24)



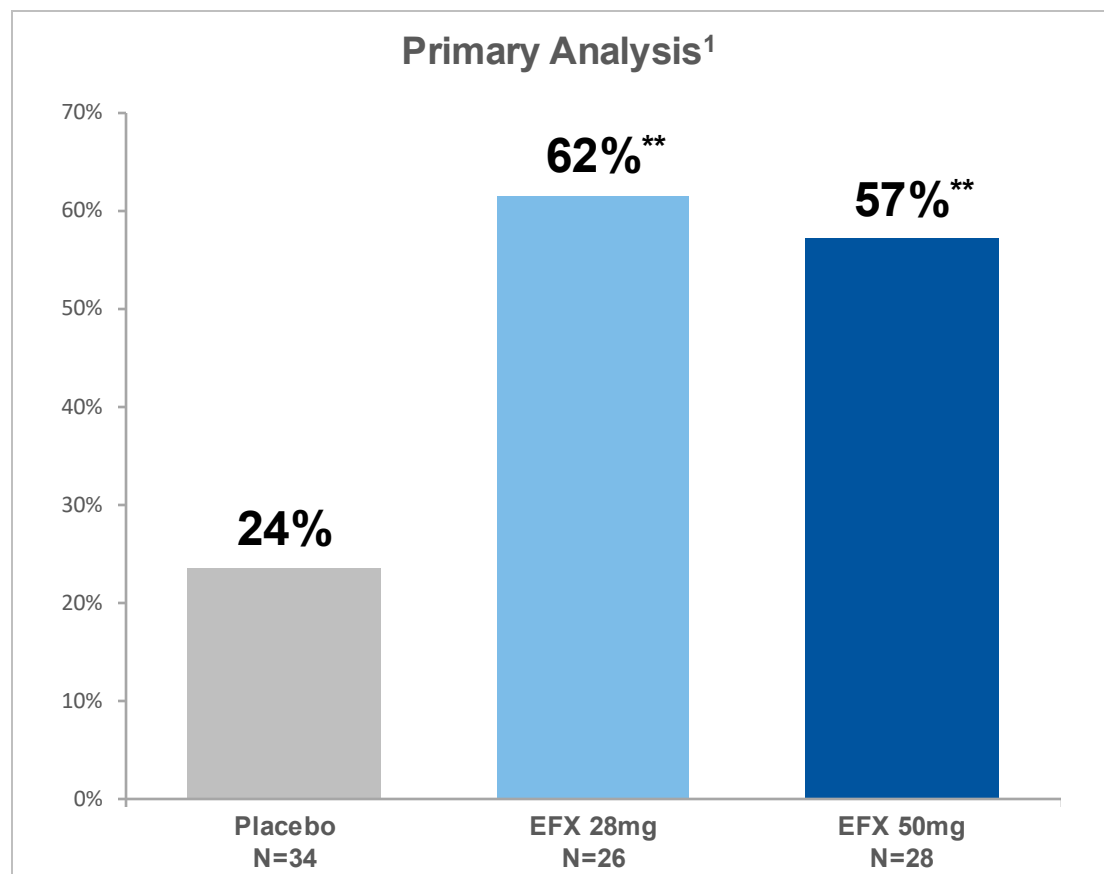
¹ Proportion with **histological fibrosis response** (improvement ≥ 1 stage without MASH worsening); ² Proportion with **liver stiffness response** ($\geq 30\%$ reduction by FibroScan [VCTE]); ³ Proportion with **ELF response** (≥ 0.5 reduction in ELF Score); ⁴ None: Proportion without any of fibrosis improvement, liver stiffness response, or ELF response; ⁵ All Three: proportion with fibrosis improvement, liver stiffness response, and ELF response



MASH Resolution & No Worsening of Fibrosis:

Statistically Significant Response Observed for Both EFX Groups

MASH Resolution & No Worsening of Fibrosis at Week 96



¹ All subjects with baseline and Week 96 biopsies

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

ITT Analysis²

Placebo (N=43)	EFX 28mg (N=40)	EFX 50mg (N=43)
19%	40%*	37%*

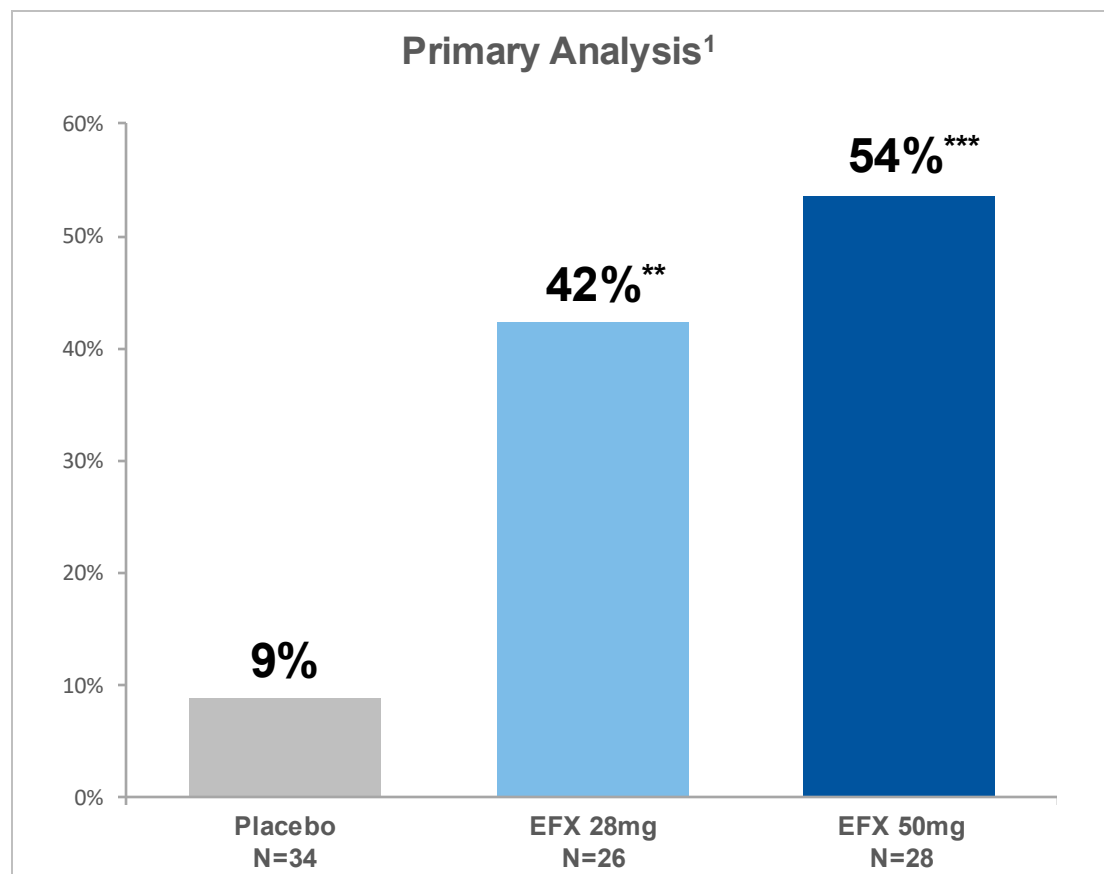
² Subjects with missing biopsies are imputed as non-responders

* p<0.05, versus placebo (CMH test)



≥1 Stage Fibrosis Improvement AND MASH Resolution: Statistically Significant Response Observed for Both EFX Groups

Fibrosis Improvement ≥1 Stage AND MASH Resolution at Week 96



¹ All subjects with baseline and Week 96 biopsies

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

ITT Analysis²

Placebo (N=43)	EFX 28mg (N=40)	EFX 50mg (N=43)
7%	28%**	35%**

² Subjects with missing biopsies are imputed as non-responders

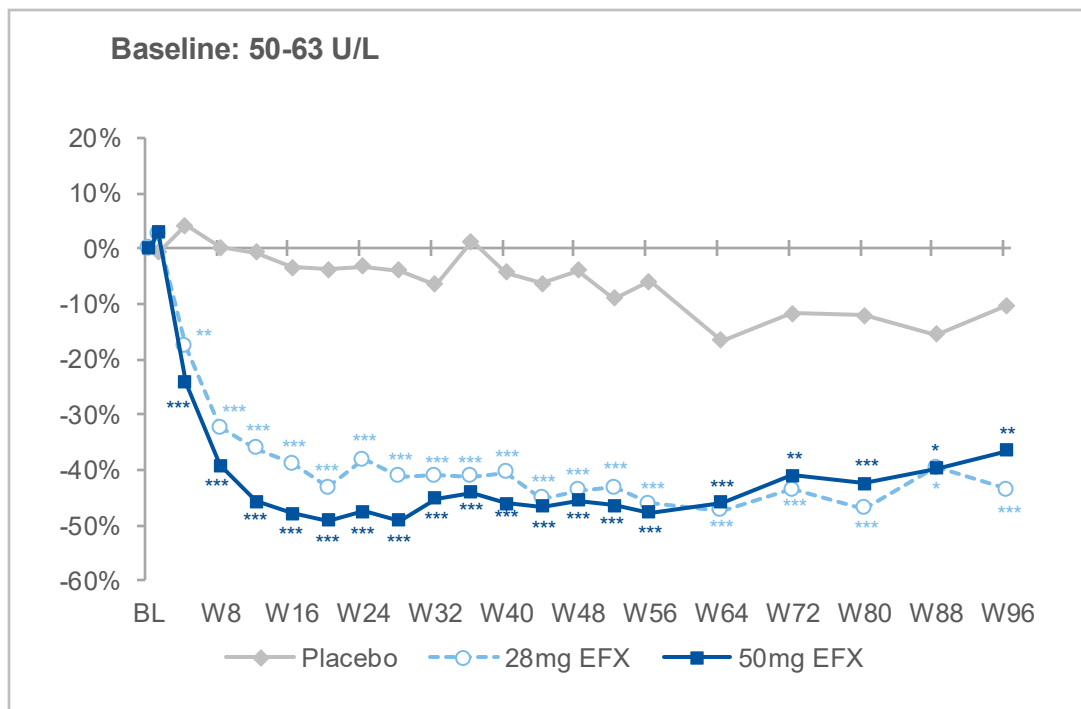
** p<0.01, versus placebo (CMH)



Statistically Significant Improvements in Markers of Liver Injury Sustained Through Week 96

ALT

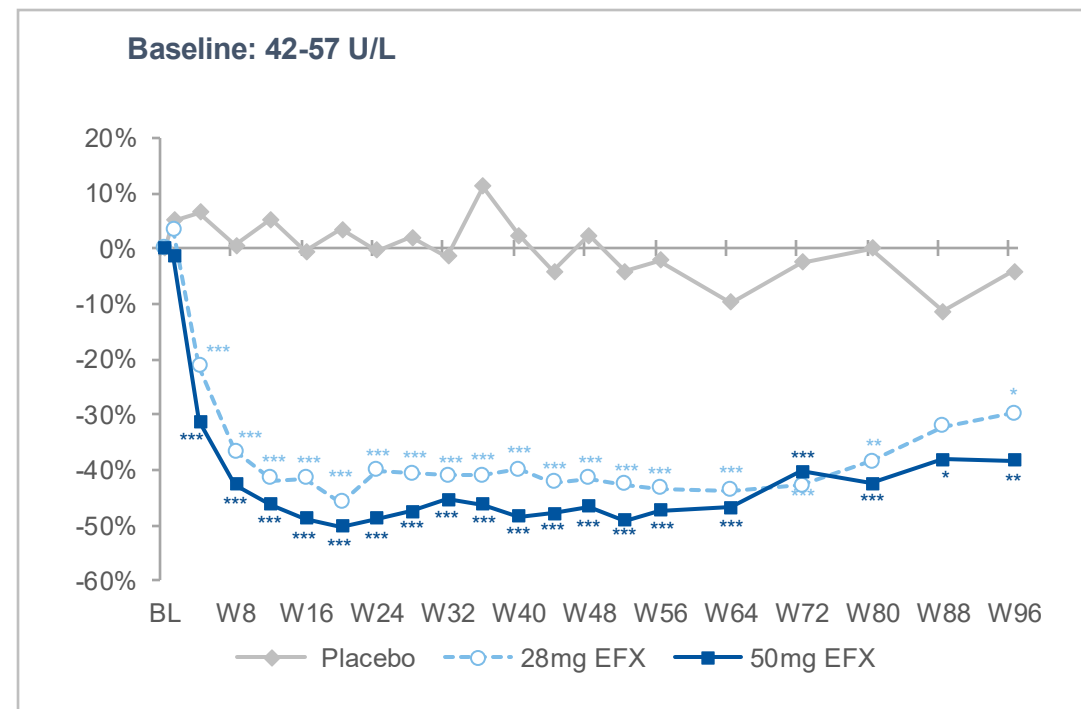
LS Mean Percent Change from Baseline



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

AST

LS Mean Percent Change from Baseline



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



Treatment-Emergent Adverse Events (TEAE)

From Baseline through Week 96

TEAE Overview	Placebo (N=43)	EFX 28mg (N=40)	EFX 50mg (N=43)
TEAE Leading to Death	0 (0%)	0 (0%)	0 (0%)
Serious Adverse Event (SAE)	4 (9%)	4 (10%)	7 (16%)
Drug-Related SAE	0 (0%)	1 (2%) ^a	1 (2%) ^b
Drug-Related TEAE Leading to Discontinuation	0 (0%)	4 (10%) ^{c,d}	3 (7%) ^{e,f}
Most Frequent (≥15%) Drug-Related TEAEs	Placebo	EFX 28mg	EFX 50mg
Diarrhea	7 (16%)	16 (40%)	16 (37%)
Nausea	5 (12%)	12 (30%)	14 (33%)
Increased Appetite	3 (7%)	7 (18%)	10 (23%)
Injection Site Erythema	6 (14%)	8 (20%)	7 (16%)
Injection Site Bruising	2 (5%)	6 (15%)	3 (7%)

^a Post week 24: pancreatitis (not confirmed on imaging and discharged within 24 hours)

^b Previously reported: esophagitis

^c Previously reported: (1) increased appetite & weight gain; (2) diarrhea;

^d Post week 24: (1) pancreatitis (SAE reported above); (2) diarrhea

^e Previously reported: (1) esophagitis & vomiting; (2) nausea

^f Post week 24: (1) diarrhea

Blood Pressure

- No statistical difference versus placebo in systolic & diastolic BP at week 96

Markers of Liver Function and Hemostasis

- Remained stable, including platelets, bilirubin, INR¹, MELD² and CP³ score

Progression to Cirrhosis

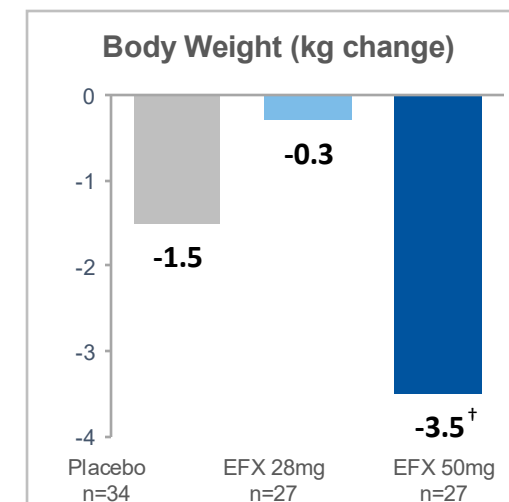
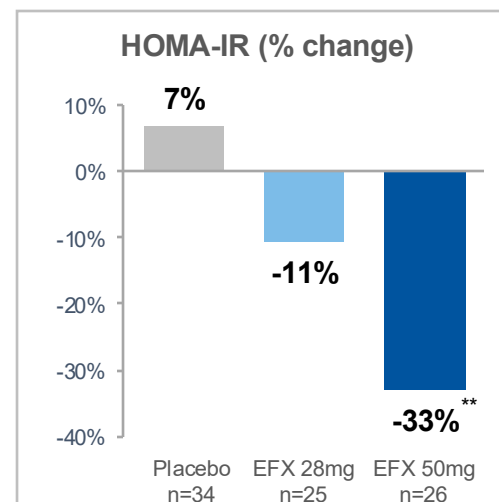
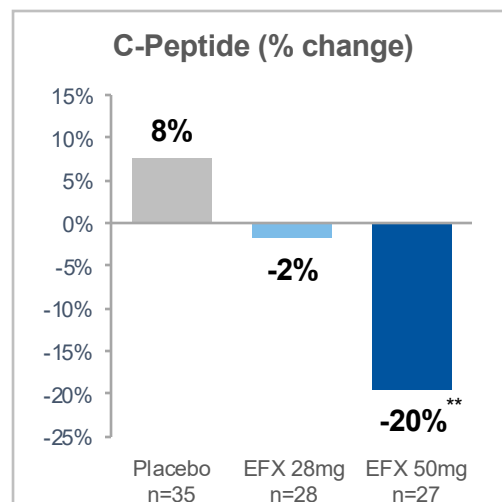
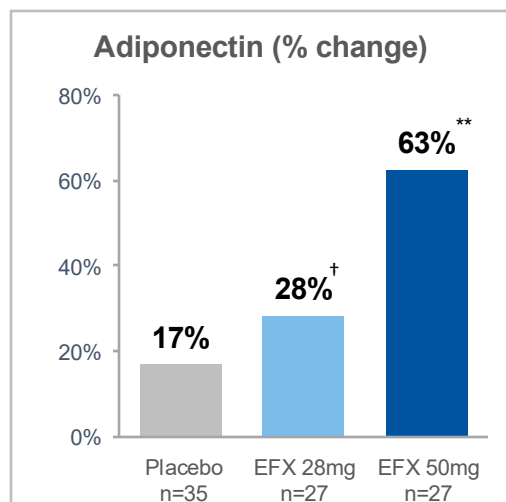
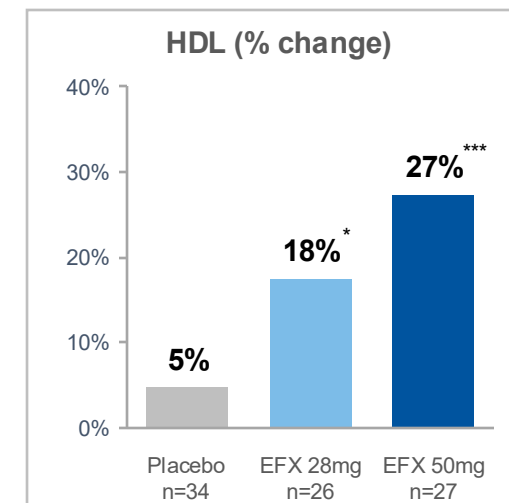
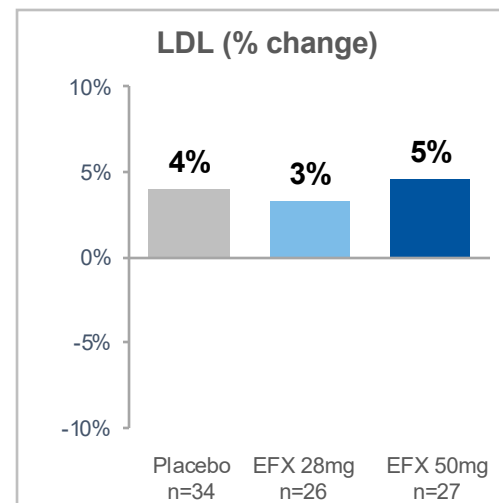
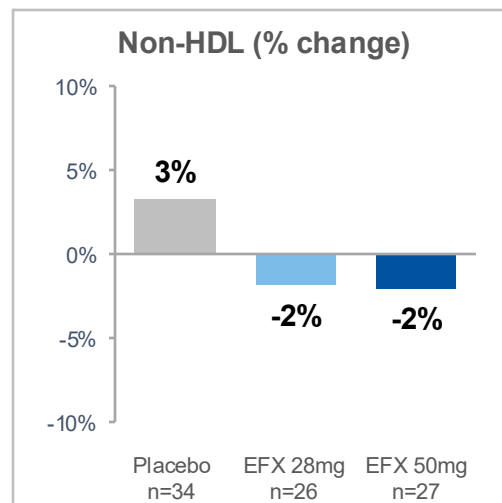
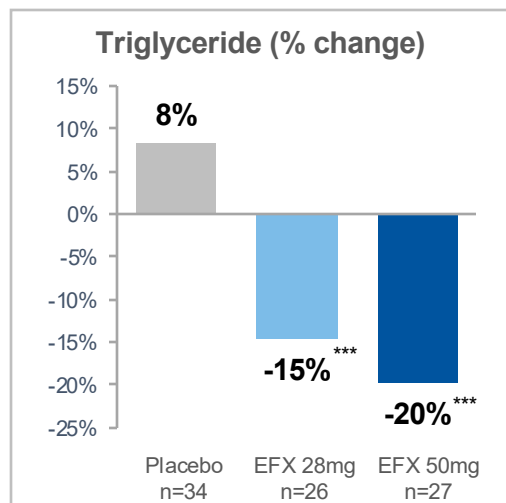
- Balanced across dose groups

Bone Mineral Density

- At week 48, no significant changes versus placebo for lumbar spine and femoral neck regions
- At week 96, significant reductions versus placebo for lumbar spine (3-4%, both EFX groups) and femoral neck regions (< 3%, 50mg EFX only)
- One vertebral fracture (L1) observed in placebo group; no vertebral fractures observed in EFX groups



Improvement in Lipoproteins, Markers of Insulin Sensitivity and Body Weight After 96 Weeks, LS Mean Change From Baseline

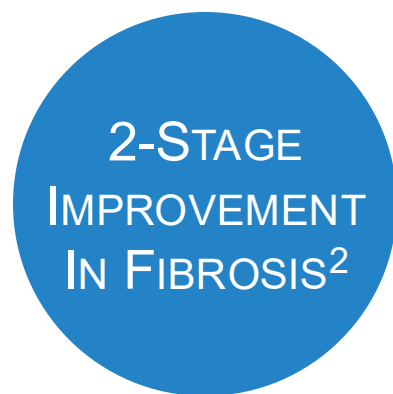


Unprecedented



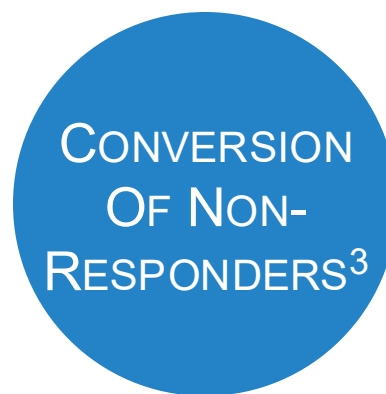
75%* vs. 24%**
(50mg EFX vs. Placebo)

Deep



36%* vs. 3%**
(50mg EFX vs. Placebo)

Broad



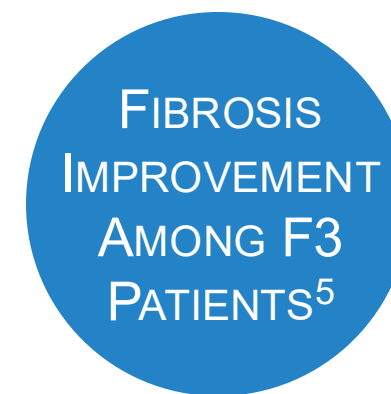
63% vs. 20%⁶
(50mg EFX vs. Placebo)

Durable



92% vs. 40%⁶
(50mg EFX vs. Placebo)

Advanced



68%* vs. 14%**
(50mg EFX vs. Placebo)

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

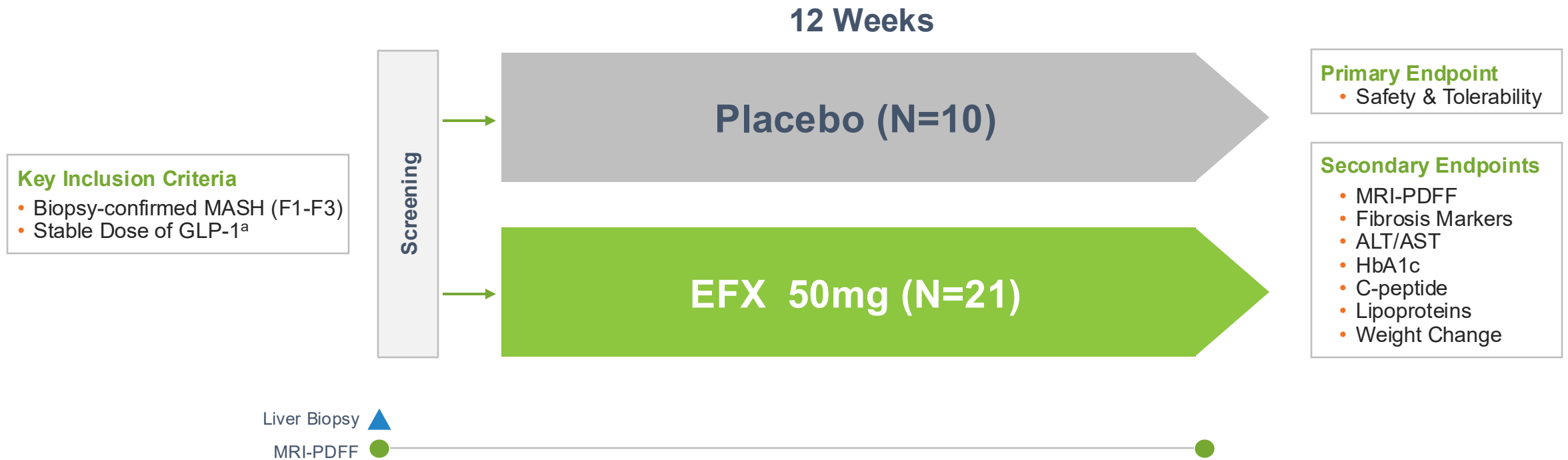
¹ ≥1 stage improvement in fibrosis without worsening of MASH; ² 2 stages improvement in fibrosis without worsening of MASH; ³ proportion of Week 24 non-responders who converted to week 96 responders;

⁴ proportion of Week 24 responders who were also week 96 responders; ⁵ ≥1 stage improvement in fibrosis without worsening of MASH among patients with week 96 biopsies and F3 fibrosis at baseline;

⁶ Not evaluated for statistical significance

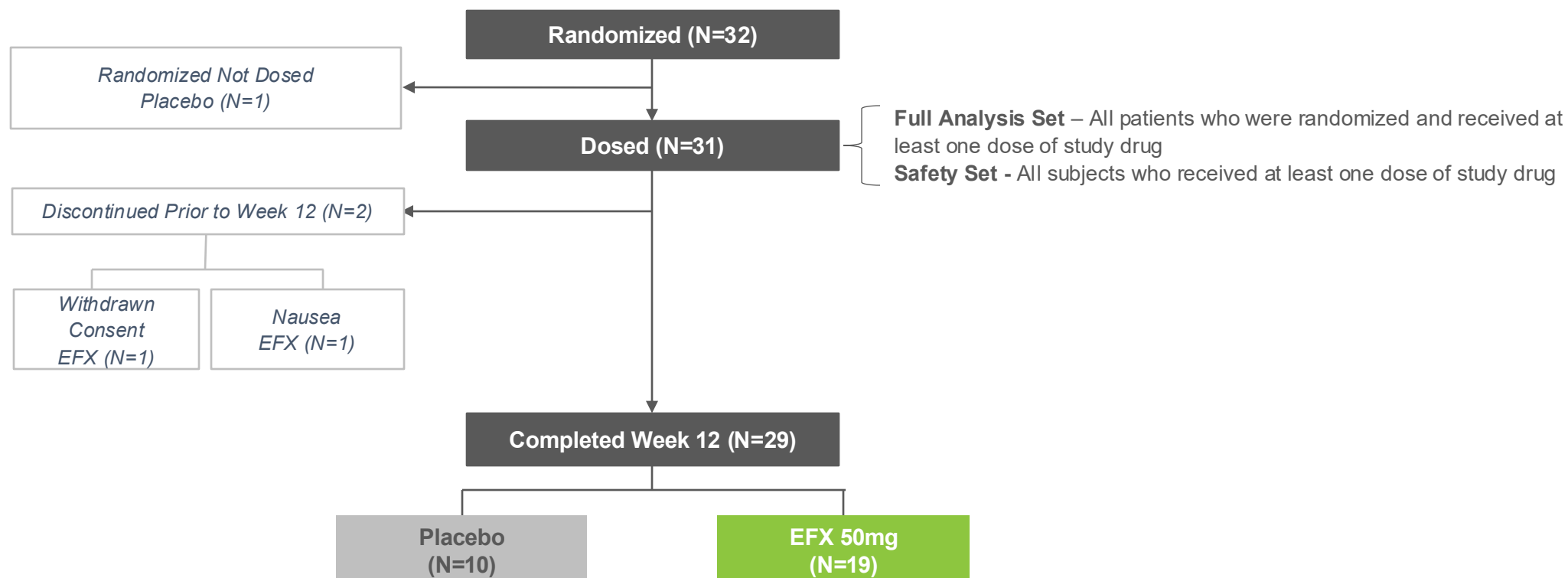
Backup Slides

» Cohort D Trial Design: EFX in Combination with GLP-1 Receptor Agonist Therapy (GLP-1) at Diabetic Doses



^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.

» Cohort D: Week 12 Patient Disposition & Key Analysis Sets



» Cohort D: 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

» Cohort D: 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.



Cohort D Primary Endpoint: Comparable Safety and Tolerability Across Both Treatment Groups

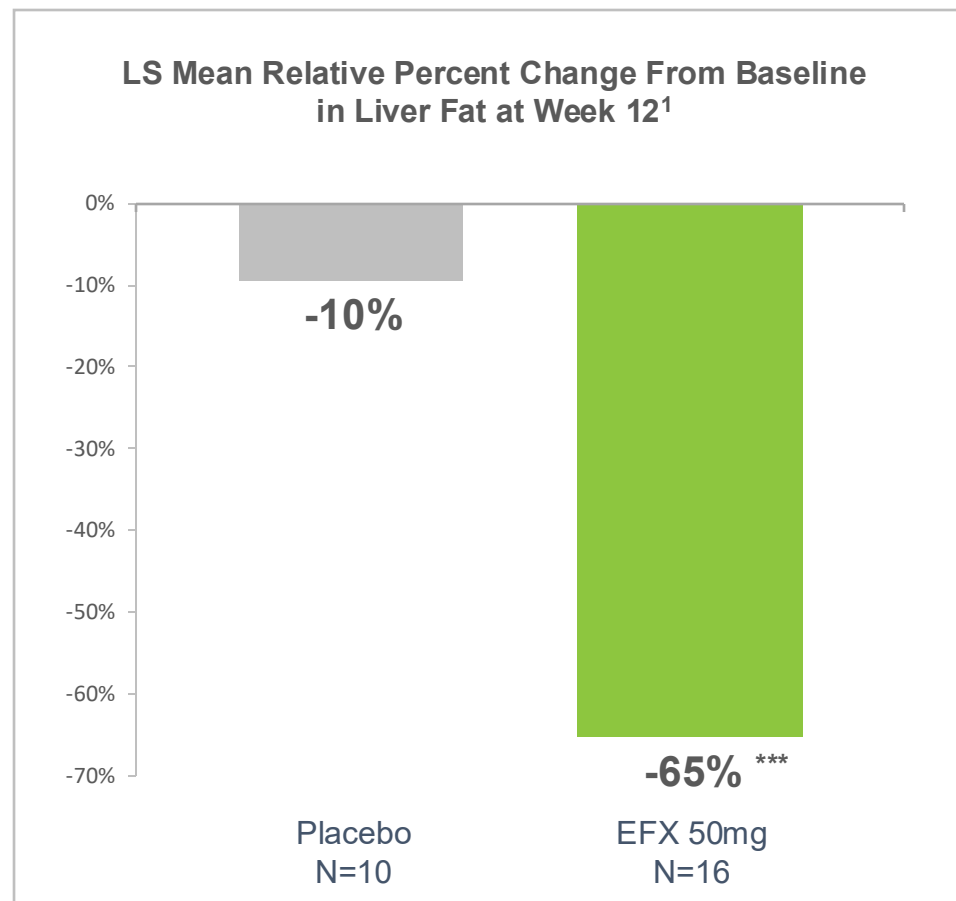
Treatment-Emergent Adverse Event (TEAE) Overview	Placebo (N=10)	EFX 50mg (N=21)
TEAE Leading to Death	0 (0%)	0 (0%)
Drug-Related Serious Adverse Event (SAE)	0 (0%)	0 (0%) ^a
Drug-Related TEAE Leading to Discontinuation	0 (0%)	1 (5%) ^b
Most Frequent (≥15%) Drug-Related TEAEs	Placebo	EFX 50mg
Diarrhea	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



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

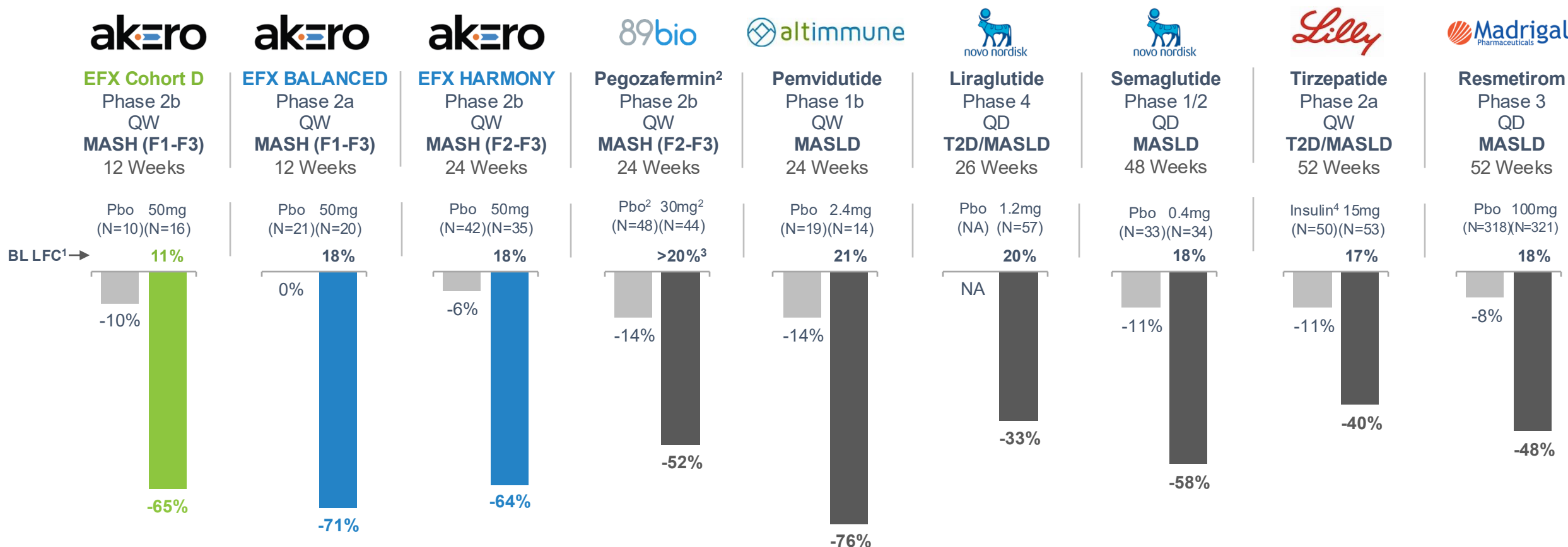


*** p<0.001, versus placebo (Analysis of Covariance [ANCOVA])

¹ Including the baseline MRI-PDFF measurements for three subjects with baseline MRI-PDFF measurements after the first dose lowers the LS Mean result for the EFX group from -65.3% to -63.2% (N=19) and the placebo group from -9.6% to -9.0% (N=10)

Source Data: MRI-PDFF Analysis Set (all subjects with pre-dose baseline and on-study measurement assessed by MRI-PDFF [N=16]); Topline preliminary data

» EFX Liver Fat Reduction in Context: MASLD & Pre-Cirrhotic MASH



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

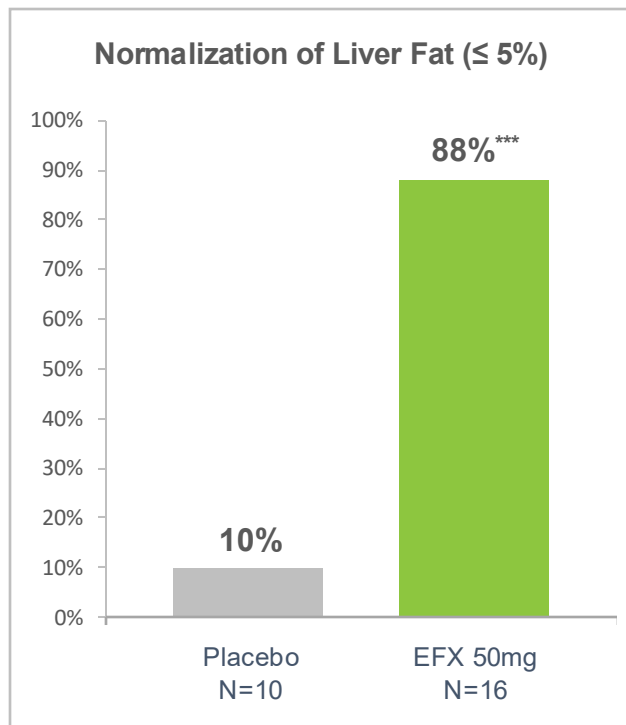
⁴ Insulin Degludec

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.

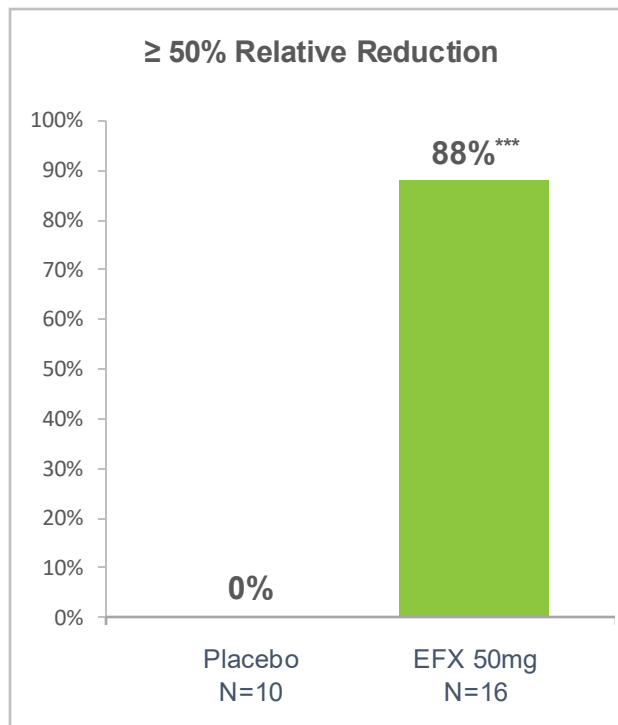


More Patients Treated with EFX Combined with GLP-1 Met Higher Thresholds of Liver Fat Reduction and Normalization than GLP-1 Alone

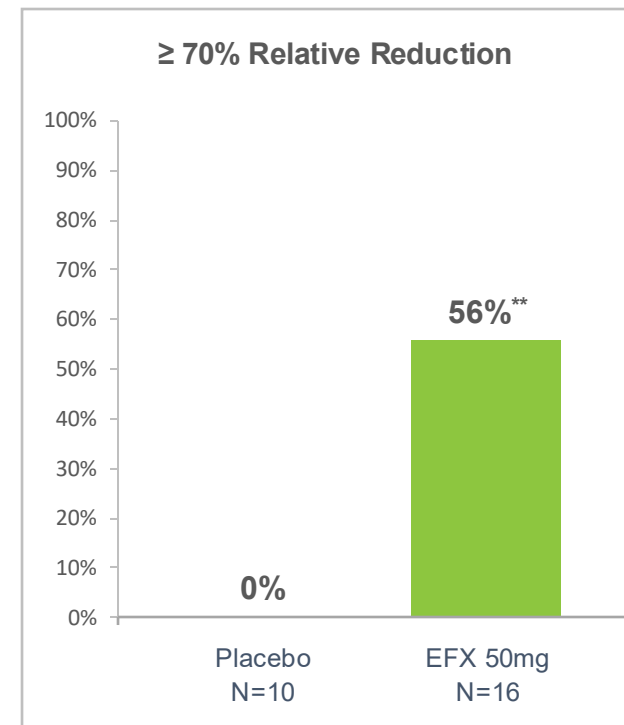
Proportion of Patients Achieving Liver Fat Reduction Thresholds at Week 12¹



*** $p < 0.001$, versus placebo (CMH²)



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



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

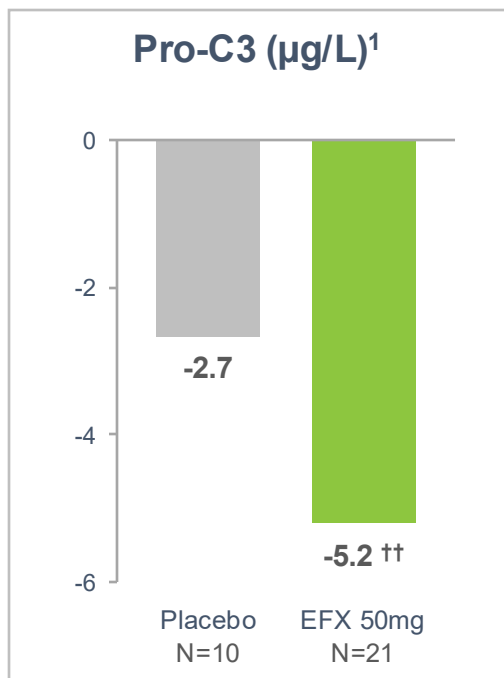
In the HARMONY Study, patients whose liver fat was normalized had 3-fold higher odds of achieving MASH Resolution and Fibrosis Improvement

¹ When three EFX-treated patients with baseline measurements after the first dose are included in liver fat analyses, normalization of liver fat increased from 87.5% (14 of 16) to 89.5% (17 of 19) and the proportion of patients achieving $\geq 50\%$ and $\geq 70\%$ relative reduction in liver fat decreased, respectively, to 84.2% (16 of 19) and 52.6% (10 of 19); ² Cochran–Mantel–Haenszel test

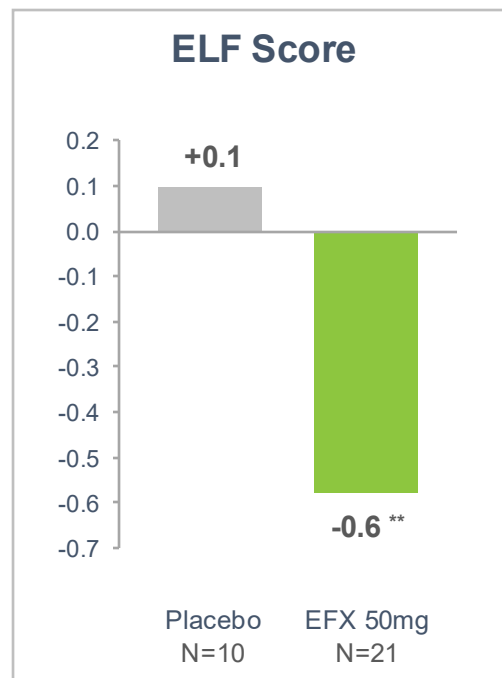


Greater Reductions in Markers of Fibrosis for EFX Combined with GLP-1 than GLP-1 Alone

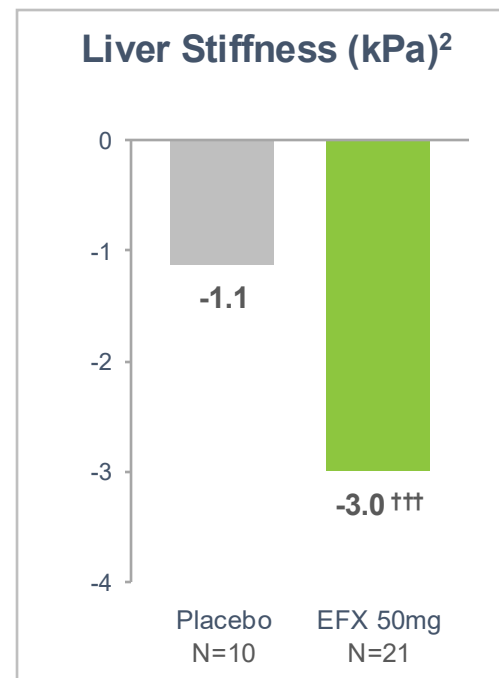
LS Mean Change From Baseline to Week 12



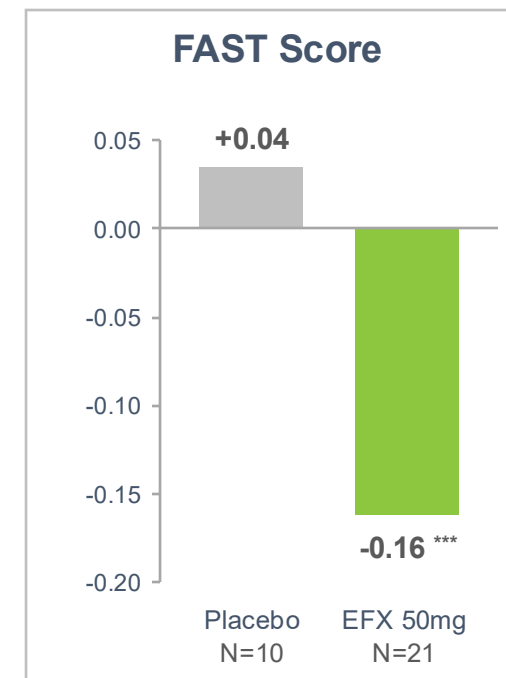
†† $p < 0.01$, versus baseline (MMRM¹)



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



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



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

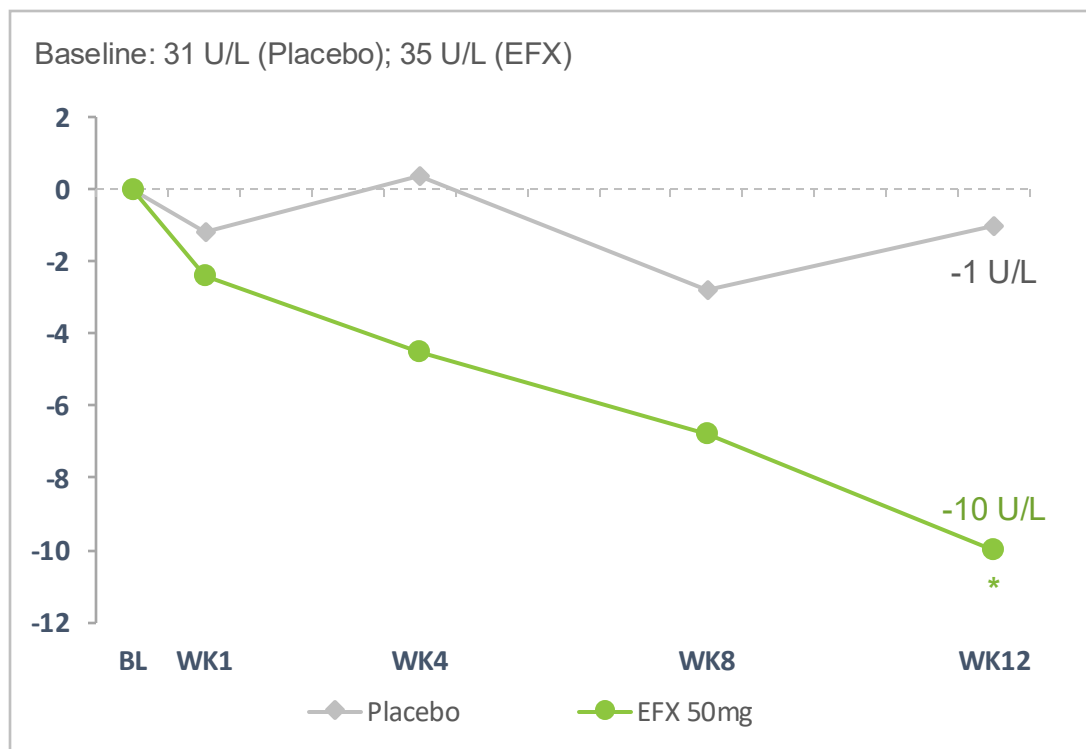
¹ Mixed Model Repeated Measures; ² Measured by FibroScan



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

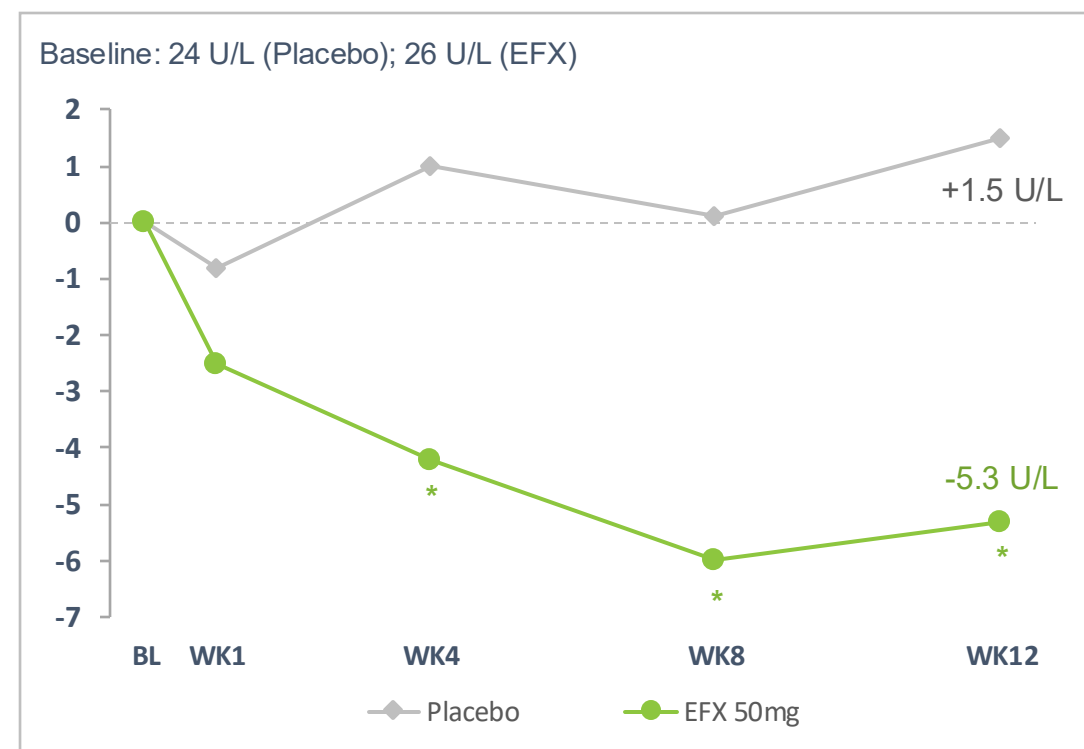
ALT

LS Mean Change from Baseline (U/L)

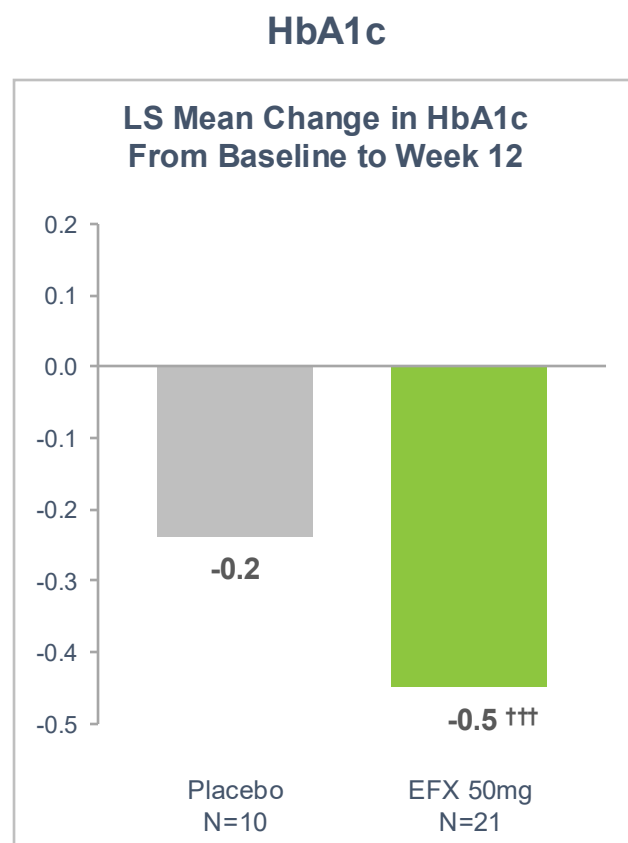


AST

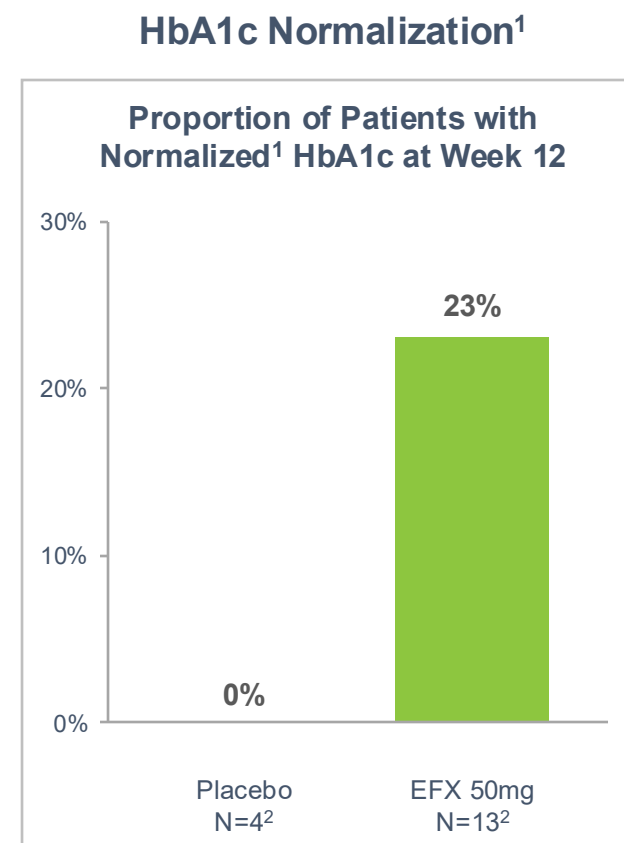
LS Mean Change from Baseline (U/L)



» Clinically Meaningful Improvements in HbA1c after Only 12 Weeks



††† p<0.001, versus baseline (MMRM)

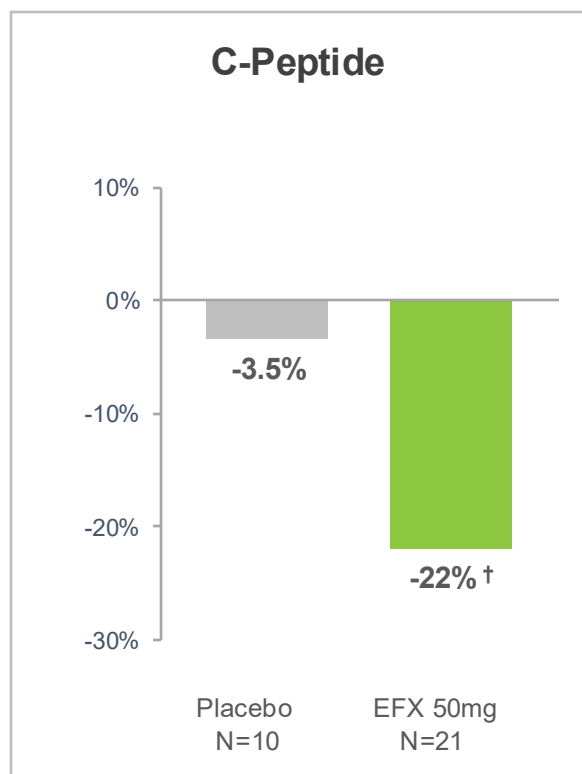


¹ Normalization of HbA1c defined as an HbA1c of ≥ 6.5 at baseline and < 6.5 at week 12

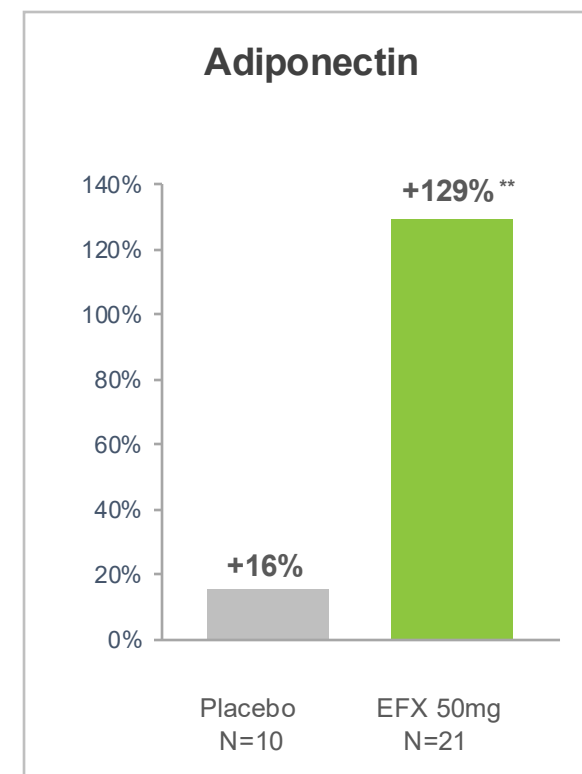
² Number of patients with HbA1c ≥ 6.5 at baseline

» EFX Complements GLP-1 by Increasing Sensitivity to Insulin

LS Mean Change From Baseline to Week 12



[†] p<0.001, versus baseline (MMRM)

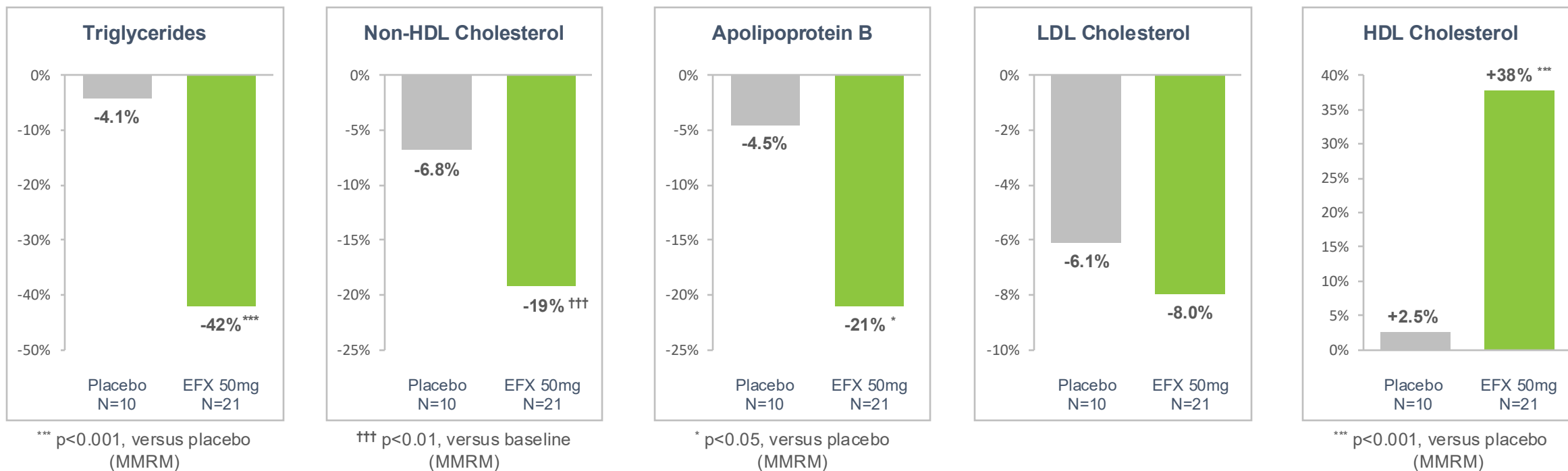


^{**} p<0.01, versus placebo (MMRM)



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



» Weight Loss Maintained for EFX Combined with GLP-1



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

Key Take-Aways

- ❖ EFX and GLP-1 have complementary mechanisms of action.
- ❖ Addition of EFX to GLP-1 in patients with MASH 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

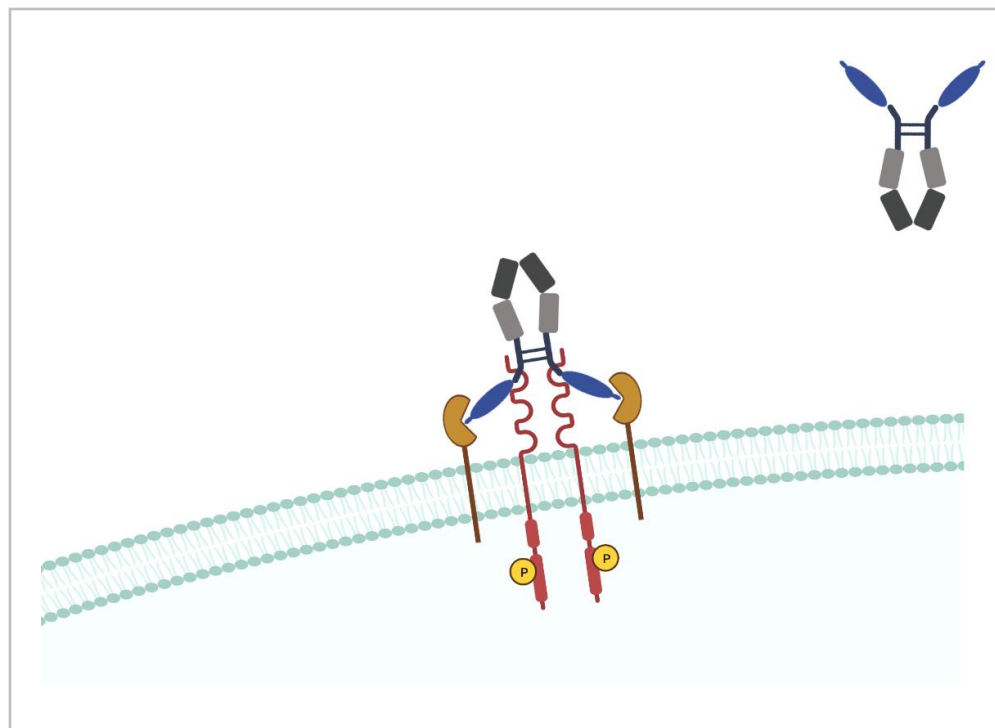
Potential for EFX on Top of GLP-1 to be More Effective than GLP-1 Alone





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

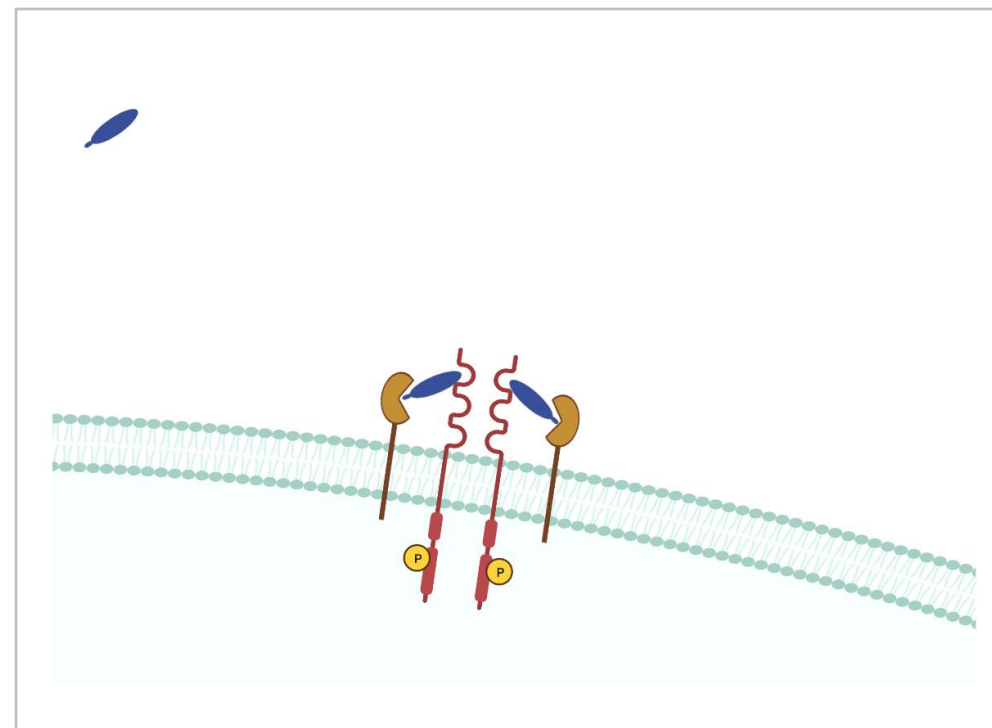
EFX



Dimer structure may enable cooperative binding and enhance avidity effects

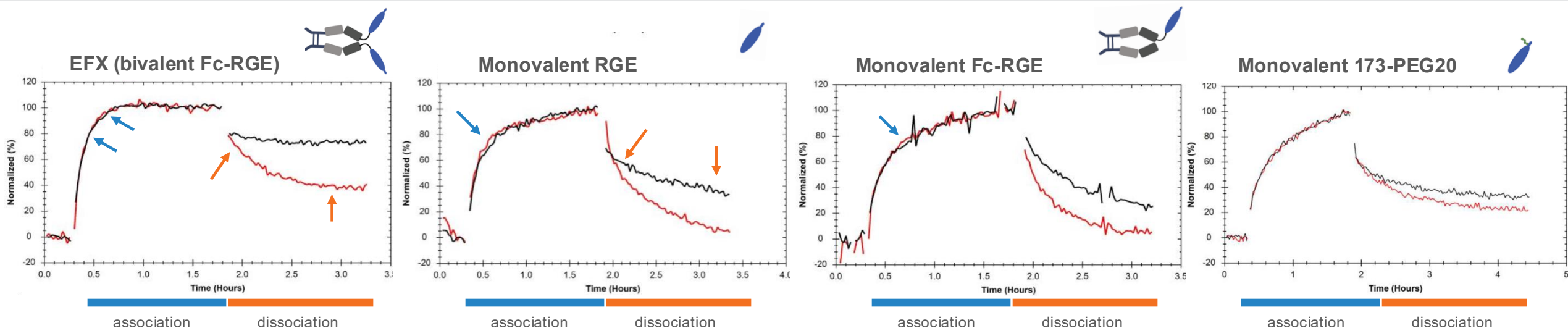
vs

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

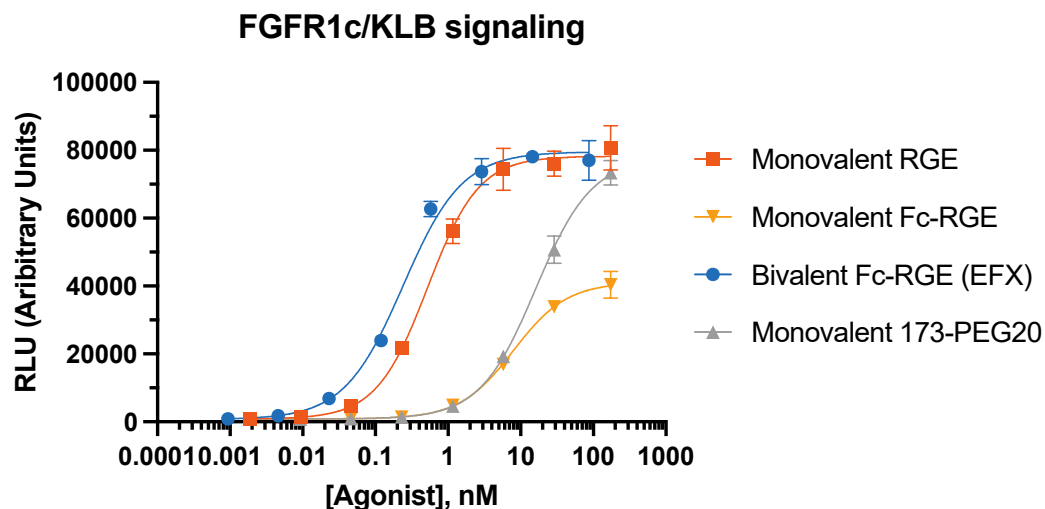
Addition of Fc or 20 kDa PEG to single-chain FGF21 analog further slows association

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]

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 EC₅₀) 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 EC₅₀)
 - *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 EC₅₀)



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