Restoring Balance. Renewing Life.

JP Morgan Presentation

Andrew Cheng, MD, PhD
President & CEO

January 14, 2025

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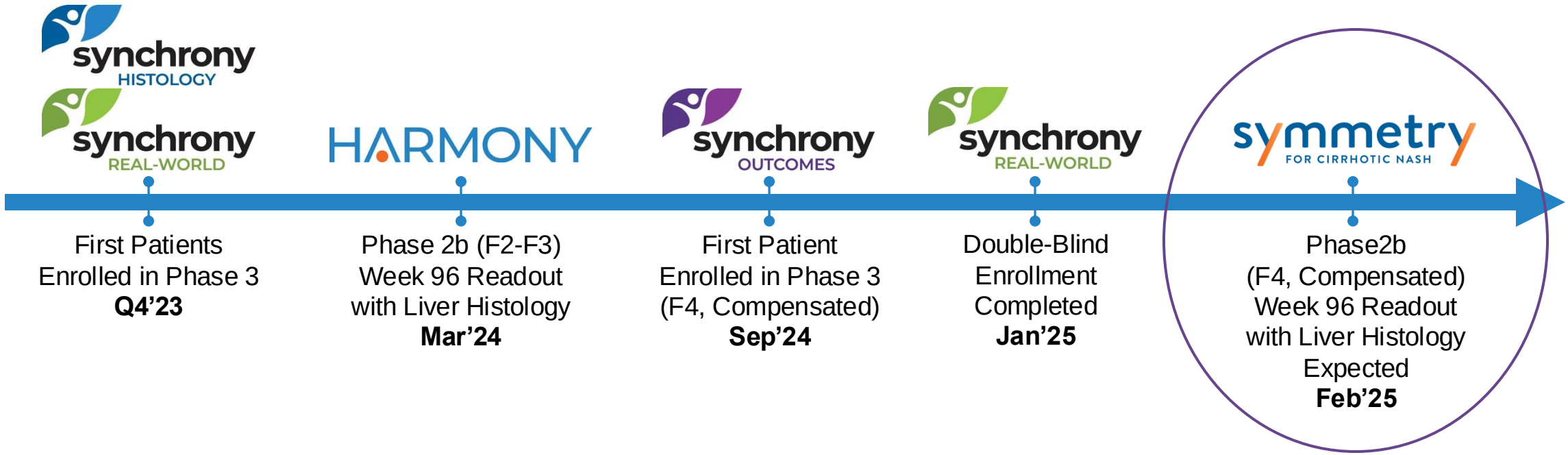
Recent Progress & Near-Term Milestones for Efruxifermin (EFX)



Cash sufficient to fund our Phase 3 SYNCHRONY *Histology* and *Real-World* studies through their respective primary endpoints and our current operating plan into the second half of 2027, with ~$787M cash on hand[1] as of September 30, 2024

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[1] Cash, cash equivalents, and short-term marketable securities

SYNCHRONY Real-World Enrollment Completed in ~1 Year

Akero Therapeutics Completes Enrollment of the Double-Blind Portion of the Phase 3 SYNCHRONY *Real-World* Study Evaluating Efruxifermin (EFX) in Patients with Non-Invasively Diagnosed MASH or MASLD

-- 601patients have been enrolled in the double-blind portion of the SYNCHRONY Real-World *study since initiation in November 2023 --*

-- Data from SYNCHRONY Real-World *study anticipated in the first half of 2026 --*

SOUTH SAN FRANCISCO, Calif., January 13, 2025 – Akero Therapeutics, Inc. (Nasdaq: AKRO), a clinical-stage company developing transformational treatments for patients with serious metabolic diseases marked by high unmet medical need, today announced it has completed enrollment of patients in the double-blind portion of the Phase 3 SYNCHRONY *Real-World* study of EFX in patients with metabolic dysfunction-associated steatohepatits (MASH) or metabolic dysfunction-associated steatotic liver disease (MASLD) (F1-F4).

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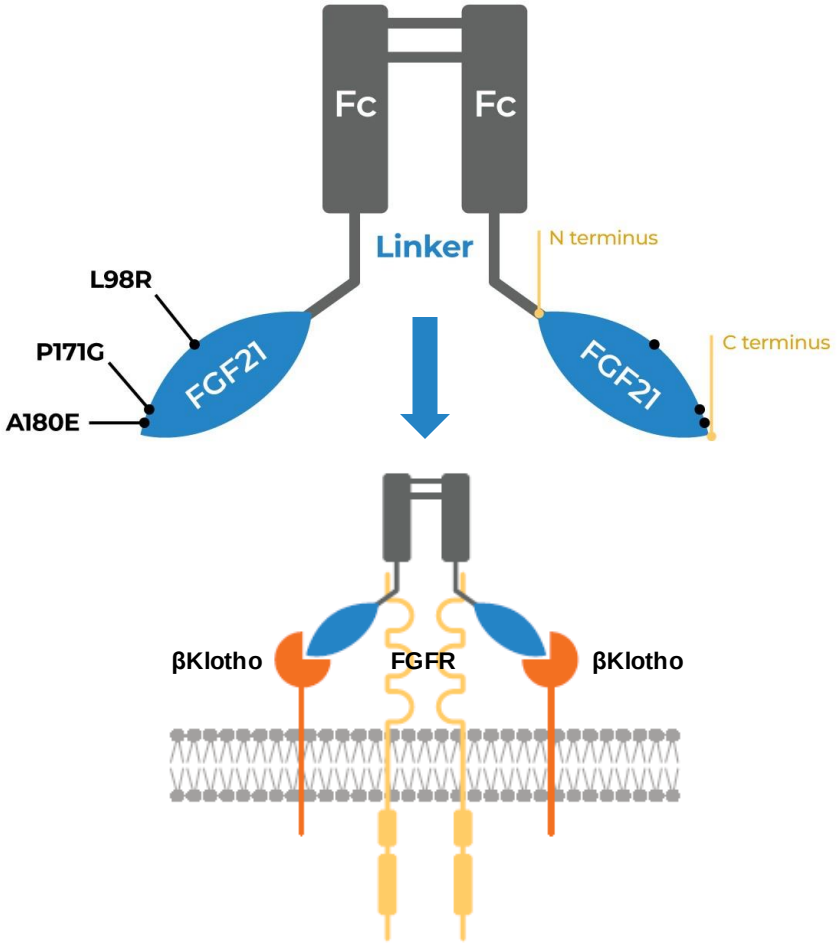
EFX Bivalent Structure Potentially Optimal for MASH Efficacy, With Convenient Once-weekly Dosing



Bivalent FGF21 Analog Brings:

- **High β-Klotho affinity**
- **High systemic exposure**
- **Maintained agonism of FGFRs throughout weekly dosing interval**
- **Sustained pharmacodynamic effect through week 96 (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; Kharitonenkov, A *et al.* (2007) Endocrinology 148(2)774-781

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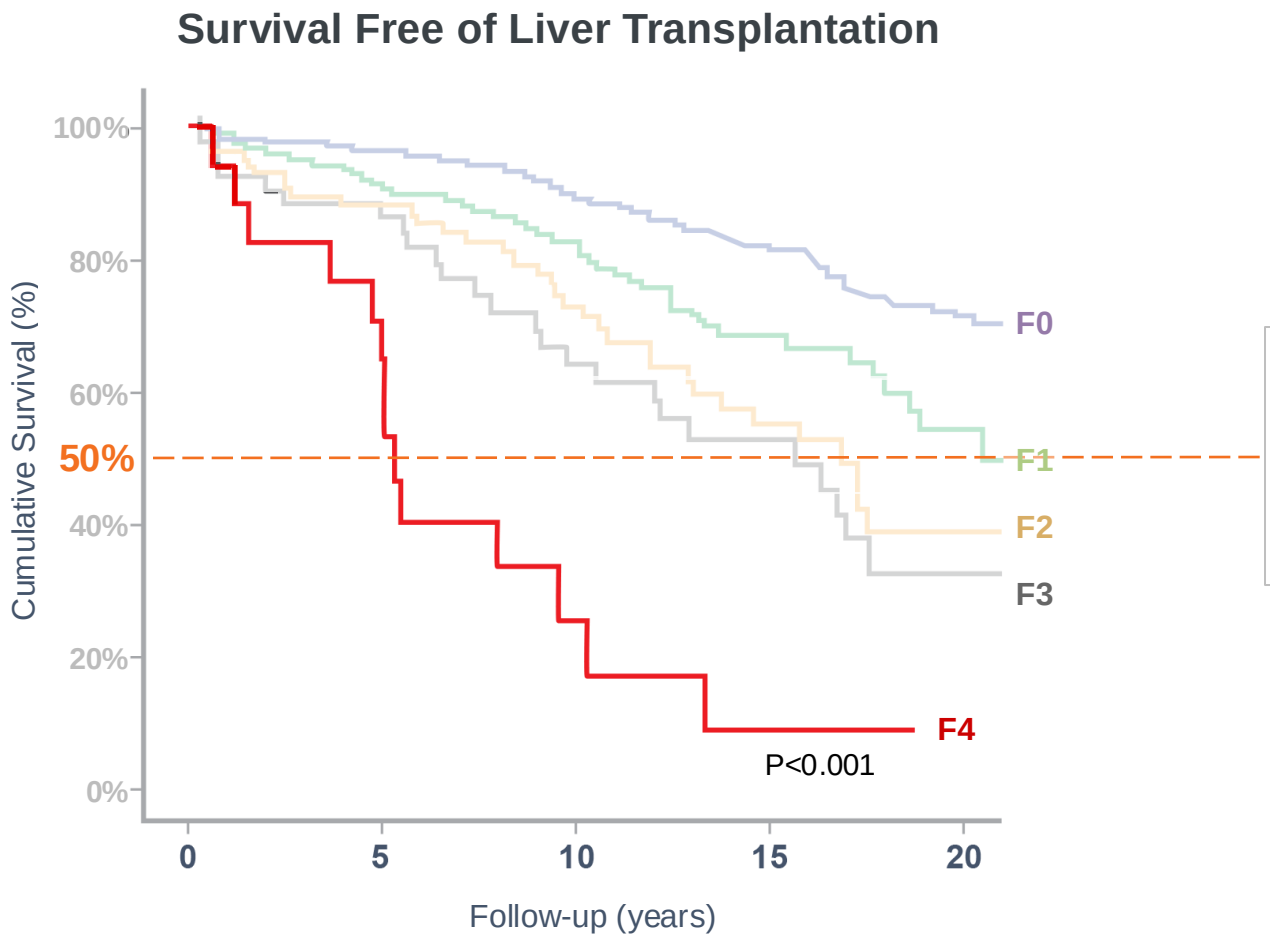
High Risk of Mortality Associated with Cirrhosis Due to MASH



~50%

5-year mortality
without liver transplant
for **F4 patients**

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

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

Key Inclusion Criteria[1]

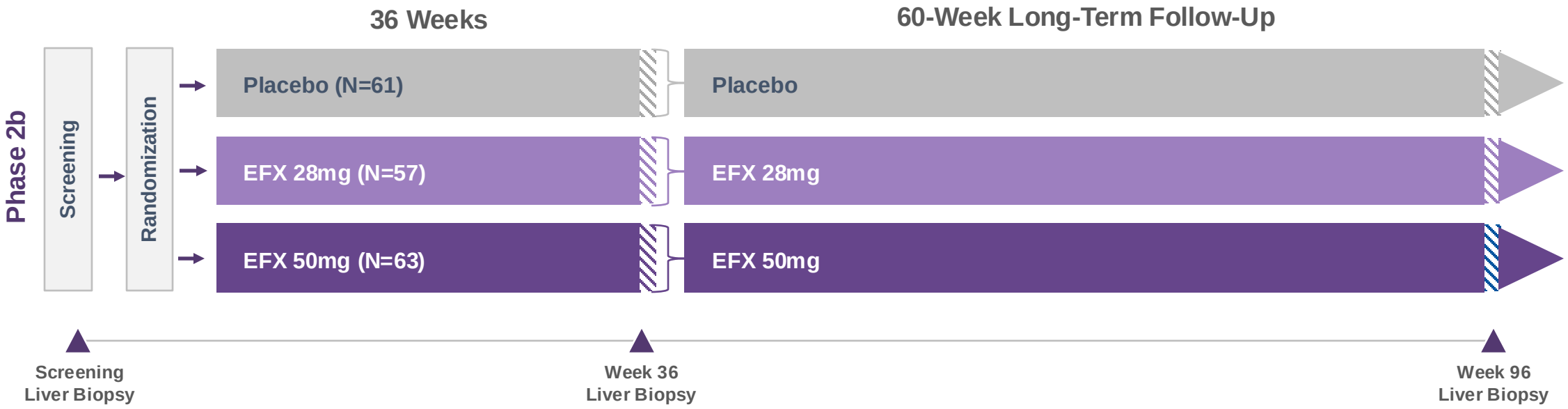
- F4 MASH (compensated)
- T2D or 2 of 4 components of metabolic syndrome[2]

Phase 2b Primary Endpoint

- ≥1 Stage Fibrosis Improvement with no Worsening of MASH at Week 36
- ***Not*** *powered for week 96 endpoints*

Key Secondary Efficacy Endpoints

- MASH 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 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.

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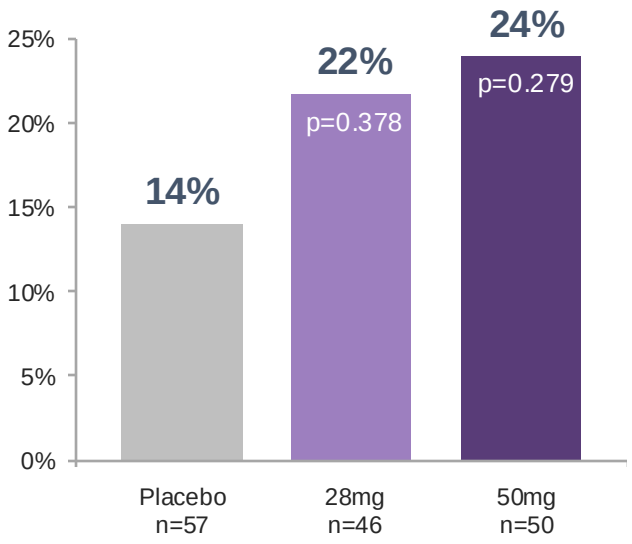
Summary of Week 36 SYMMETRY Liver Histology

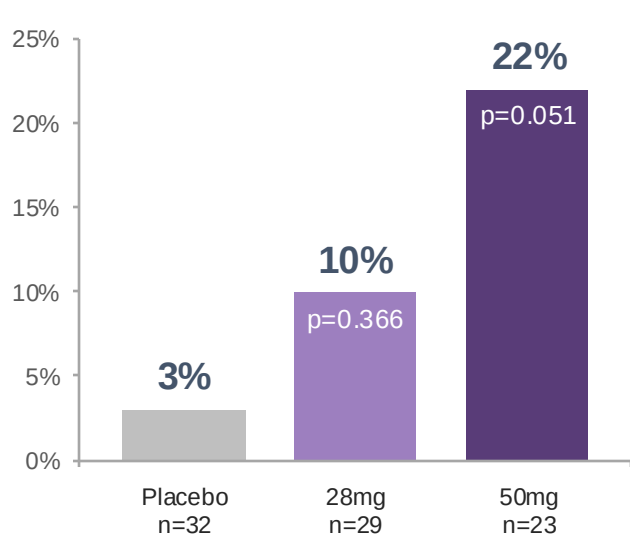
Fibrosis Improvement ≥1 Stage Without Worsening of MASH at Week 36

All Patients with Baseline and Week 36 Biopsies (Primary Endpoint) (N=153)



Statistically significant fibrosis improvement without worsening of MASH in patients with cirrhosis has not been reported for any investigational drug to date.

Subgroup: Cirrhosis Diagnosed ≥ 6 Months or Cryptogenic Cirrhosis (N=84)



Longer duration of cirrhosis at baseline may increase proportion of liver with features of F4 cirrhosis versus F3, thus reducing probability of reversal to F3 for placebo patients.

4 patients experienced 3- or 2-stage fibrosis improvement without worsening of MASH at Week 36

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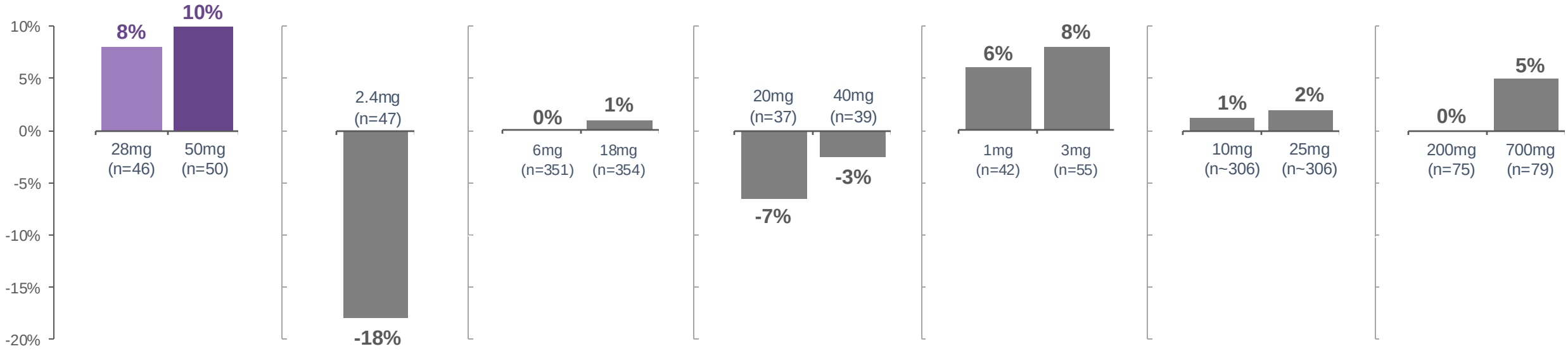
Source Data: Week 36 Interim Liver Biopsy Analysis Set; Topline preliminary data

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

	Fc-FGF21	GLP-1	ASK-1	Peg-FGF21	FGF19	FXR	LOXL-2
	Efruxifermin	Semaglutide[1]	Selonsertib[2]	Pegbelfermin[3]	Aldafermin[4]	Obeticholic acid[5]	Simtuzumab[6]
	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



[1] *Loomba, R et al. (2023) Lancet Gastro Hep 8:511-22;* [2] *Harrison, SH et al. (2020) J Hepatol 73(1):26-39;* [3] *Abdelmalek, MF et al. (2023) Clinical Gastro Hep 23:S1542-3565;* [4] *NGM Bio (2023) September Corporate Overview;* [5] *Intercept (2022) September 30 Press Release;* [6] *Harrison, SA et al. (2018) Gastroenterology 155:1140–1153. 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 (EFX, semaglutide, selonsertib, pegbelfermin, obeticholic acid) or only ≥ 1-stage fibrosis improvement (aldafermin, simtuzumab); numerical values represent percent responders. 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.*

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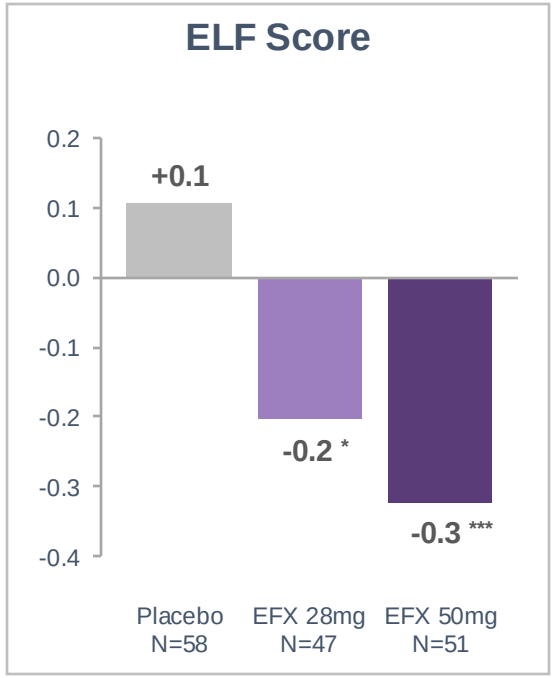
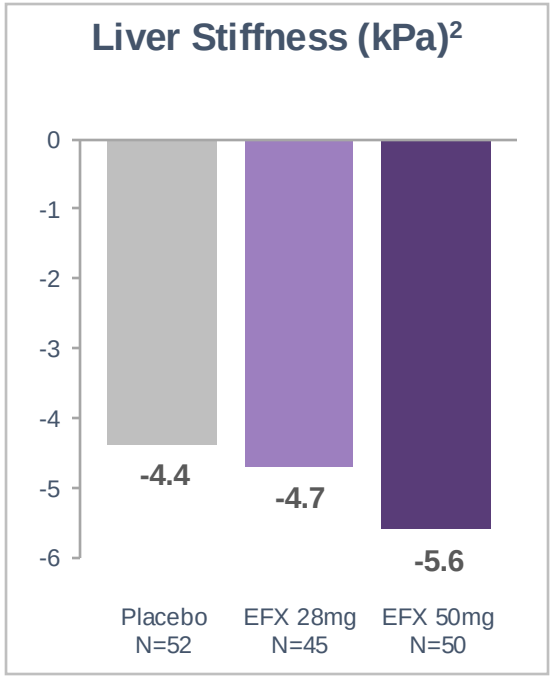
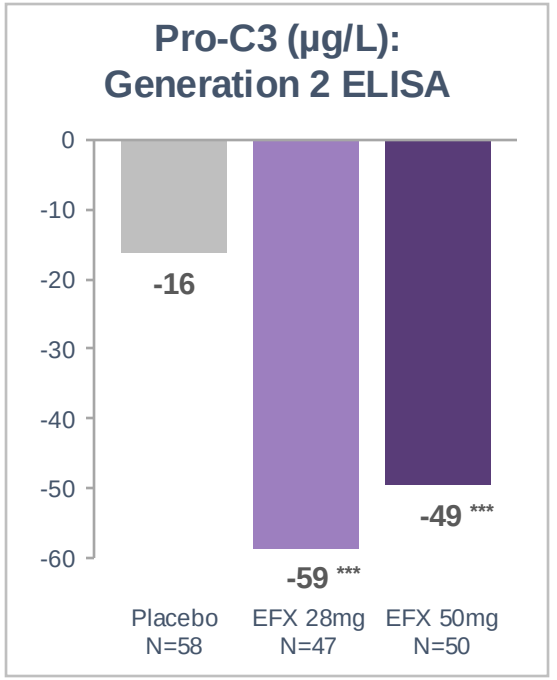
Evidence of Anti-Fibrotic Activity:
Analysis of Noninvasive Fibrosis Markers

Change[1] From Baseline to Week 36







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

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

[1] LS Mean (ELF Score, Pro-C3 and FAST Score); Arithmetic Mean (Liver Stiffness); [2] Measured by FibroScan

Source Data: Week 36 Interim Full Analysis Set (non-missing values only, no imputation); Topline preliminary data

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Case Study: 3-Stage Fibrosis Improvement & MASH Resolution

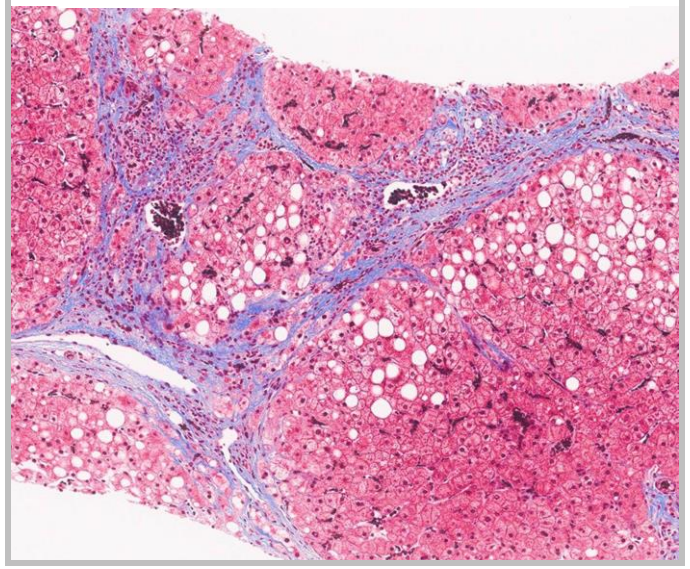
Histological Observations Consistent with Noninvasive Tests

Patient Background & Weight Loss During Study

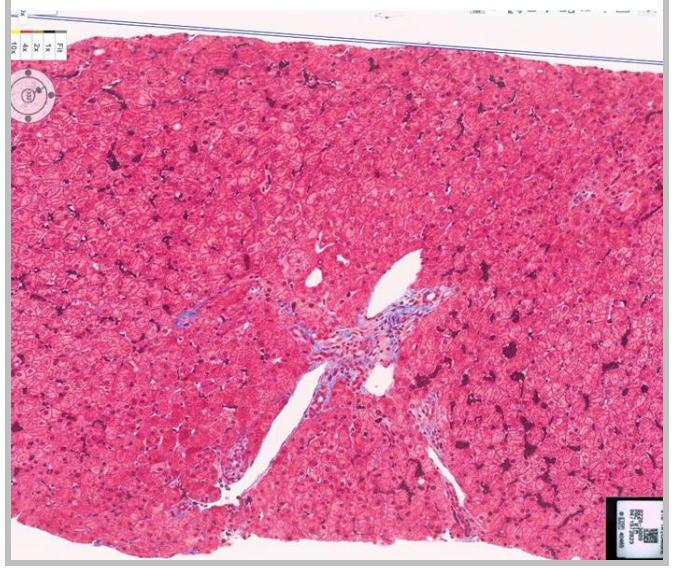
69-year-old female; T2D; cirrhosis diagnosed 17.4 months prior to first dose; no GLP-1 use at baseline; weight loss of 2 Kg (-3%) at Week 36

Comparison of Biopsy Features

Baseline Biopsy



Week 36 Biopsy



Comparison of Histology and Fibrosis Markers

Fibrosis Stage

Measure	Baseline	Week 36	Change
Fibrosis Stage	4	1	**-3**

MASLD Activity Score

Measure	Baseline	Week 36	Change
Total Score	**5**	**0**	**-5**
Steatosis	1	0	**-1**
Ballooning	2	0	**-2**
Lobular Inflammation	2	0	**-2**

Non-Invasive Fibrosis Markers

Measure	Baseline	Week 36	Change
ALT (U/L)	29	14	**-52%**
AST (U/L)	32	20	**-38%**
Pro-C3 (µg/L)	73	54	**-26%**
ELF Score	10.57	9.44	**-1.13**
FAST Score	0.45	0.15	**-0.30**

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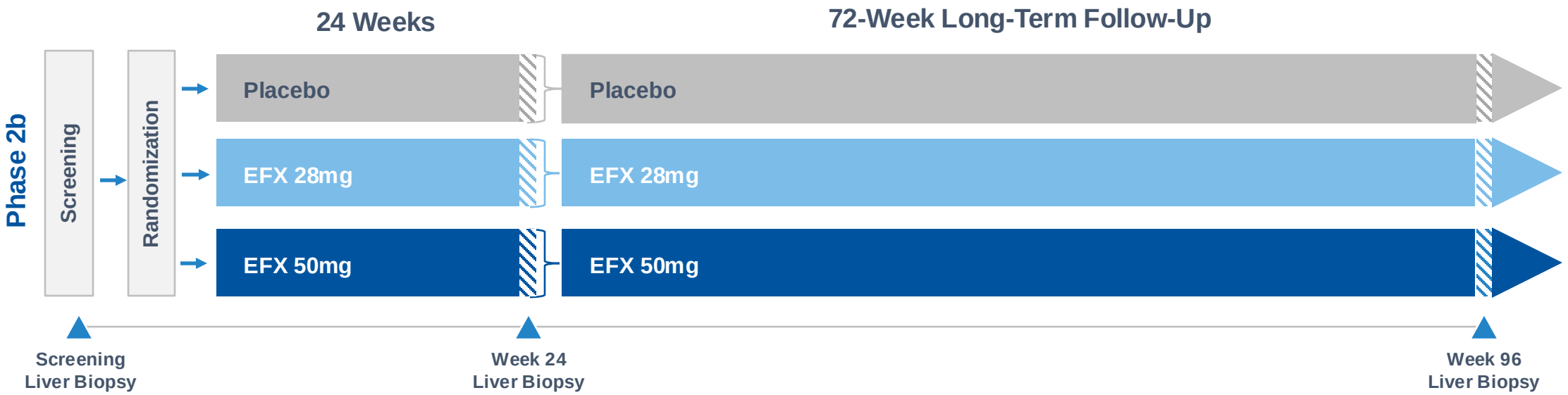
Phase 2b HARMONY Trial Design: Pre-Cirrhotic (F2-F3) MASH with Liver Histology at 24 and 96 weeks

Week 24 Primary Endpoint

- ≥ 1 stage fibrosis improvement & no worsening of MASH

Week 96 Primary Analyses

- ≥ 1 or 2 stages fibrosis improvement & no worsening of MASH
- MASH Resolution & No Worsening of Fibrosis
- Fibrosis Improvement & MASH Resolution
- *Fully powered for week 24 primary endpoint; **not** fully powered for week 96 endpoints*



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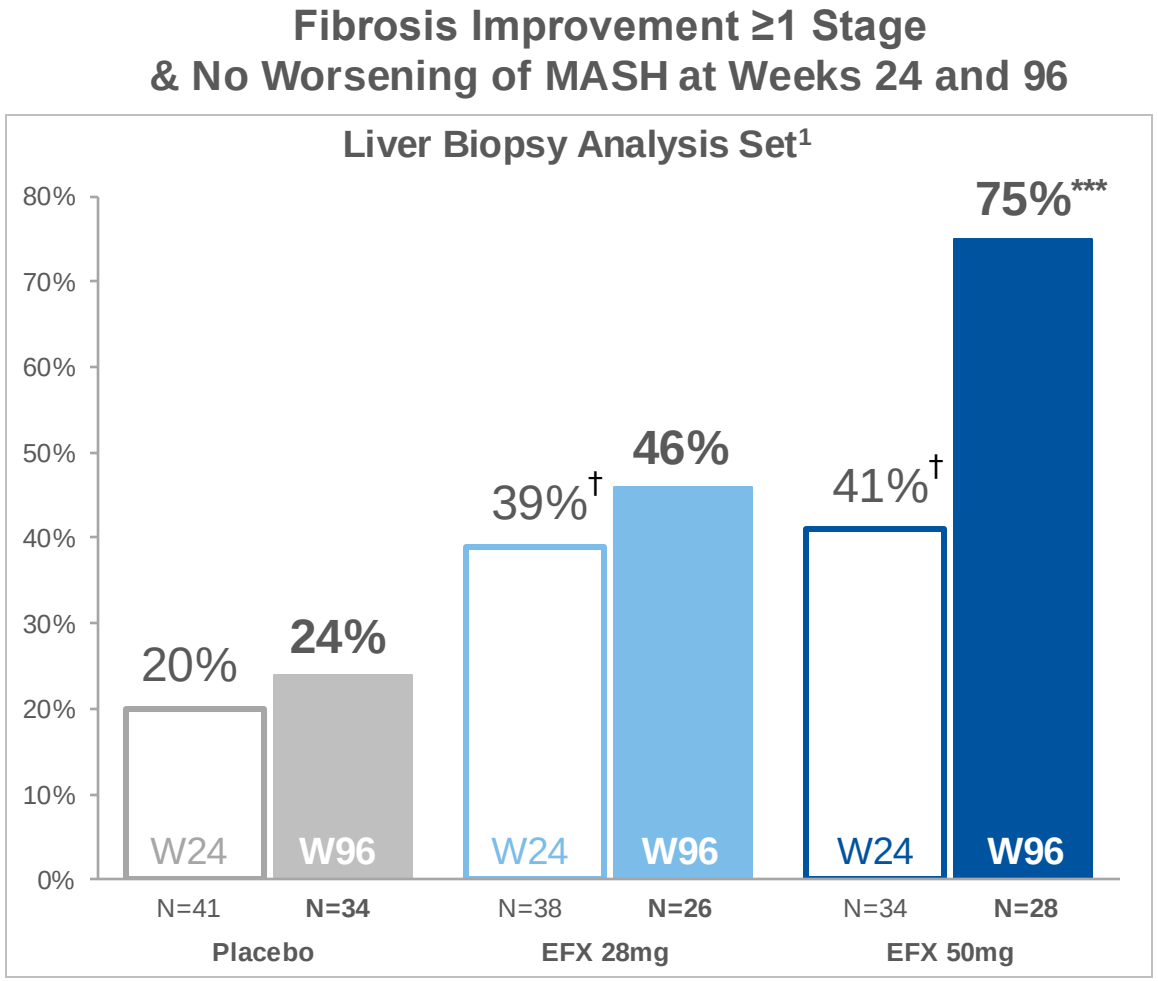
Substantial Improvement in Fibrosis Between Weeks 24 and 96 for Participants Treated with 50mg EFX



[1] All participants with baseline and specified timepoint
†p<0.05, versus placebo at W24; *** p<0.001, versus placebo at W96 (Cochran-Mantel-Haenszel Test [CMH])

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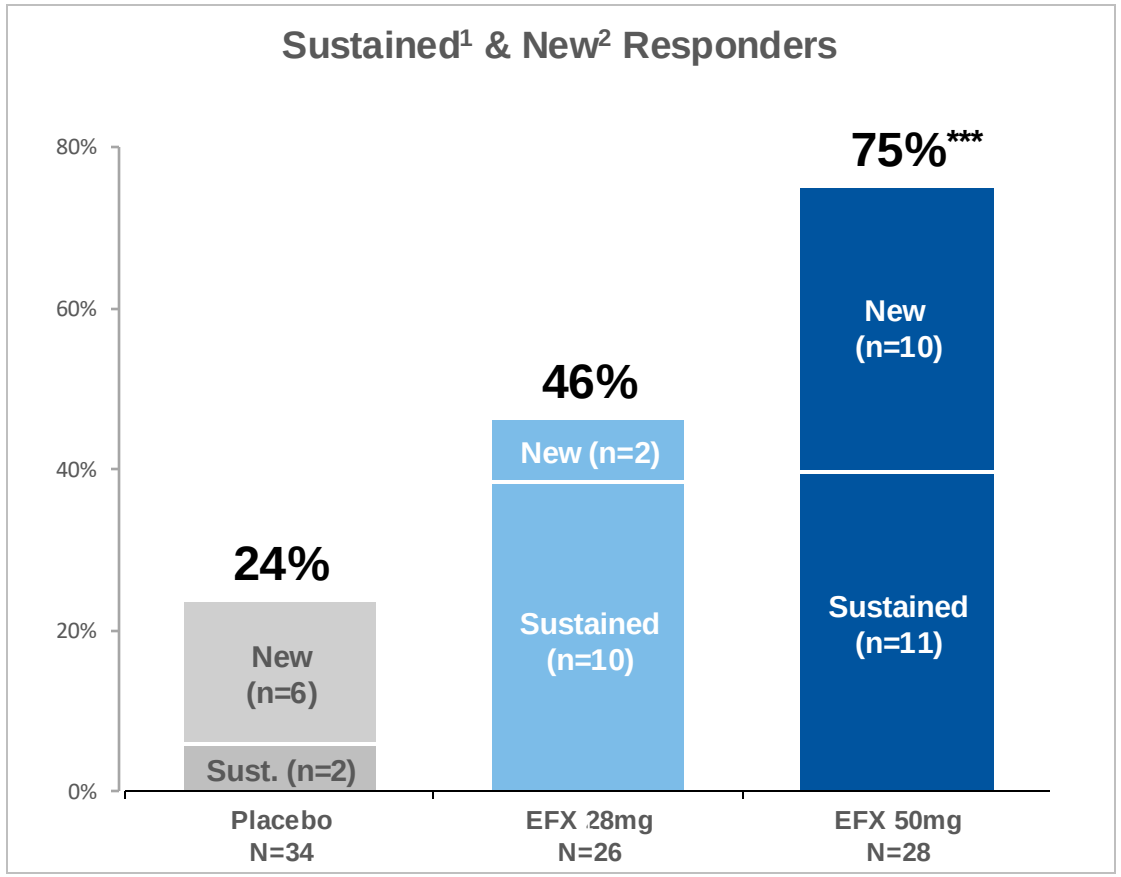
≥1 Stage Fibrosis Improvement & No Worsening of MASH:
Sustained, Broad and Durable Response

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
[3] Among Week 24 non-responders with Week 96 biopsies
[5] Not analyzed for statistical significance

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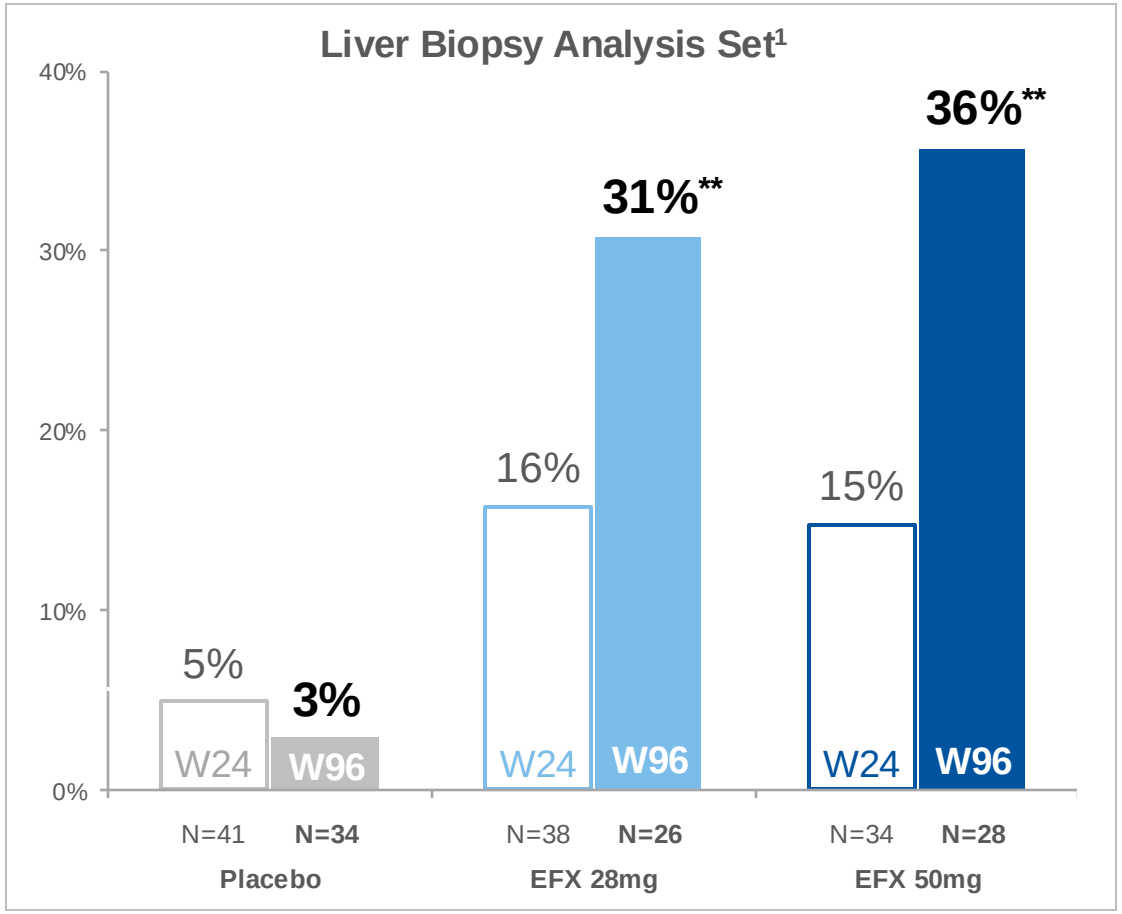
HARMONY

Source Data: LBAS-96

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

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



[1] All subjects with baseline and Week 24 or Week 96 biopsies

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

Source Data: LBAS-96; ITT

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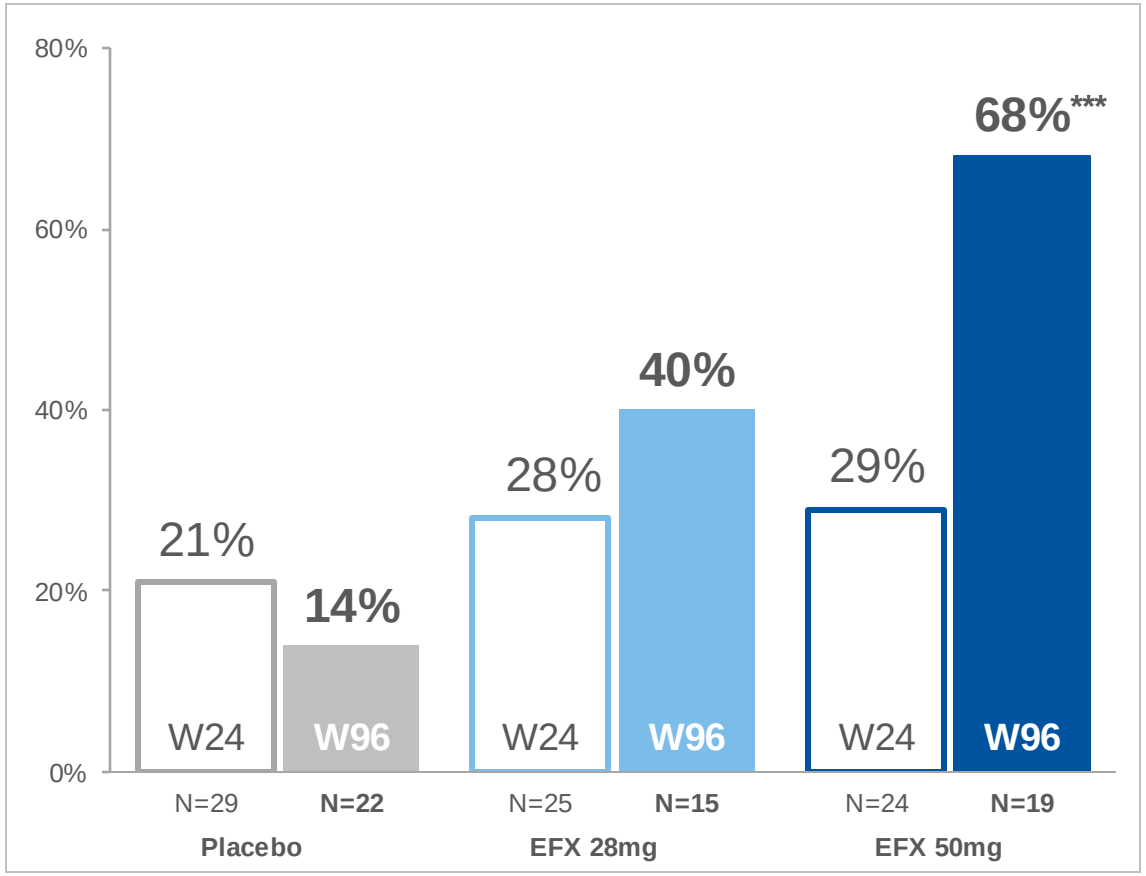
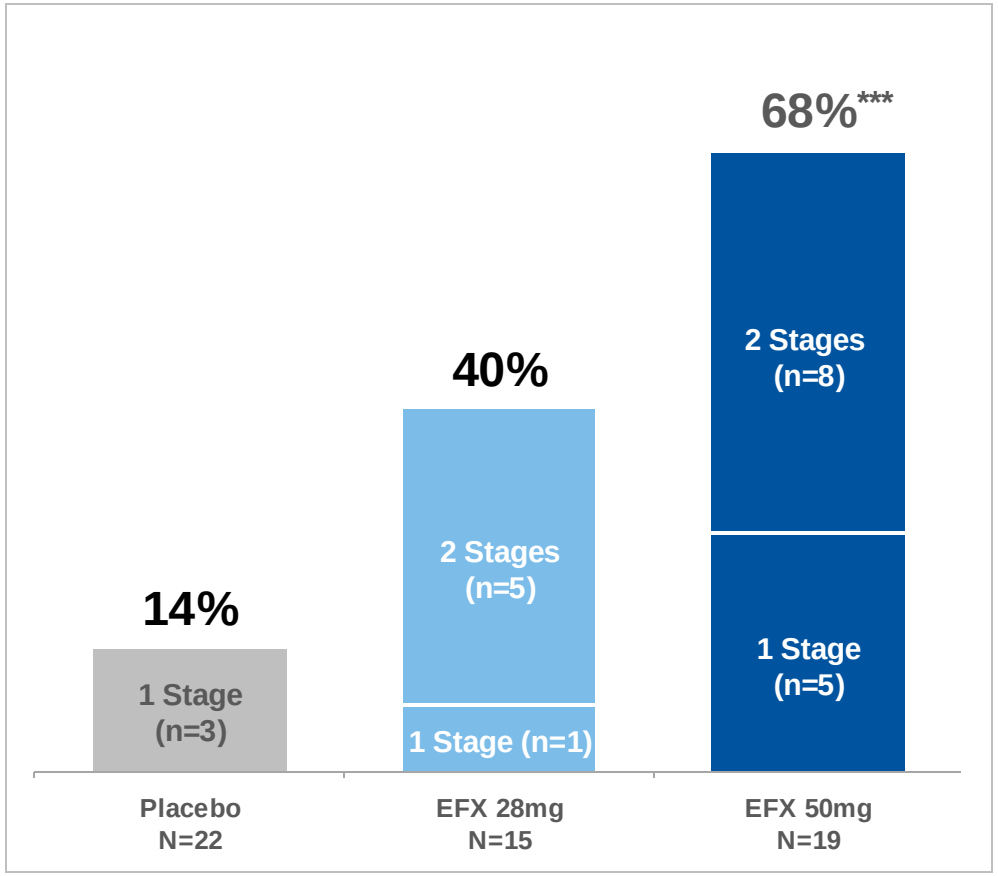
Substantial Improvement in Fibrosis Between Weeks 24 and 96 for EFX-Treated Patients with **F3 Fibrosis** at Baseline

Fibrosis Improvement ≥1 Stage & No Worsening of MASH[1] at Weeks 24 and 96



[1] All participants with baseline F3 fibrosis and on-treatment biopsy at specified timepoint
*** p<0.001, versus placebo at W96 (CMH])

1- vs 2-Stage Fibrosis Improvement & No Worsening of MASH[2] at Week 96



[2] All participants with baseline F3 fibrosis and Week 96 biopsy
*** p<0.001, versus placebo (CMH)

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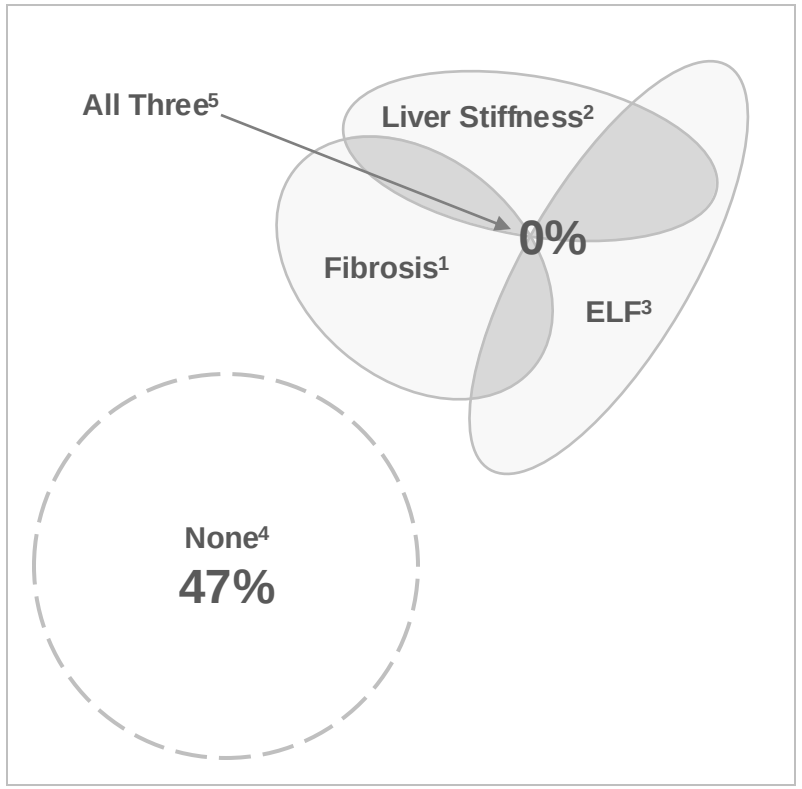
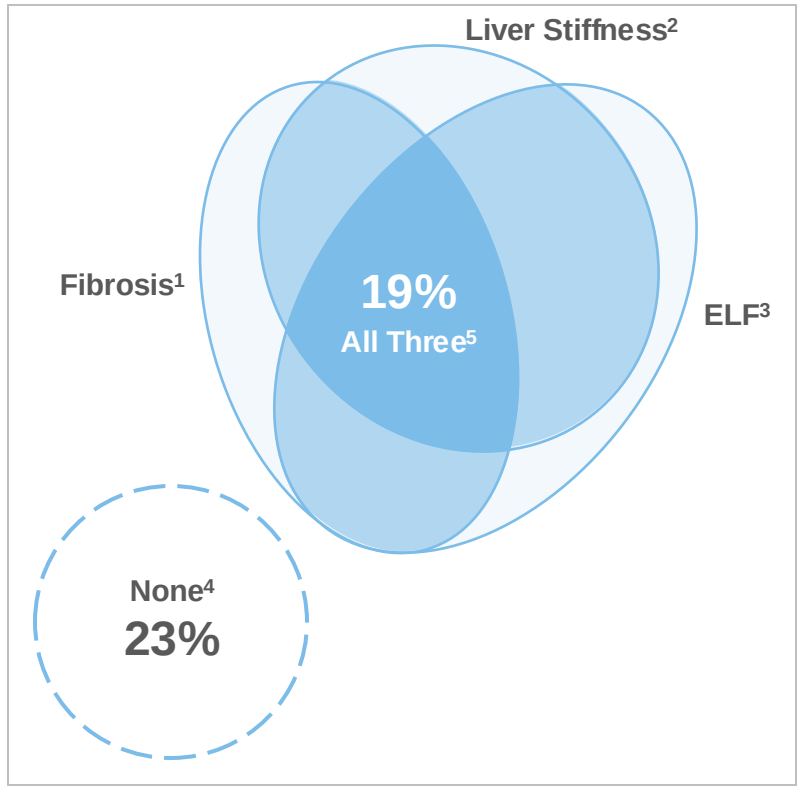
Overlap of Imaging and Circulating Biomarkers of Fibrosis at 96 Weeks Corroborates Conventional Histopathology only in EFX-treated Individuals

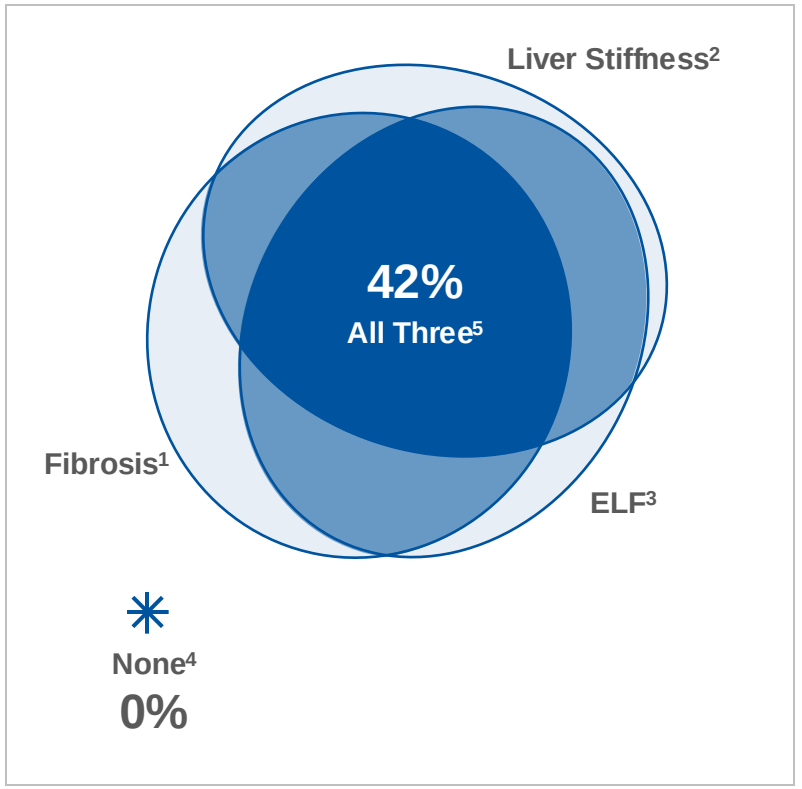
Placebo (N=32)



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** (≥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

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HARMONY

Areas, including overlaps, are proportional to response percentage

Source Data: Subset of the LBAS-W96 with available data

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

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Safety Overview

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, INR[1], MELD[2] and CP[3] 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

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[1] Prothrombin International Normalized Ratio; [2] Model for End-Stage Liver Disease; [3] Child-Pugh

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

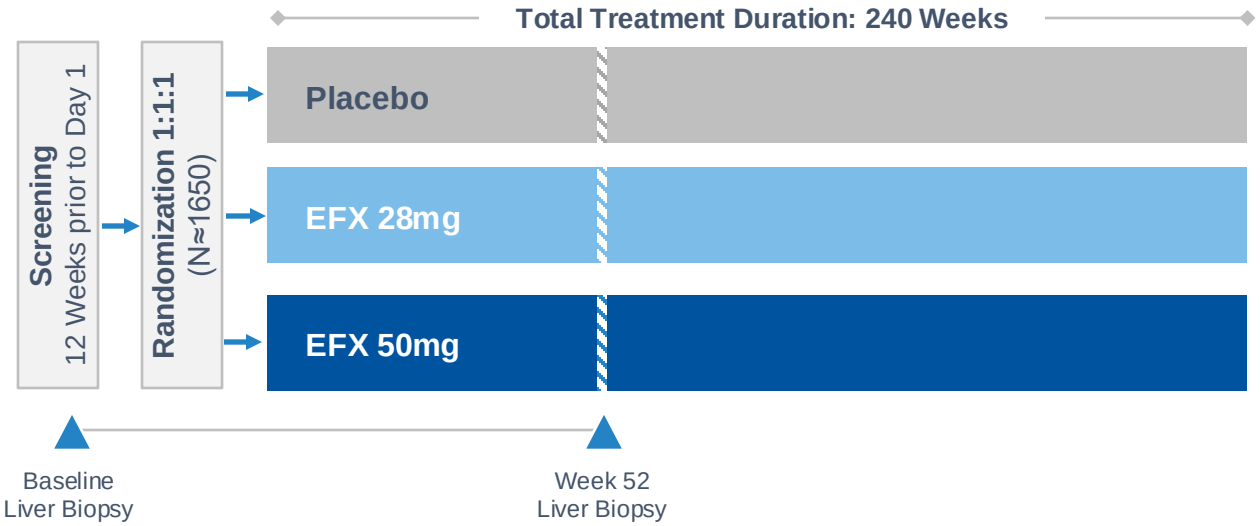
synchrony HISTOLOGY

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

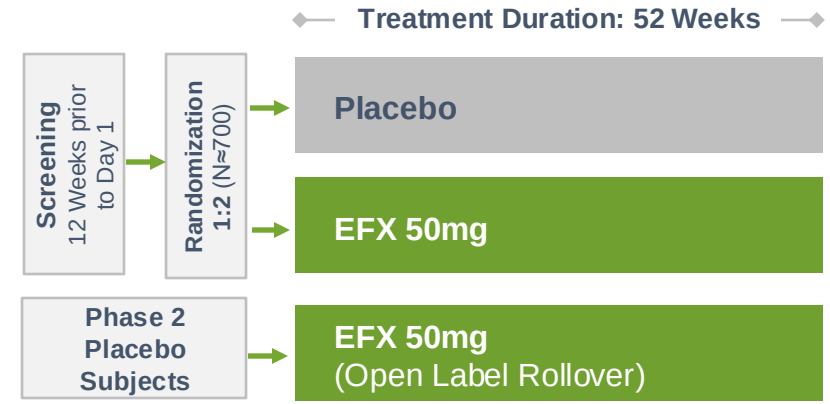


synchrony REAL-WORLD

Primary Endpoint
Safety & Tolerability

Patient Population
MASH/MASLD

Readout Expected
1H 2026



Double-Blind Enrollment Completed

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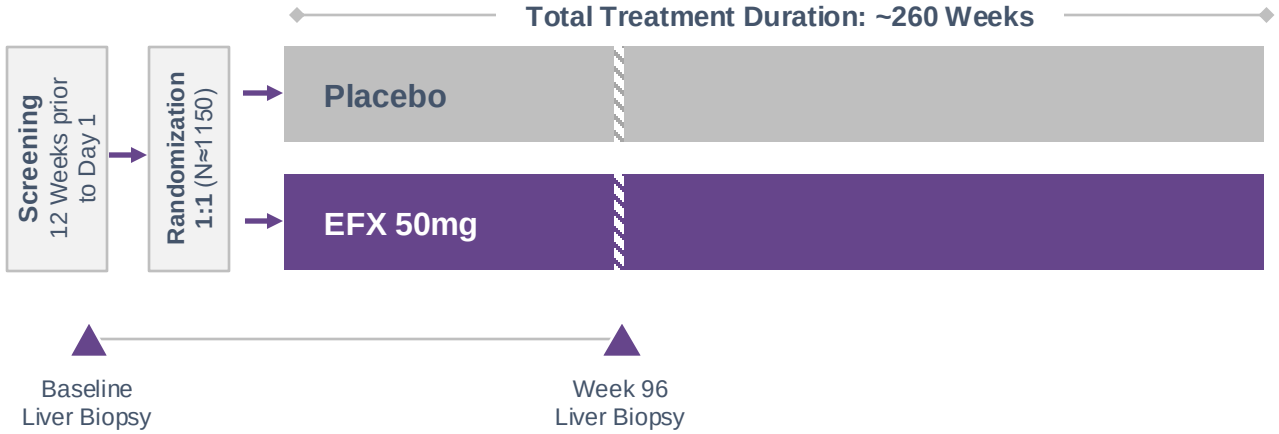
Phase 3 SYNCHRONY Trial Design:
Outcomes (F4, Compensated)

synchrony OUTCOMES

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

Patient Population
Cirrhosis Due to MASH (F4, Compensated)

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

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