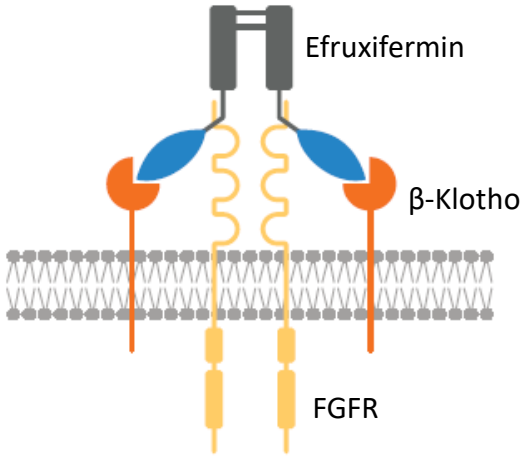
American College of Gastroenterology Annual Scientific Meeting
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Efruxifermin induced a rapid and direct antifibrotic response that was sustained through 96 weeks in phase 2b trials of participants with MASH and F2/F3 fibrosis or cirrhosis

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Introduction and Aim

Efruxifermin and target receptor



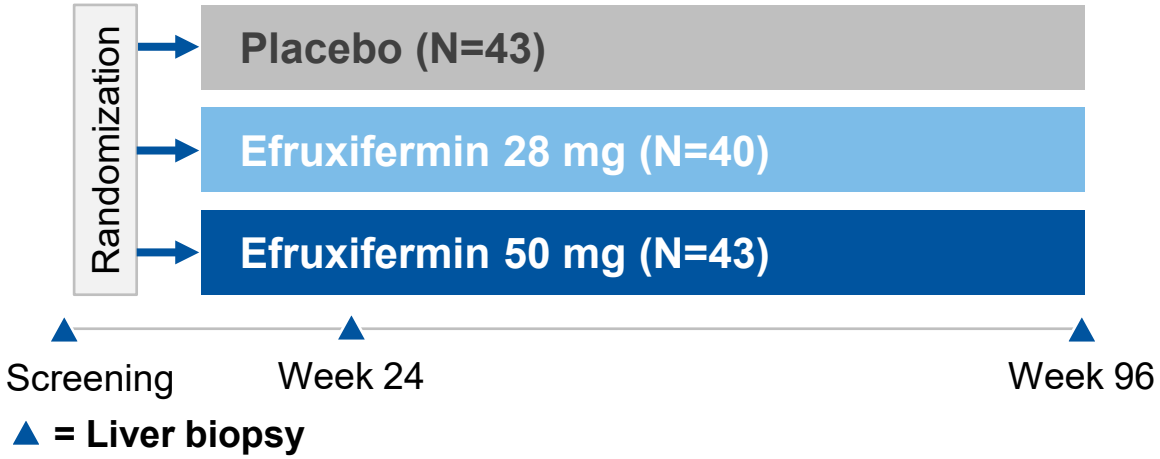
- Metabolic dysfunction-associated steatohepatitis (MASH) is a progressive liver disease characterized by excess hepatic fat accumulation, which can lead to fibrosis, cirrhosis, liver failure, and hepatocellular carcinoma.
- There are no approved treatments for MASH cirrhosis.
- Efruxifermin is a bivalent Fc-FGF21 analog with balanced agonism of FGFR1c, 2c, and 3c that is in development for treatment of MASH.
- In phase 2b trials, efruxifermin improved fibrosis and cardiometabolic markers in participants with MASH and moderate to advanced (F2/F3) fibrosis or compensated cirrhosis (F4c).[1,2]

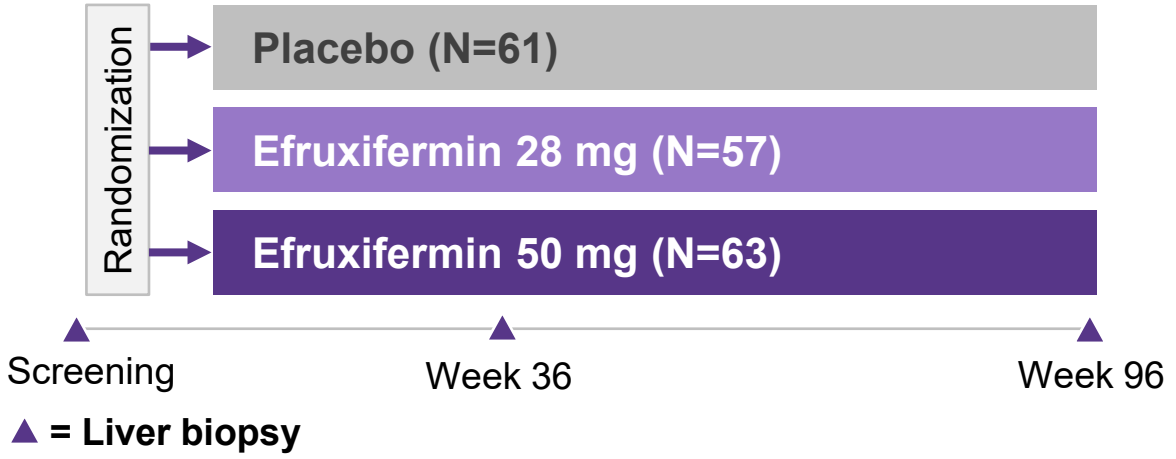
AIM: Evaluate the time course of fibrosis improvement with efruxifermin in participants with MASH and moderate to advanced (F2/F3) fibrosis or compensated cirrhosis (F4c).

[1] Noureddin et al. Lancet. 2025;406(10504):719–730. [2] Noureddin et al. N Engl J Med. 2025;392(24):2413–2424.

Design of Phase 2b Trials of Efruxifermin

	HARMONY: F2/F3 MASH[1]	SYMMETRY: F4c MASH[2]
Population	• 126 randomized and dosed • 88 with Week 96 liver biopsy	• 181 randomized and dosed • 134 with Week 96 liver biopsy
Participants	Age 55 years, 62% female, 70% T2D, 16% GLP-1 RA* BMI 38 kg/m^2, 66% F3	Age 61 years, 67% female 80% T2D, 35% GLP-1 RA* BMI 36 kg/m^2



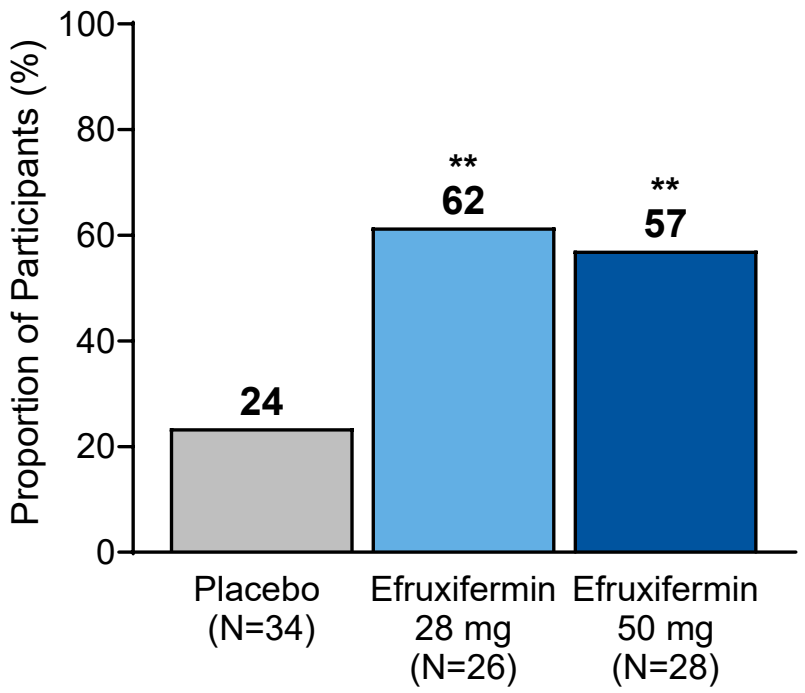


[1] Noureddin et al. Lancet 2025;405(10504):719-730; [2] Noureddin et al. N Engl J Med. 2025;392(24):2413–2424. *GLP-1 RA reflects proportion of participants with concomitant use at any time in the study.
BMI, body mass index; GLP-1 RA, glucagon-like peptide-1 receptor agonist; MASH, metabolic dysfunction-associated steatohepatitis; T2D, type 2 diabetes.

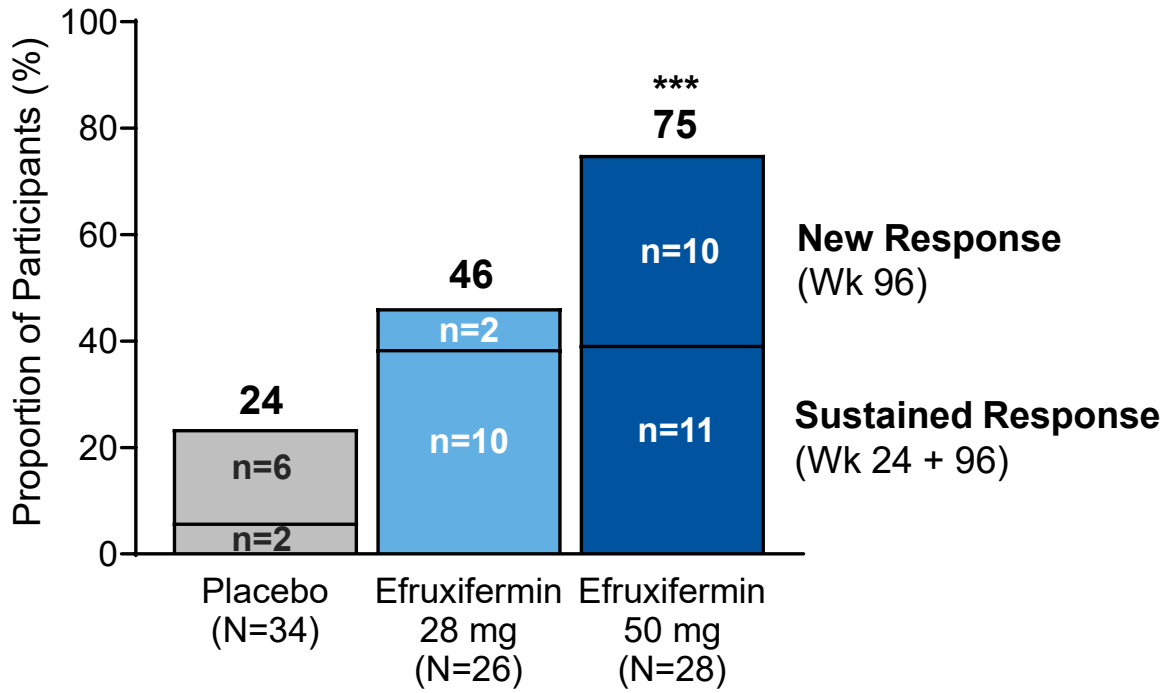
HARMONY: F2/F3 MASH

Efruxifermin Improved MASH and Fibrosis[1,2]

MASH Resolution without Fibrosis Worsening at Week 96



≥1-Stage Fibrosis Improvement without MASH Worsening at Week 96



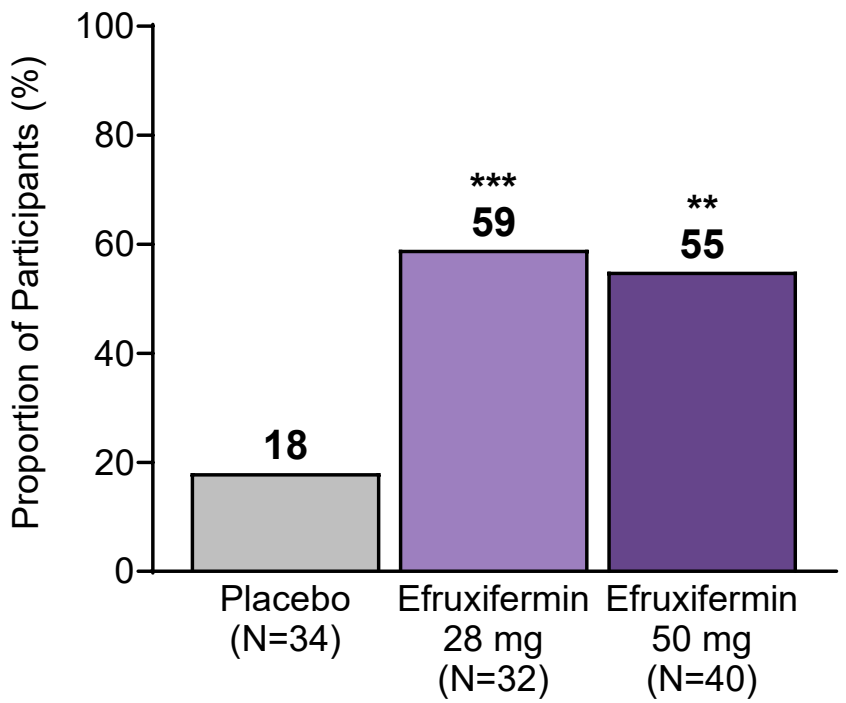
New Response	Week 96 response only
Sustained Response	Week 24 **and** Week 96 Response

[1] Harrison et al. Lancet Gastroenterol Hepatol. 2023 Dec;8(12):1080-1093; [2] Noureddin et al. Lancet 2025;405(10504):719-730. *p<0.05, **p<0.01, ***p<0.001 vs placebo (Cochran-Mantel-Haenszel test).
Data are for participants with baseline, Week 24, and Week 96 liver biopsies (N=88). MASH, metabolic dysfunction-associated steatohepatitis.

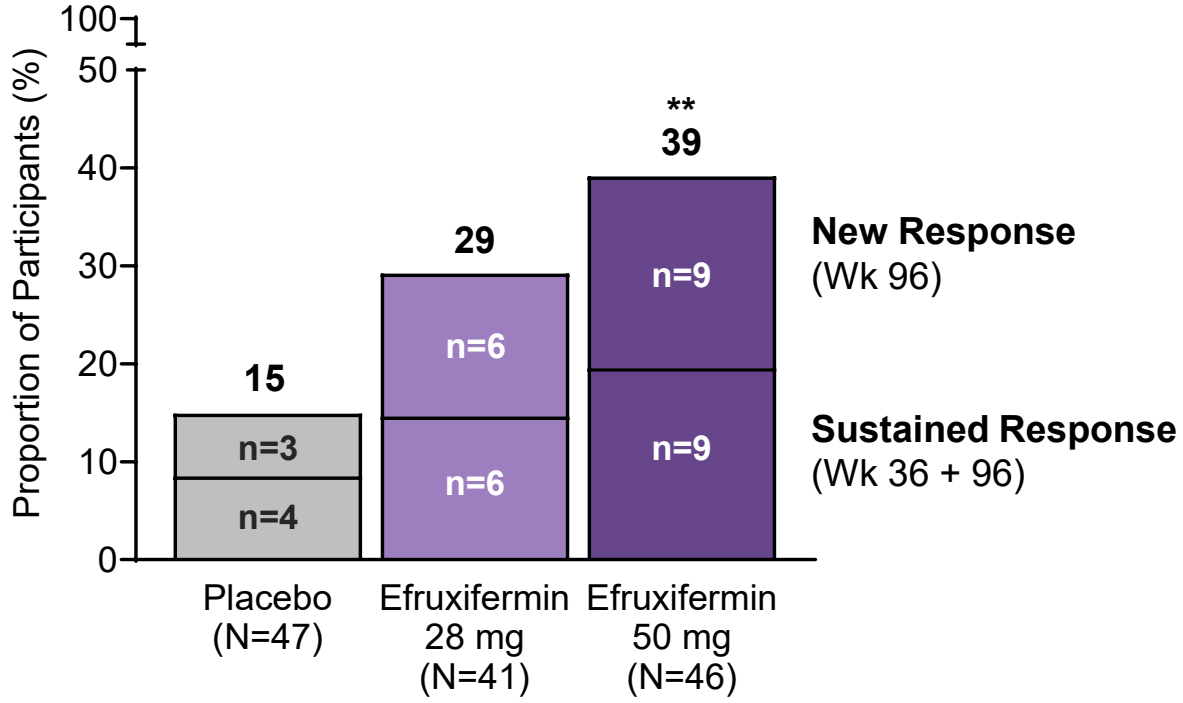
SYMMETRY: F4c MASH

Efruxifermin Improved MASH and Fibrosis[1]

MASH Resolution without Fibrosis Worsening at Week 96



≥1-Stage Fibrosis Improvement without MASH Worsening at Week 96

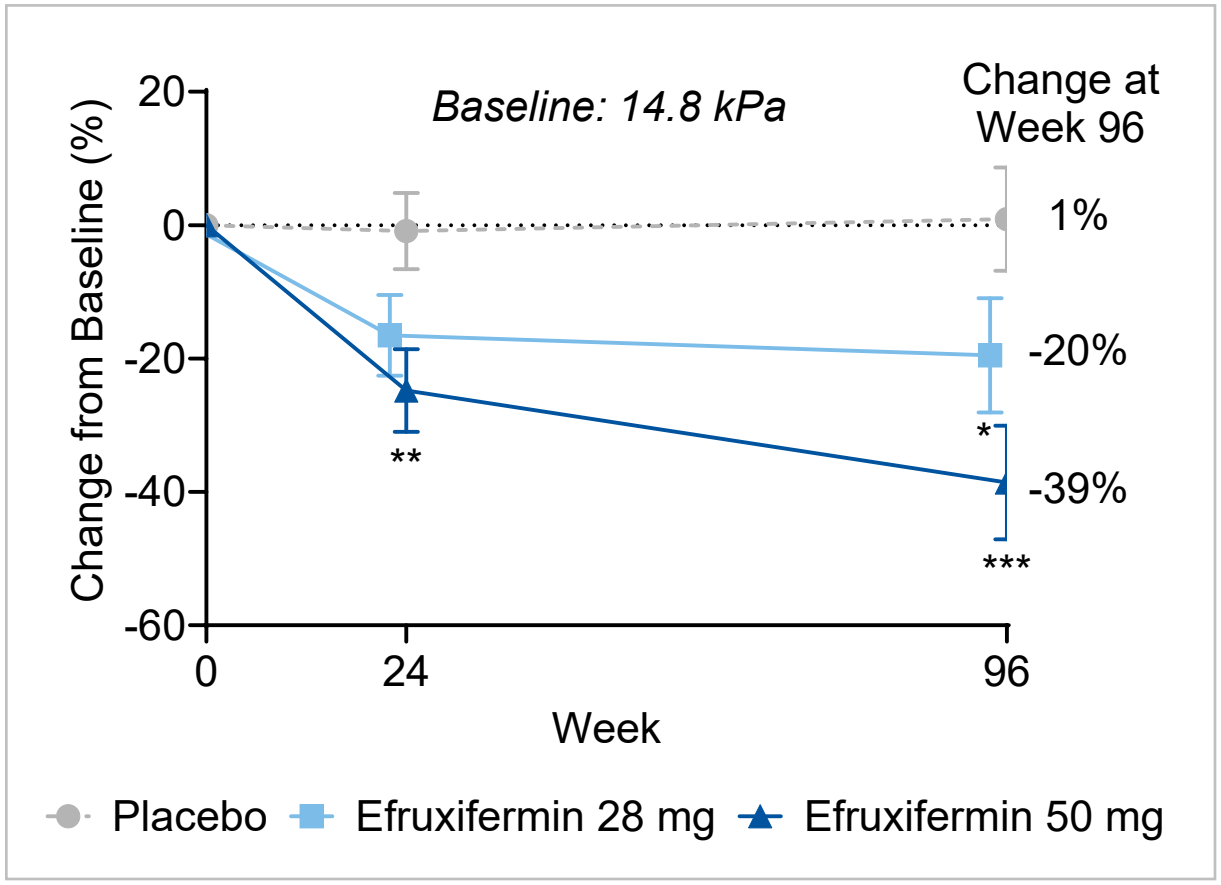


New Response	Week 96 response only
Sustained Response	Week 36 **and** Week 96 Response

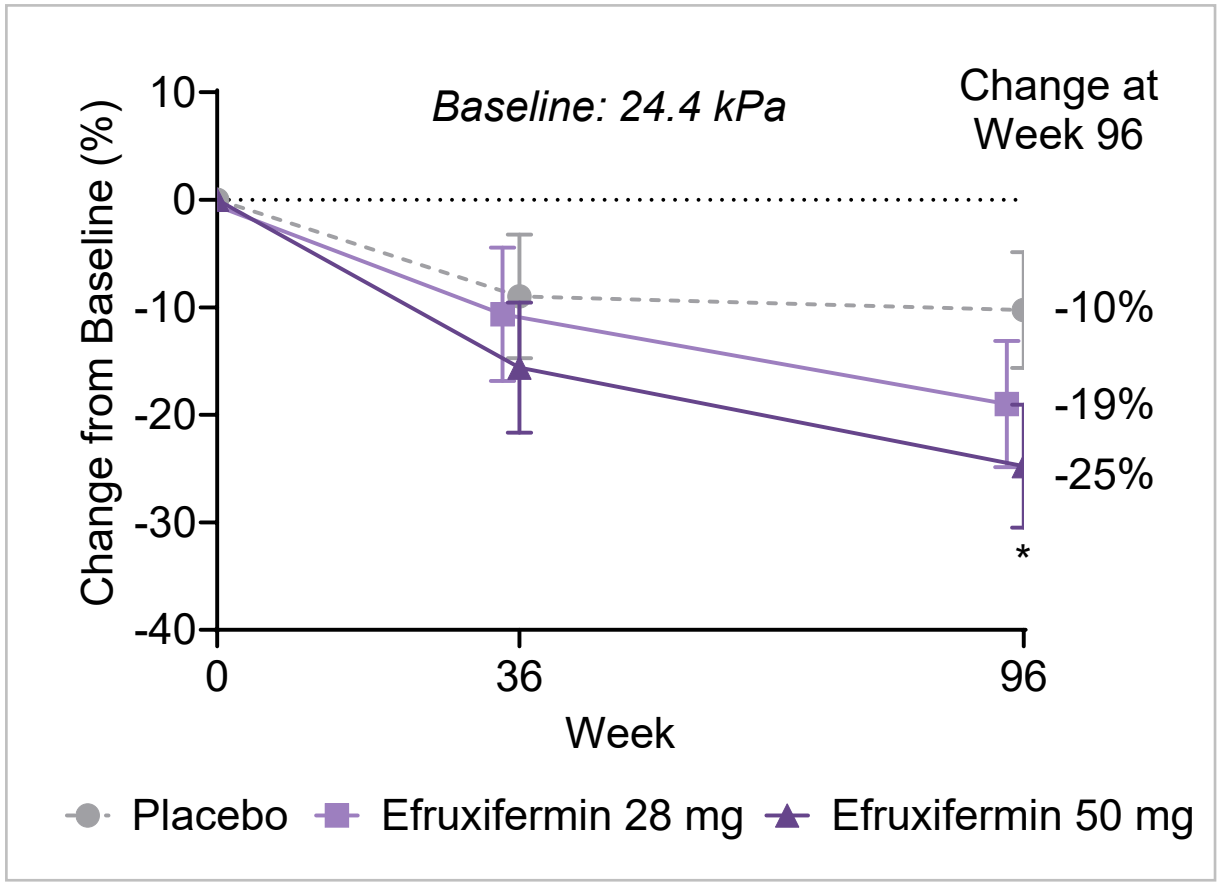
[1] Noureddin et al. N Engl J Med 2025;392(24):2413-2424. *p<0.05, **p<0.01, ***p<0.001 vs placebo (Cochran-Mantel-Haenszel test). MASH resolution data are for participants with biopsy-defined MASH at baseline (N=106). Data are for participants with baseline, Week 36, and Week 96 liver biopsies (N=134). MASH, metabolic dysfunction-associated steatohepatitis.

Liver Stiffness by VCTE: Rapid Improvement that Increased at Week 96

HARMONY: F2/F3 MASH



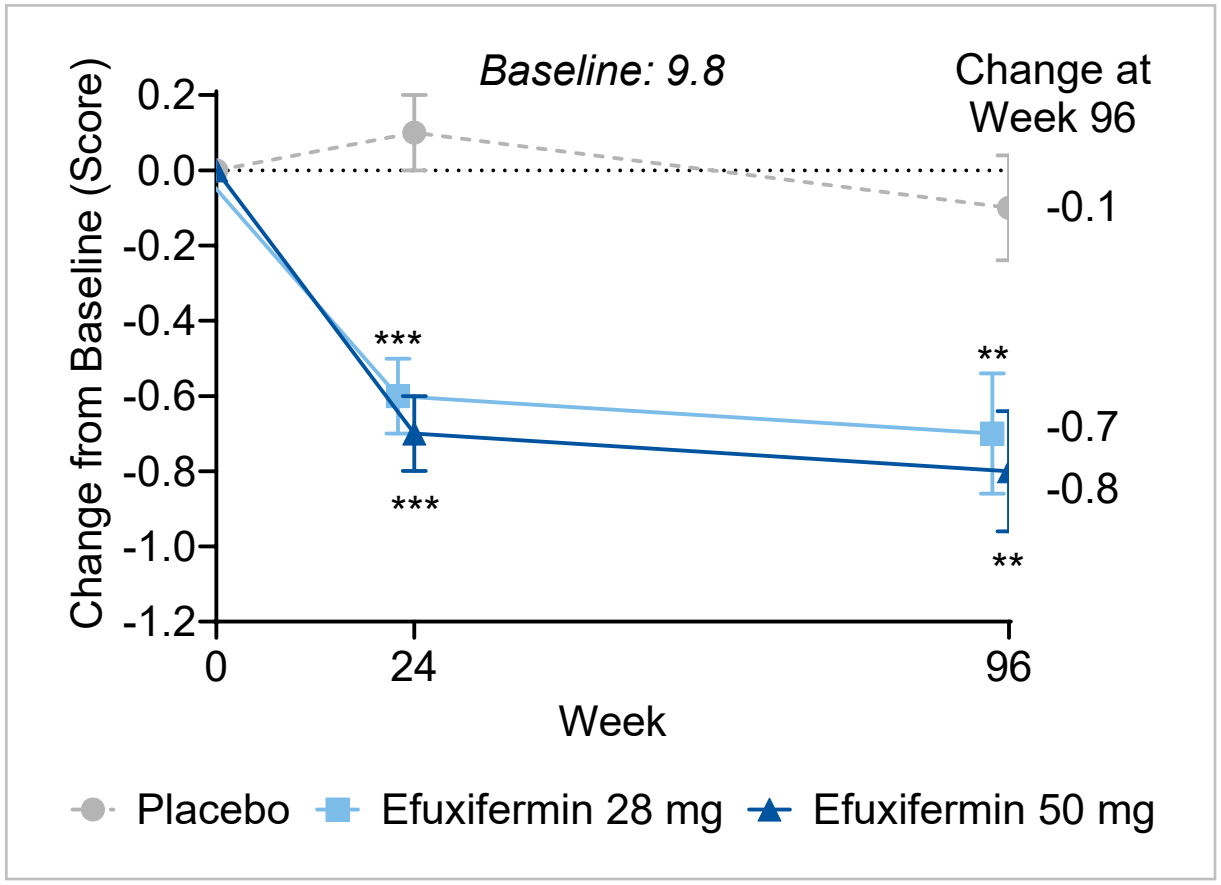
SYMMETRY: F4c MASH



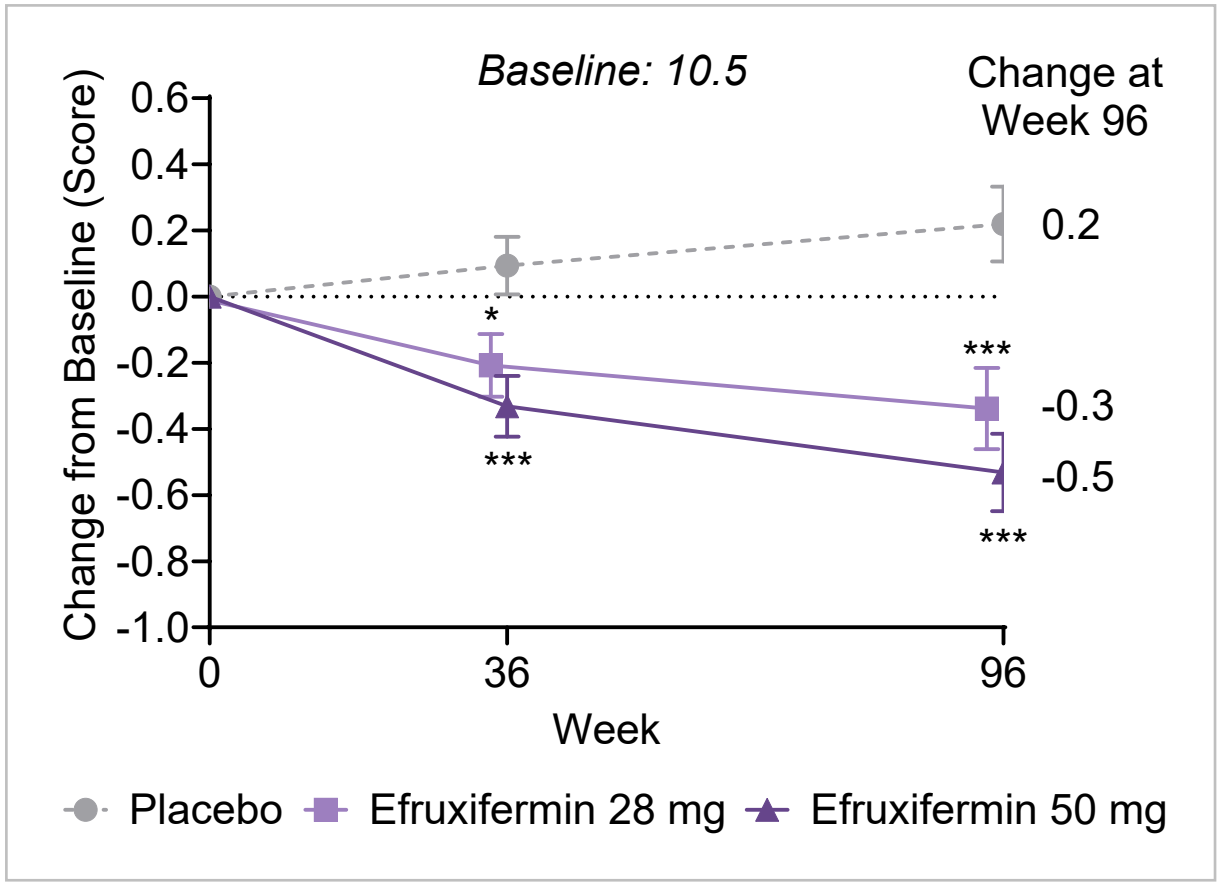
Data are LS mean and SE. *p<0.05, **p<0.01, ***p<0.001 vs placebo (MMRM analysis). F2/3 MASH data are observed values for the mITT population (N=126) at Week 96 in HARMONY. F4c MASH data are observed values for the ITT population (N=181) at Week 96 in SYMMETRY. Liver stiffness was assessed by vibration-controlled transient elastography (FibroScan).

ELF: Rapid and Sustained Improvement at Week 96

HARMONY: F2/F3 MASH



SYMMETRY: F4c MASH



Data are LS mean and SE. *p<0.05, **p<0.01, ***p<0.001 vs placebo (MMRM analysis). F2/3 MASH data are observed values for the mITT population (N=126) at Week 96 in HARMONY. F4c MASH data are observed values for the ITT population (N=181) at Week 96 in SYMMETRY. ELF, Enhanced Liver Fibrosis test.

Efruxifermin Safety and Tolerability Across Phase 2b Trials

- Most common AEs were gastrointestinal, mild-to-moderate, transient, and generally occurred early in treatment. No signal for other AEs of interest.
  - Despite AEs of increased appetite, mean body weight was generally unchanged.
- Small but statistically significant reductions in BMD at Week 96, clinical relevance to be determined. No increase in fractures.
- No reported events of DILI. Liver function and hemostasis markers remained stable.

	HARMONY: F2/F3 MASH			SYMMETRY: F4c MASH		
	Placebo N=43	Efruxifermin 28 mg N=40	Efruxifermin 50 mg N=43	Placebo N=61	Efruxifermin 28 mg N=57	Efruxifermin 50 mg N=63
AE leading to discontinuation	0	10%	7%	3%	11%	17%
Any SAE	0	0	9%	18%	26%	24%
Frequent AEs						
Diarrhea	30%	58%	44%	30%	42%	54%
Nausea	30%	40%	44%	30%	30%	46%
Increased appetite	7%	20%	23%	7%	16%	40%
Injection site erythema	19%	25%	19%	10%	23%	25%

Data are for the safety analysis sets HARMONY (N=126), SYMMETRY (N=181).
AE, adverse event; BMD, bone mineral density; DILI, drug-induced liver injury; SAE, serious adverse event.

Conclusions and Phase 3 Trials of Efruxifermin

- In phase 2b trials, efruxifermin improved MASH and fibrosis in participants with MASH and F2/F3 fibrosis or compensated cirrhosis.
- Most participants with early fibrosis response maintained their response through Week 96. Additional early nonresponders had a fibrosis response at Week 96, supporting the strong hepatic antifibrotic effect of efruxifermin.
- Efruxifermin was generally well tolerated. Most common AEs were gastrointestinal and transient.

Phase 3 program enrolling individuals with MASH and fibrosis or cirrhosis

synchrony HISTOLOGY	synchrony OUTCOMES
• **Currently enrolling:** NCT06215716 • F2/F3 MASH: Biopsy-defined moderate to advanced fibrosis due to MASH • 28 and 50 mg efruxifermin	• **Currently enrolling:** NCT06528314 • F4c MASH: Biopsy-defined or **noninvasively diagnosed** compensated cirrhosis due to MASH • 50 mg efruxifermin