THE FORUM
For Collaborative Research℠
Berkeley's Hub for Regulatory Science

Company Updates

UC Berkeley Public Health

Madrigal Update

Becky Taub

9-26

Pam, patient advocate

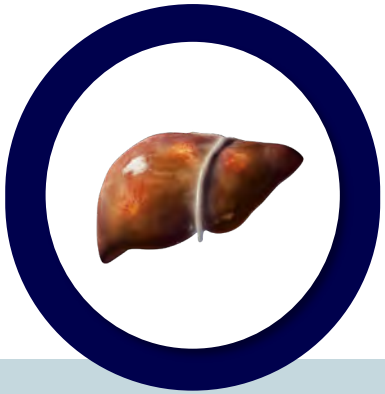
Madrigal Portfolio

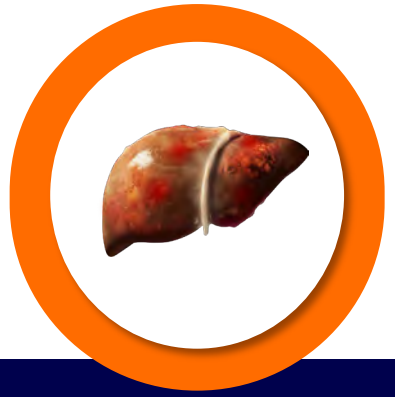
	MOA	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Launched
Rezdiffra® resmetirom tablets	THR-β agonist	MASH F2/F3					
	THR-β agonist	MASH F4c					
Ervogastat/resmetirom combo[1]	Oral DGAT-2 inhibitor	MASH					
MGL-2086/resmetirom combo[2]	Oral GLP-1 receptor agonist	MASH					
ARO-PNPLA3/resmetirom combo[3]	siRNA	MASH					
Undisclosed/resmetirom combo	siRNA (6)	MASH					
Additional MASH Assets in varying stages of development	Exploratory oral assets (3)	MASH					

1. Ervogastat monotherapy Phase 2b trial completed by Pfizer; drug-drug (resmetirom/ervogastat) interaction (DDI) trial expected to initiate in 4Q26; Phase 2 combination trial expected to initiate in 2027 following regulatory discussions; 2. MGL-2086 Phase 1 single ascending dose (SAD) trial expected to initiate in 2Q26; 3. ARO-PNPLA3 monotherapy Phase 1 trial completed by Arrowhead; **MOA**: Mechanism of action; **THR-β:** Thyroid hormone receptor beta; **DGAT-2:** Diacylglycerol *O*-acyltransferase 2; **GLP-1:** Glucagon-like peptide-1; **siRNA:** Small interfering RNA.

Phase 3 MAESTRO Clinical Development Program

MAESTRO clinical trials are intended to provide a comprehensive dataset in patients with MASH





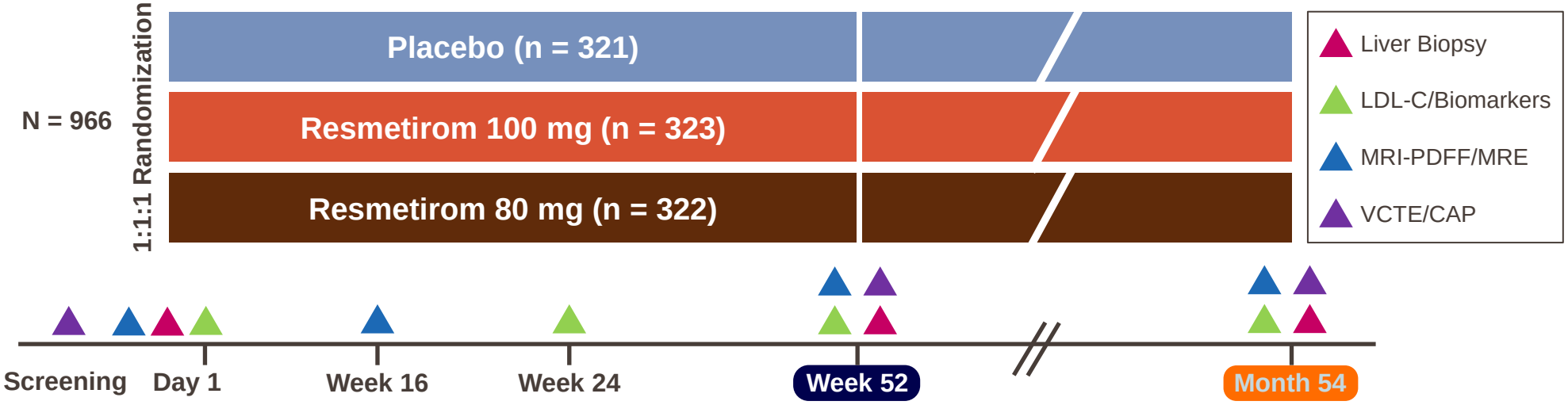
MAESTRO NAFLD-1[1]	MAESTRO NAFLD-OLE[2,3]	MAESTRO NASH[4]	MAESTRO NASH OUTCOMES[5]
Safety and tolerability as measured by incidence of TEAEs	Safety and tolerability as measured by incidence of TEAEs (extension to MAESTRO-NAFLD-1)	MASH resolution and/or fibrosis improvement on liver biopsy and composite clinical events	Event-driven trial evaluating progression to hepatic decompensation in patients with well-compensated MASH cirrhosis
52 weeks (completed)	52 weeks (ongoing)	52 weeks biopsy (completed); 54 months clinical outcomes (ongoing)	~36 months (ongoing)
1143 patients	1000 patients (estimated)	1050 patients (52 weeks) 1759 patients (54 months)	845 patients

Resmetirom is not approved by the United States Food and Drug Administration to treat cirrhosis and the safety and effectiveness of resmetirom for the treatment of cirrhosis has not been established.
aNo efficacy or safety data available yet. The study duration is expected to be 2-3 years for accrual of the required number of composite clinical outcome events.
MASH, metabolic dysfunction–associated steatohepatitis; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; OLE, open-label extension; TEAE, treatment-emergent adverse event.
1. Harrison SA et al. Nat Med. 2023;29(11):2919-2928. 2. Alkhouri N et al. Presented at EASL International Liver Congress: May 7-10 2025; Amsterdam, the Netherlands. 3. A Phase 3 Study to Evaluate Safety and Biomarkers of Resmetirom (MGL-3196) in Patients With Non-alcoholic Fatty Liver Disease (NAFLD), MAESTRO-NAFLD-Open-Label-Extension (MAESTRO-NAFLD-OLE). Updated August 3, 2025. Accessed August 12, 2025. https://clinicaltrials.gov/study/NCT04951219/ 4. Harrison SA et al. N Engl J Med. 2024;390:497-5096. 5. Schattenberg JM et al. Poster SAT-424. Presented at EASL International Liver Congress: May 7-10, 2025; Amsterdam, the Netherlands.

MAESTRO-NASH (M-NASH) Trial Design[1,2]

Key inclusion criteria

- 18 years of age or older
- ≥3 metabolic risk factors
- VCTE-LSM ≥8.5 kPa, CAP ≥280 dB/m
- Biopsy confirmed MASH with fibrosis stage F1B, F2 and F3 (no more of 15% F1B)
- ELF ≥9
- ≥8% liver fat on MRI-PDFF



Week 52 Primary analysis

- **Dual primary endpoints**
  - MASH resolution: (ballooning = 0, inflammation =0/1), and ≥ 2 point improvement in NAS with no worsening of fibrosis
  - Fibrosis improvement ≥1 stage with no worsening of NAS
- **Key secondary endpoint**
  - LDL-C lowering at Week 24

Month 54 Primary Analysis

- **Composite Clinical Outcomes**
  - Hepatic decompensation events
  - Histologic progression to cirrhosis
  - All-cause mortality
  - MELD score increase < 12 to ≥15
  - Liver transplant

MAESTRO-NASH trial is ongoing

[a]Patients were stratified at randomization by fibrosis stage (F2 or F3) or T2D status (present or absent) at baseline.
CAP, controlled attenuation parameter; ELF, enhanced liver fibrosis test; F, (F1: mild fibrosis, F2: moderate fibrosis, F3: advanced fibrosis); kPa, kilopascal; LDL-C, low-density lipoprotein cholesterol; LSM, liver stiffness measurement; MASH, metabolic dysfunction–associated steatohepatitis; MRE, magnetic resonance elastography; MRI-PDFF, magnetic resonance imaging proton density fat fraction; NAS, nonalcoholic fatty liver disease activity score; VCTE, vibration-controlled transient elastography.

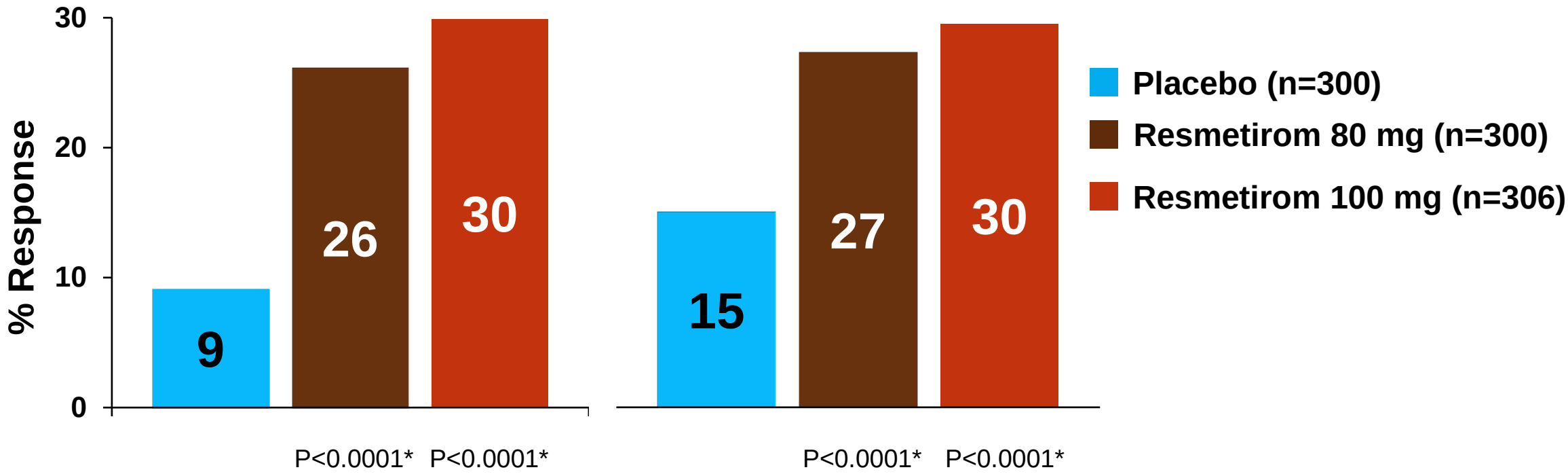
1. Harrison SA et al. *N Engl J Med*. 2024;390:497-509. 2. Harrison SA et al. *Aliment Pharmacol Ther*. 2024;59(1):51-63.

Published 2026: Secondary Analyses of the MAESTRO-NASH Trial

- Online in EMA review, and in new a manuscript (APT), reanalysis of primary endpoint with placebo response and multiple imputation analyses of the F2/F3 population
- Secondary analysis of MAESTRO-NASH using qFibrosis, “Quantitative regression of qFibrosis with resmetirom: Exploratory histologic endpoints from the MAESTRO-NASH phase III clinical trial”
- Prespecified analysis of MAESTRO-NASH “Effects of MASH risk genotypes on resmetirom efficacy in patients with MASH and fibrosis”, *JHEP in press*
- “Machine Learning Models of Non-Invasive Tests to Predict Metabolic Dysfunction-Associated Steatohepatitis and Fibrosis Stage”; *Hepatology communications in press*

MAESTRO-NASH F2 F3 Population (SAP defined population and analysis*)

NASH Resolution Response[a] ≥1 Stage Fibrosis Improvement[b]

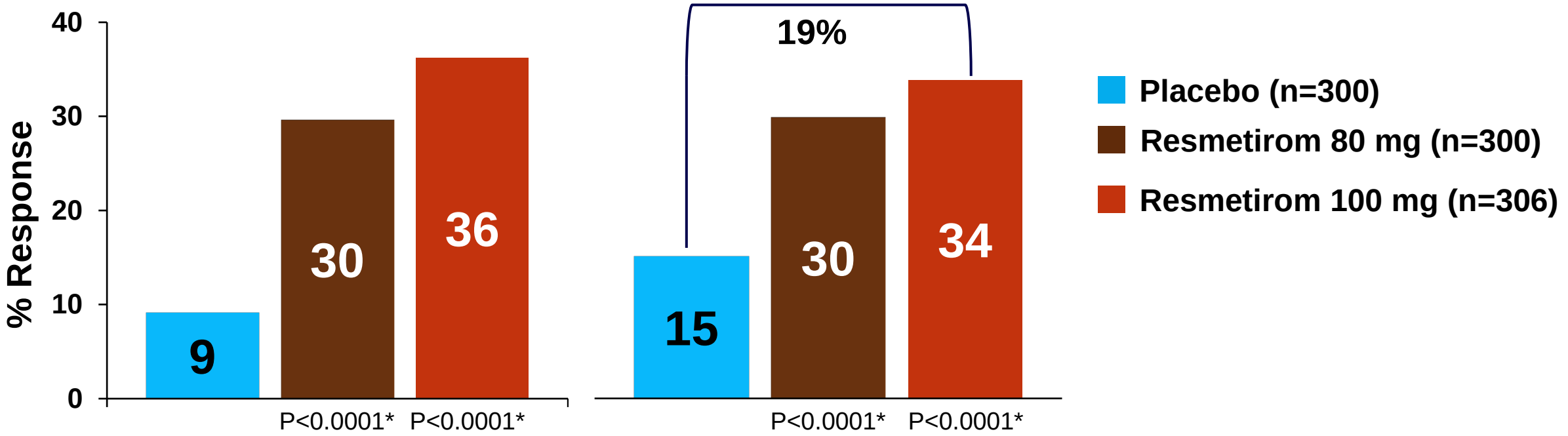


- MAESTRO-NASH biopsy responses show a greater than **3-fold benefit relative to placebo on NASH Resolution and 2-fold benefit on Fibrosis Improvement**
- More than half of resmetirom treated patients have a response on NASH and/or Fibrosis endpoints

[a] * Placebo response imputation
NASH Resolution response: NASH resolution (ballooning 0,1) with at least a 2-point improvement in NAS and no worsening of fibrosis
[b] Fibrosis improvement response: ≥1 stage improvement in fibrosis with no worsening of NAS
* All P values are nominal.

MAESTRO-NASH: Treatment Assignment Based Imputation

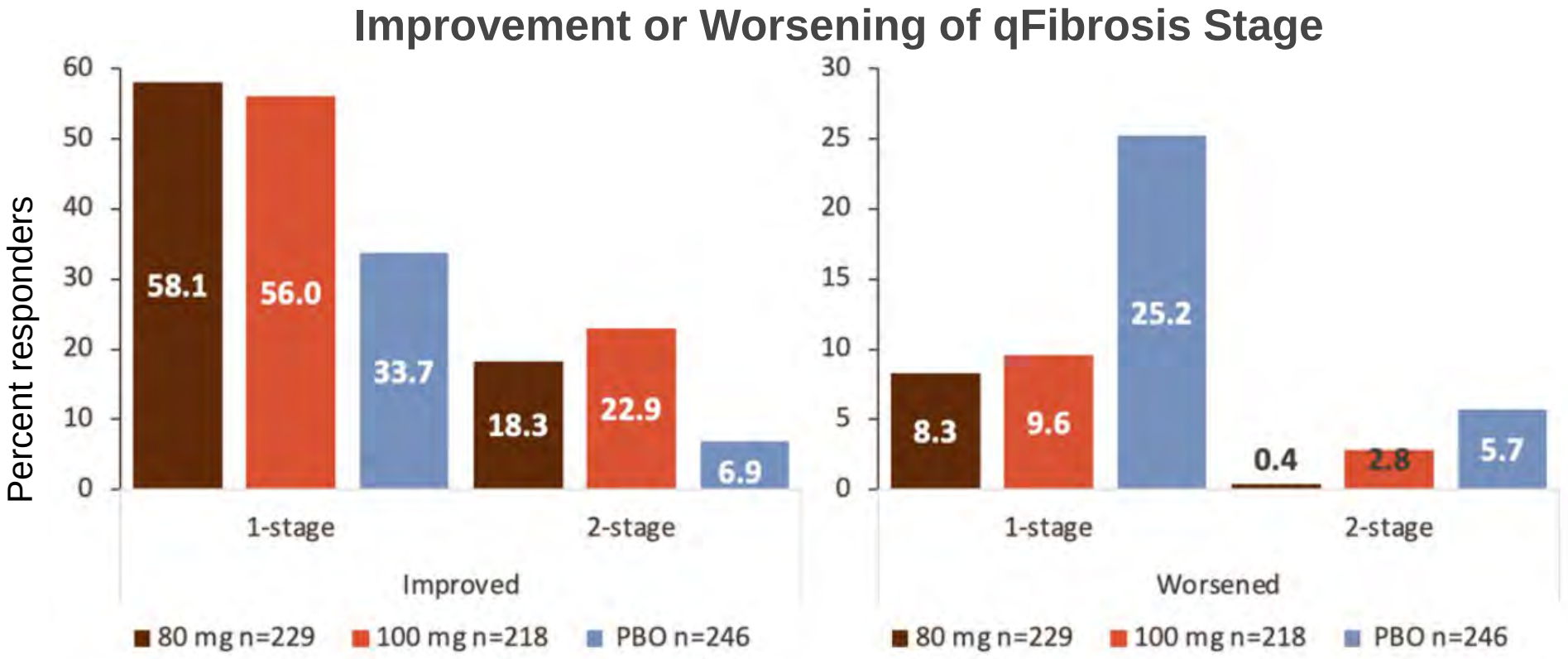
NASH Resolution Response[a] ≥1 Stage Fibrosis Improvement[b]



- Using a treatment response imputation or completer biopsy analysis similar to analyses of biopsy studies in Phase 2 studies, the difference in NASH Resolution response in resmetirom patients is ~ 30% and fibrosis improvement ~20% greater than placebo, **at least comparable or more robust than other mechanisms in development**

[a] NASH Resolution response: NASH resolution (ballooning 0,1) with at least a 2-point improvement in NAS and no worsening of fibrosis
[b] Fibrosis improvement response: ≥1 stage improvement in fibrosis with no worsening of NAS
* All P values are nominal.

Quantitative regression of qFibrosis with resmetirom: Exploratory histologic endpoints from MAESTRO-NASH



80 mg (N=229)	100 mg (N=218)	Placebo (N=246)	80 mg - Placebo	100 mg - Placebo
Overall qFC Change from Baseline (LS mean, 95% CI)			Mean Difference (95% CI)	
-1.1 (-1.3, -0.9)	-1.2 (-1.4, -1.0)	-0.2 (-0.3, 0.0)	-1.0 (-1.2, -0.7)	-1.1 (-1.3, -0.8)

Effects of MASH risk genotypes on resmetirom efficacy in patients with MASH and fibrosis

Background

In a phase 3 randomized, controlled trial, resmetirom significantly improved MASH and fibrosis in patients with MASH and F2/F3.

Aim

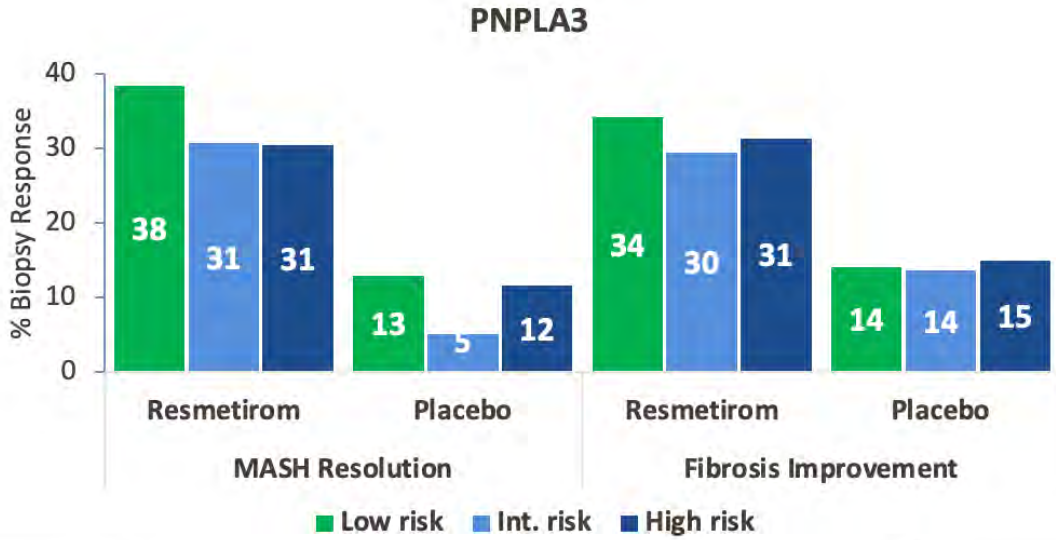
We interrogated the effect of select MASH genetic variants (*PNPLA3*, *HSD17B13*, *TM6SF2*, *MTARC1*, *MBOAT7*, and *SERPINA1)* on histological and biomarker responses to resmetirom among MAESTRO NASH participants.

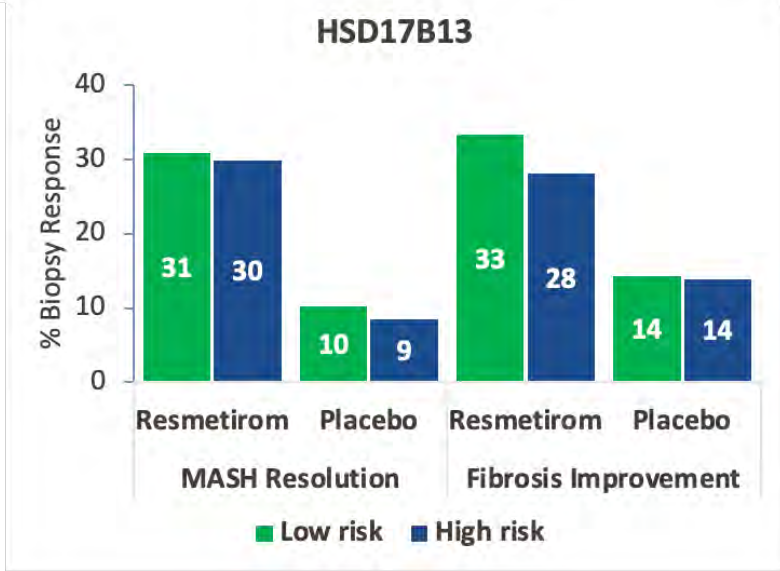
Research Design

This analysis cohort consisted of 742 of 966 randomized participants who had consented for DNA collection and had genotyping and week 52 end-of-treatment biopsy.

Conclusion

The efficacy of resmetirom on improvement in MASH, liver fibrosis, MRI-PDFF, and MASH biomarkers in patients with MASH appears to be independent of their background MASH genetic architecture.





Liver Forum – Novo Nordisk Update

MICHELLE T LONG, MD, MS

INTERNATIONAL MEDICAL VP, MASH

NOVO NORDISK

Semaglutide received conditional regulatory approval from EMA[1] and FDA[2] for treatment of MASH

EMA granted conditional marketing authorization throughout the EU on 26th March 2026[1]

ESSENCE study ongoing (2029) to verify clinical benefit

novo nordisk®

company announcement

Wegovy® approved in the US for the treatment of MASH

Bagsværd, Denmark, 15 August 2025 – Novo Nordisk today announced that the US Food and Drug Administration (FDA) has approved an additional indication for Wegovy® (semaglutide 2.4 mg) based on a supplemental New Drug Application (sNDA) for treatment of noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH) in adults with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis), in combination with a reduced calorie diet and increased physical activity.

The accelerated approval is based on part 1 of the ESSENCE trial, in which Wegovy® demonstrated a statistically significant and superior improvement in liver fibrosis with no worsening of steatohepatitis, as well as resolution of steatohepatitis with no worsening of liver fibrosis compared to placebo.

The clinical data from ESSENCE showed that at week 72, 36.8% of people treated with Wegovy® achieved improvement in liver fibrosis with no worsening of steatohepatitis compared to 22.4% treated with placebo. 62.9% of people treated with Wegovy® achieved resolution of steatohepatitis with no worsening of liver fibrosis compared to 34.3% treated with placebo.

FDA, Food and Drug Administration; EMA, European Medicines Agency; 1. EMA conditional approval https://www.ema.europa.eu/en/documents/overview/kayshild-epar-medicine-overview_en.pdf [Accessed 31 Aug 2026] 2. FDA approval FDA Approves Treatment for Serious Liver Disease Known as 'MASH' | FDA [Accessed 31 Aug 2026]

Efruxifermin is being evaluated in the phase 3 SYNCHRONY programme for the treatment of moderate to advanced MASH, including cirrhosis

F1–F4 SYNCHRONY REAL-WORLD[1]
Placebo-controlled

Participants: **700**

Status: **FINISHED ENROLMENT**

Treatment Duration
52 weeks

Primary Outcome:
Safety and tolerability

F2–F3 SYNCHRONY HISTOLOGY[2]
Placebo-controlled

Participants: **1650**

Status: **ENROLLING**

Treatment Duration
~4.5 years

Primary Outcome:
Efficacy and Safety/tolerability

F4* SYNCHRONY OUTCOMES[3]
Placebo-controlled

Participants: **2150**

Status: **ENROLLING**

Treatment Duration
~5 years

Primary Outcome:
Efficacy and Safety/tolerability

**Compensated cirrhosis. †Planned sample.*
F, fibrosis stage; FGF21, fibroblast growth factor 21; MASH, metabolic dysfunction-associated steatohepatitis.
1. clinicaltrials.gov/study/NCT06161571; 2. clinicaltrials.gov/study/NCT06215716; 3. clinicaltrials.gov/study/NCT06528314.

Kriya

The Durable Medicines Company

Durable FGF21 Gene Therapy for Steatotic Liver Disease

Liver Forum 2026, Paris, France

Michele Stone, PhD
Chief Scientific Officer

Safe Harbor

This presentation contains "forward-looking" statements that involve risks, uncertainties and assumptions, and actual results may differ substantially from those projected or expected in the forward-looking statements. Forward-looking statements include, but are not limited to: any projections of financial information; any statements about future development, clinical or regulatory events; any statements concerning Kriya's plans, strategies or objectives; and any other statements of expectation or belief regarding future events. These statements are based on estimates and information available to Kriya at the time of this presentation and are not guarantees of future performance. Any projected financial information constitutes forward-looking information and is for illustrative purposes only and should not be relied upon as necessarily being indicative of future results. The assumptions and estimates underlying such projected financial information are inherently uncertain and are subject to a wide variety of significant business, economic, competitive and other risks and uncertainties that could cause actual results to differ materially from those contained in the prospective financial information. Actual results could differ materially from Kriya's current expectations as a result of many factors including, but not limited to: Kriya's ability to develop successful products that obtain market acceptance; Kriya's ability to estimate future product demand or growth in a nascent and uncertain field; Kriya's ability to obtain additional financing to fund its operations; unexpected delays or results in clinical trials; uncertainties regarding obtaining regulatory approvals; uncertainties regarding the ability to protect Kriya's intellectual property; uncertainties regarding market acceptance of any products for which Kriya is able to obtain regulatory approval, if any; the effects of competition; and other market and general economic conditions. Kriya assumes no obligation for and does not intend to update these forward-looking statements, except as required by law. Accordingly, undue reliance should not be placed upon the forward-looking statements.

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Redesigning Durable Medicine to Reach the Many, Not the Few

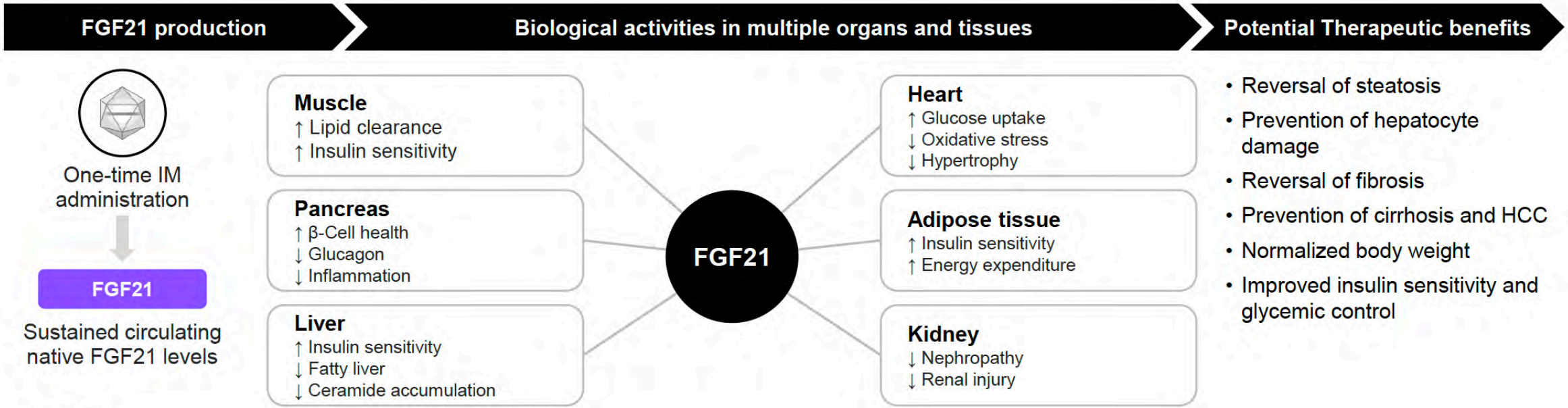
	Conventional Gene Therapy	Kriya The Durable Medicines Company
Cost of Goods	$$$$$	**$$**
Price	Expensive	**Accessible**
Number of Patients	Few	**Common**
Route of Delivery	Systemic or Complex Procedure	**Focal**
Administration	Infusion Centers or In-Hospital Surgeries	**Outpatient, In-Office Procedures**
Treatment Center	Highly Specialized Center of Excellence	**Clinics in the Community**
Practice Economics	Negative / Neutral	**Favorable / Neutral**

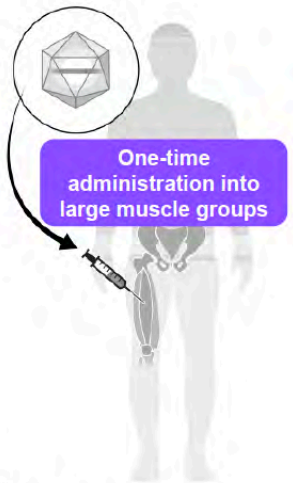
Kriya

Note that the conventional gene therapy include some FDA-approved gene therapy products, while Kriya's pipeline candidates are investigational and have not been approved as safe or effective by any regulatory health authority. Claims are relative and for hypothesis-generating purpose only.

Transformative Potential of FGF21 in Steatotic Liver Disease

KRIYA-497 is a one-time FGF21 gene therapy designed to prevent and reverse fibrosis





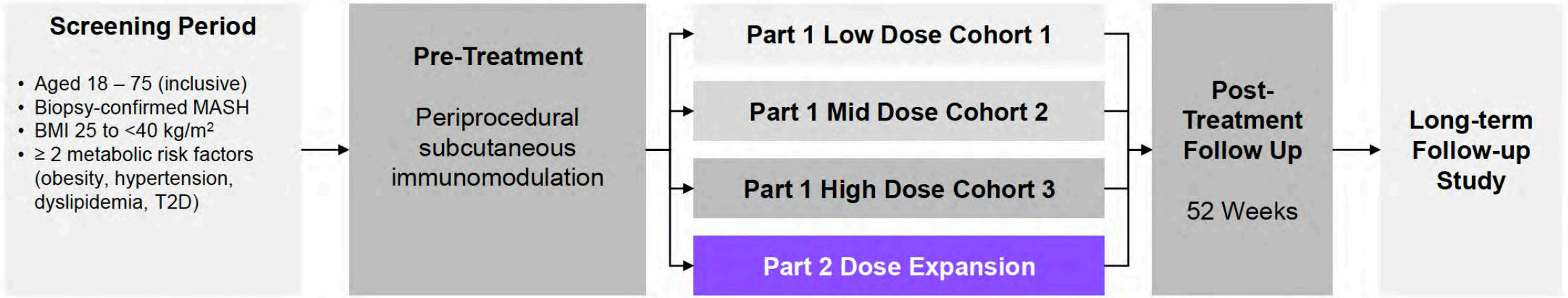
Kriya's gene therapy has the potential for:

- **Robust Anti-Fibrotic Activity** from steady expression of native FGF21 protein to drive natural ligand / receptor interactions and enhance biodistribution across multiple organs
- **Continuous, Steady Expression of Native FGF21** may limit Cmax-driven issues seen with other FGF21 therapies
- **Minimal Treatment Burden** to potentially drive a lifetime of therapeutic benefit with a one-time outpatient administration

Source: Jimenez, Molecular Therapy, 2024.

The RESTORE study

A Phase 1/2 first-in-human study of KRIYA-497 in adults with MASH | NCT07732400



Primary Endpoints:

- Parts 1 and 2: Safety assessments
- Part 1: Improvement in overall metabolic health as determined by changes in serum biomarkers
- Part 2: Changes in liver fat content via MRI-PDFF and CAP by FibroScan

Key Secondary Endpoints (Parts 1 and 2):

- Change in liver stiffness via transient elastography by FibroScan and MRE
- Change in lipoproteins, triglycerides, markers of glycemic control, adiponectin, liver enzymes, and non-invasive inflammatory and fibrosis biomarkers
- Peak and steady-state concentrations of AAV vector-mediated FGF21 in serum

The RESTORE study is actively enrolling

Kriya

MRI-PDFF, Magnetic Resonance Imaging Proton Density Fat Fraction; CAP, Controlled Attenuation Parameter; MRE, Magnetic Resonance Elastography

NX-GBL-EFI-PRST-260002
August 2026

Efimosfermin Program Update

Liver Forum- MASH 2026

Patricia Mendez
Clinical Development Lead

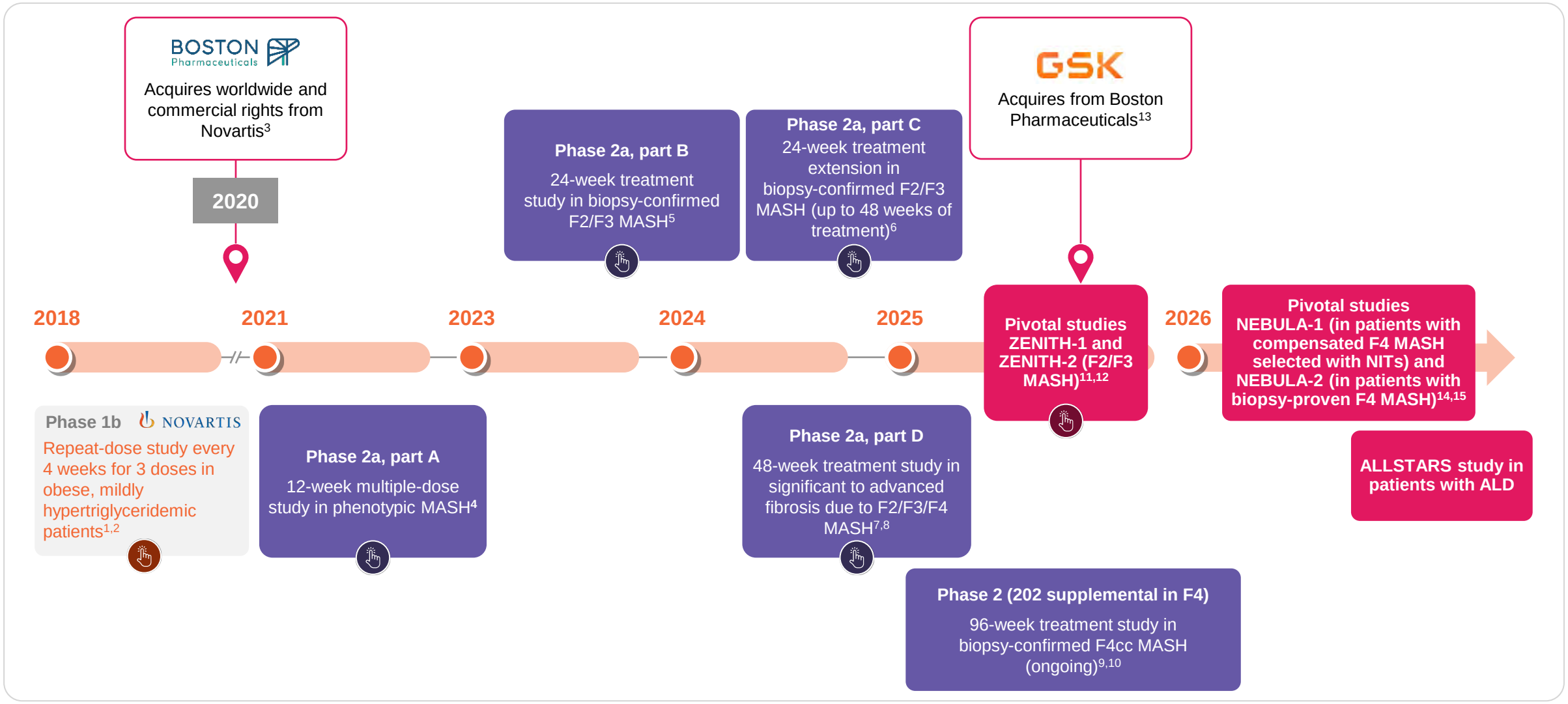
Conflict of Interest

GSK

Ahead Together

I am a GSK Employee

Efimosfermin Clinical Development Progress



Note: The protocols for ALL STARS is under development currently.
F2, fibrosis stage 2; F3, fibrosis stage 3; F4, fibrosis stage 4; F4cc, fibrosis stage 4, compensated cirrhosis; MASH, metabolic dysfunction-associated steatohepatitis; NIT, non-invasive test; SAD, single ascending dose.
1. ClinicalTrials.gov identifier NCT03466203. Available at: https://clinicaltrials.gov/study/NCT03466203; 2. Rader DJ, et al. *J Clin Endocrinol Metab*. 2022;107(1):e57-e70; 3. Boston Pharmaceuticals Licenses NASH Development Candidate from Novartis. Available at: Boston Pharmaceuticals Licenses NASH Development Candidate from Novartis; 4. Loomba R, et al. Lancet Gastroenterol Hepatol. 2025;10(8):734-745; 5. Noureddin M, et al. Lancet. 2026;407(10530):794-804; 6. Noureddin M, et al. *Hepatology*. 2026;83(1):E22-E70. 7. ClinicalTrials.gov identifier NCT04880031. Available at: https://clinicaltrials.gov/study/NCT04880031. 8. Data on file. 2025N569105. 9. ClinicalTrials.gov identifier NCT06920043. Available at: https://clinicaltrials.gov/study/NCT06920043 . 10. Data on file. 2025N569107. 11. ClinicalTrials.gov identifier NCT07221227. Available at: https://clinicaltrials.gov/study/NCT07221227; 12. ClinicalTrials.gov identifier NCT07221188. Available at: https://clinicaltrials.gov/study/NCT07221188; 13. GSK acquires efimosfermin. 14 ClinicalTrials.gov. identifier NCT07701993. 15. ClinicalTrials.gov. identifier NCT07704892. Available at: GSK completes acquisition of efimosfermin, a potential best-in-class specialty medicine to treat and prevent progression of steatotic liver disease (SLD) | GSK;.ALD (Alcoholic Liver Disease); F4cc (MASH stage F4)

Efimosfermin Clinical Development Plan: Addressing Patient Unmet Needs Across the Spectrum of MASH

Moderate to advanced fibrosis (consistent with F2/F3)

ZENITH–1 MASH CLINICAL STUDY

A randomised, double-blind, placebo-controlled study in adults with liver biopsy-confirmed F2- or F3-stage MASH **(N=1200)**

ZENITH–2 MASH CLINICAL STUDY

A randomized, double-blind, placebo-controlled study in adults with known or suspected F2- or F3-stage MASH using non-invasive tests **(N=1250)**

Cirrhosis (consistent with F4cc)

NEBULA–1 MASH CLINICAL STUDY

Randomized, double-blind, placebo-controlled study in compensated MASH cirrhosis **(selected with NITs, N=1740)**

NEBULA–2 MASH CLINICAL STUDY

Randomized, double-blind, placebo-controlled study in compensated F4 MASH **(biopsy proven, N=380)**

. ClinicalTrials.gov identifier NCT04880031. Available at: https://clinicaltrials.gov/study/NCT04880031. 8. Data on file. 2025N569105. 9. ClinicalTrials.gov identifier NCT06920043. Available at: https://clinicaltrials.gov/study/NCT06920043 . 10. Data on file. 2025N569107. 11. ClinicalTrials.gov identifier NCT07221227. Available at: https://clinicaltrials.gov/study/NCT07221227; 12. ClinicalTrials.gov identifier NCT07221188. Available at: https://clinicaltrials.gov/study/NCT07221188; 13. 14 ClinicalTrials.gov. identifier NCT07701993. 15. ClinicalTrials.gov. identifier NCT07704892.

GENFIT Program Highlights

1

Iqirvo® (elafibranor) in PBC and PSC

- Out licensed to Ipsen in 2021[1]
- Primary Biliary Cholangitis (PBC)
  - Launched in 2024
  - Expected peak sale €1bn[2]
- Primary Sclerosing Cholangitis (PSC)
  - Phase 3 data readout expected 2031[3]
- Royalty deal with HCRx[4]

2

NIS™ Technology platform in MASH Diagnostics

- Strong momentum from >$1B therapeutics market
  - Increased demand for patient identification
  - Increased demand for disease monitoring
- Scientific validation of the technology
  - LITMUS & NIMBLE
  - Clinical guidelines
- Two commercial pathways
  - Laboratory Developed Test (LDT)
    - Labcorp's NASHnext® reimbursed from August 2026, by Medicare under the Clinical Laboratory Fee Schedule, for patients eligible to coverage criteria[5]
  - In Vitro Diagnostics (IVD)

3

Clinical Pipeline in ACLF and CCA

- GNS561
  - PPT1 inhibitor for treatment of cholangiocarcinoma (CCA)
  - Phase 2 launch 2H26
- NTZ
  - Anti-inflammatory for treatment of Acute On-Chronic Liver Failure (ACLF)
  - Phase 2 launch 2H26

1: GENFIT: Ipsen and GENFIT enter into exclusive licensing agreement for elafibranor, a Phase III asset evaluated in Primary Biliary Cholangitis, as part of a long-term global partnership | GENFIT
2: H1-2026-Investor-Presentation.pdf
3: Study Details | NCT07387549 | A Study to Assess How Well and Safely Elafibranor Works in Adult Participants With Primary Sclerosing Cholangitis | ClinicalTrials.gov
4: GENFIT Announces Completion of Non-dilutive Royalty Financing Agreement with HCRx and Results of Repurchase Offer to 2025 OCEANEs holders | GENFIT
5: GENFIT Announces U.S. Medicare Coverage and Future Reimbursement for NASHnext®, a Non-Invasive Diagnostic Technology to Identify Patients with At-Risk MASH | GENFIT

GENFIT
TOWARDS BETTER MEDICINE

evido.

LiverPRO update

Maja Thiele, M.D. Ph.D., CSO for Evido.

2026

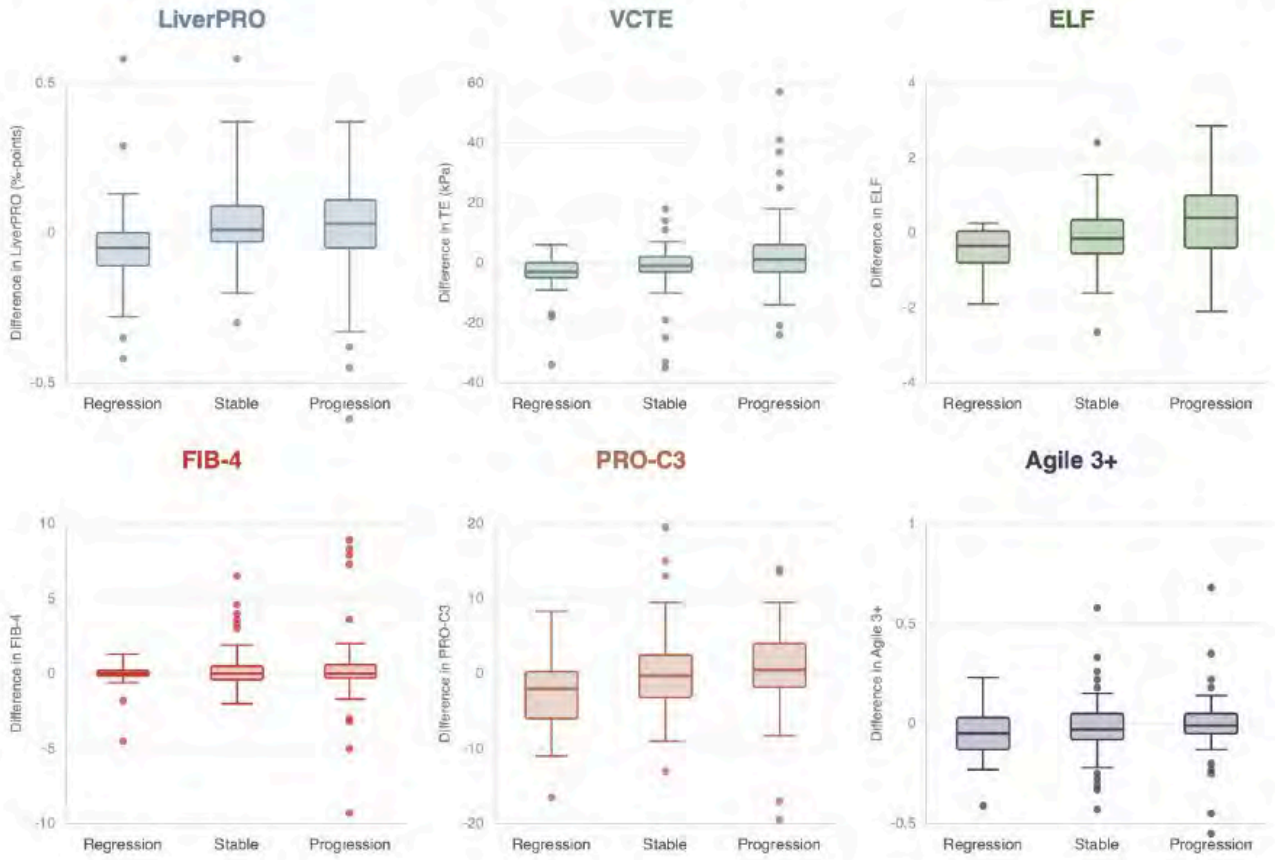
New data on treatment monitoring in MetALD/ALD

01

MetALD/ALD natural history monitoring

New study: LiverPRO for fibrosis monitoring in MetALD and ALD

Change in non-invasive tests by fibrosis improvement, stability or worsening



Change in biomarker corresponding to a 1-stage fibrosis change

Non-invasive tests	Absolute change
VCTE	4.9 kPa (3.2-6.7)
ELF	0.26 (0.11-0.41)
FIB-4	0.45 (0.10-0.81)
Agile 3+	0.02 (-0.01, 0.05)
PRO-C3	2.0 (0.22-3.79)
LiverPRO	**3 points (0.1-5)**

Cohort description

N=164 | MetALD and ALD | 75% ≥F2 | 19% =F4

Median time between biopsies: 1.9 years (IQR: 1.3)

Average fibrosis stage progression: 0.22 stage/year

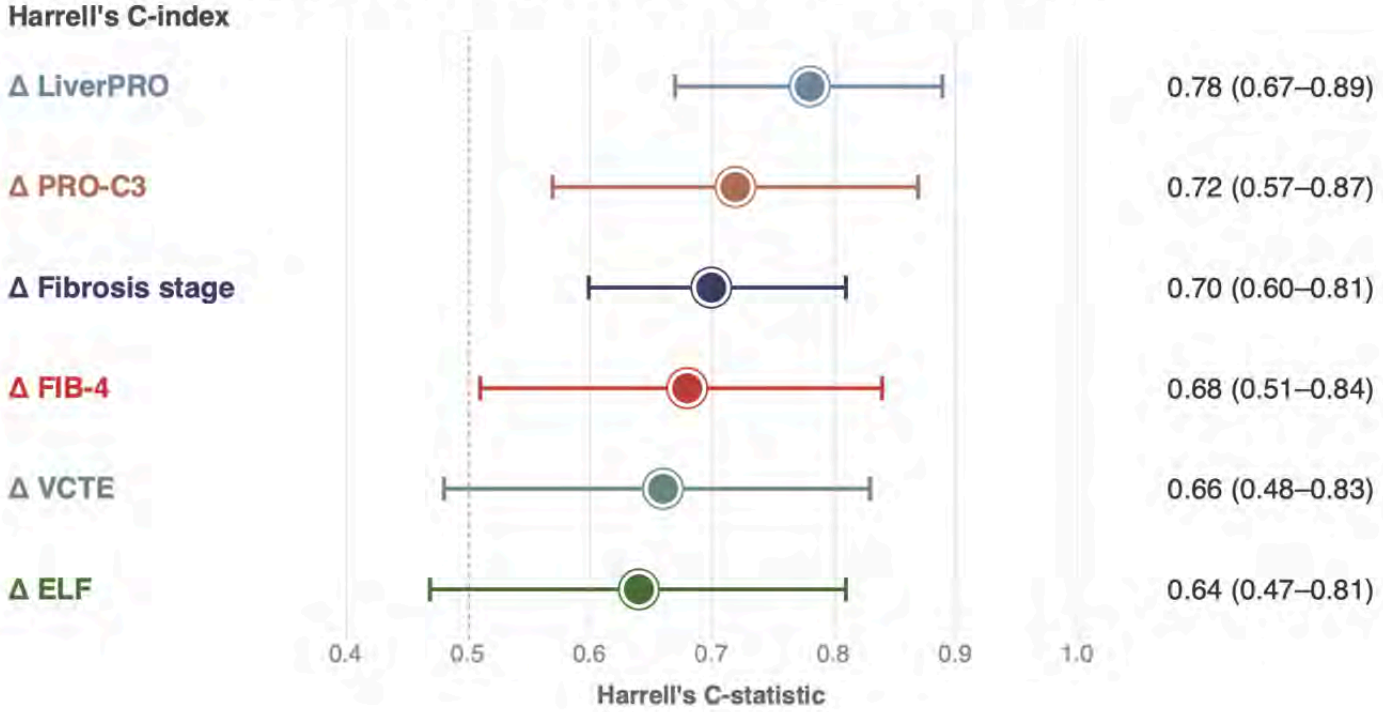
Baseline ELF: 9.7 (9.1-10.6) | LSM: 10.2 kPa (7.3-16.6)

Jensen et al. Clinical Gastroenterology and Hepatology 2026

MetALD-ALD natural history monitoring

New study: LiverPRO leads in outcome prediction for MetALD and ALD

Change in NITs to predict decompensation and death



Dot = Harrell's C-statistic; whiskers = 95% confidence interval. Dashed line at 0.5 marks no discriminative ability.

Follow up for events

Follow period after 2nd biopsy: 2.1 years

17 died and 13 decompensated in the second follow up period.
Total LRE's: 21

Jensen et al. Clinical Gastroenterology and Hepatology 2026

MetALD/ALD treatment effect monitoring

LiverPRO demonstrates changes associated with histological improvement in a Phase 2 trial in MetALD/ALD patients

Purpose

LiverPRO as a marker of histological endpoints in patients with a current or previous alcohol overuse.

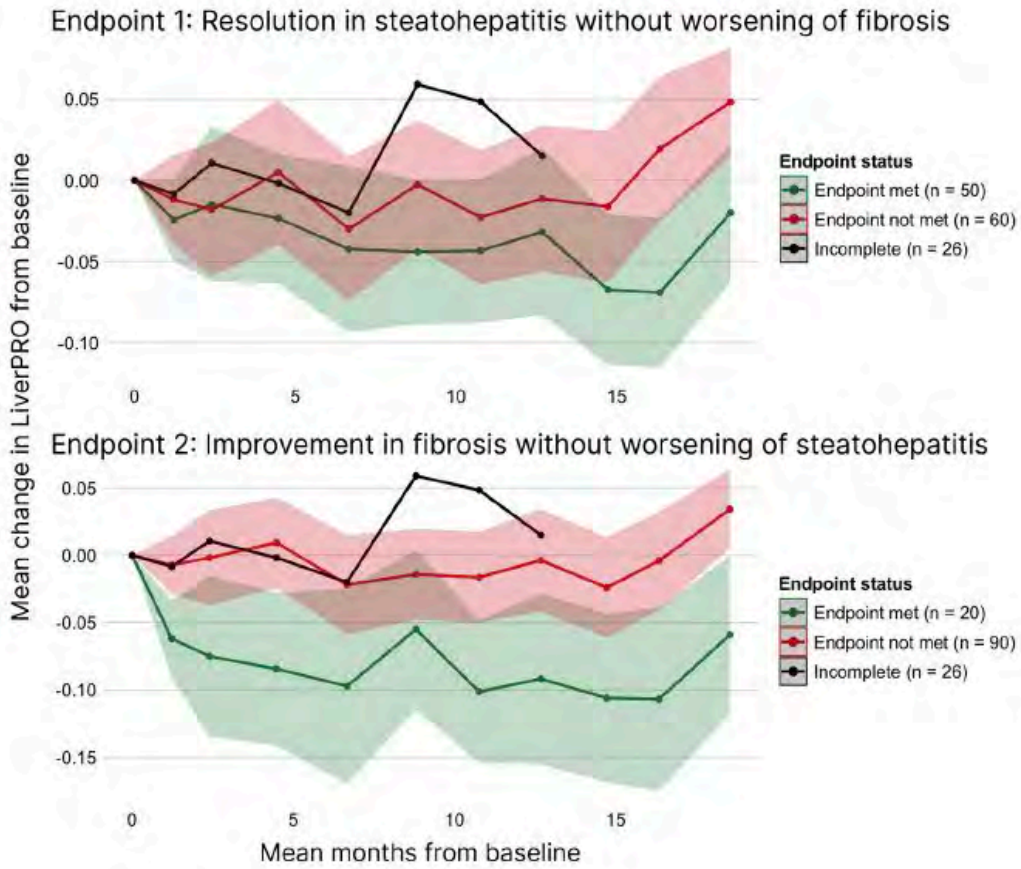
Study Characteristics

- N= 136 pts
- Duration 18 months, dual biopsy
- Rifaximin-α vs. Placebo

Poster of distinction, accepted for AASLD 2026

50 met endpoint 1

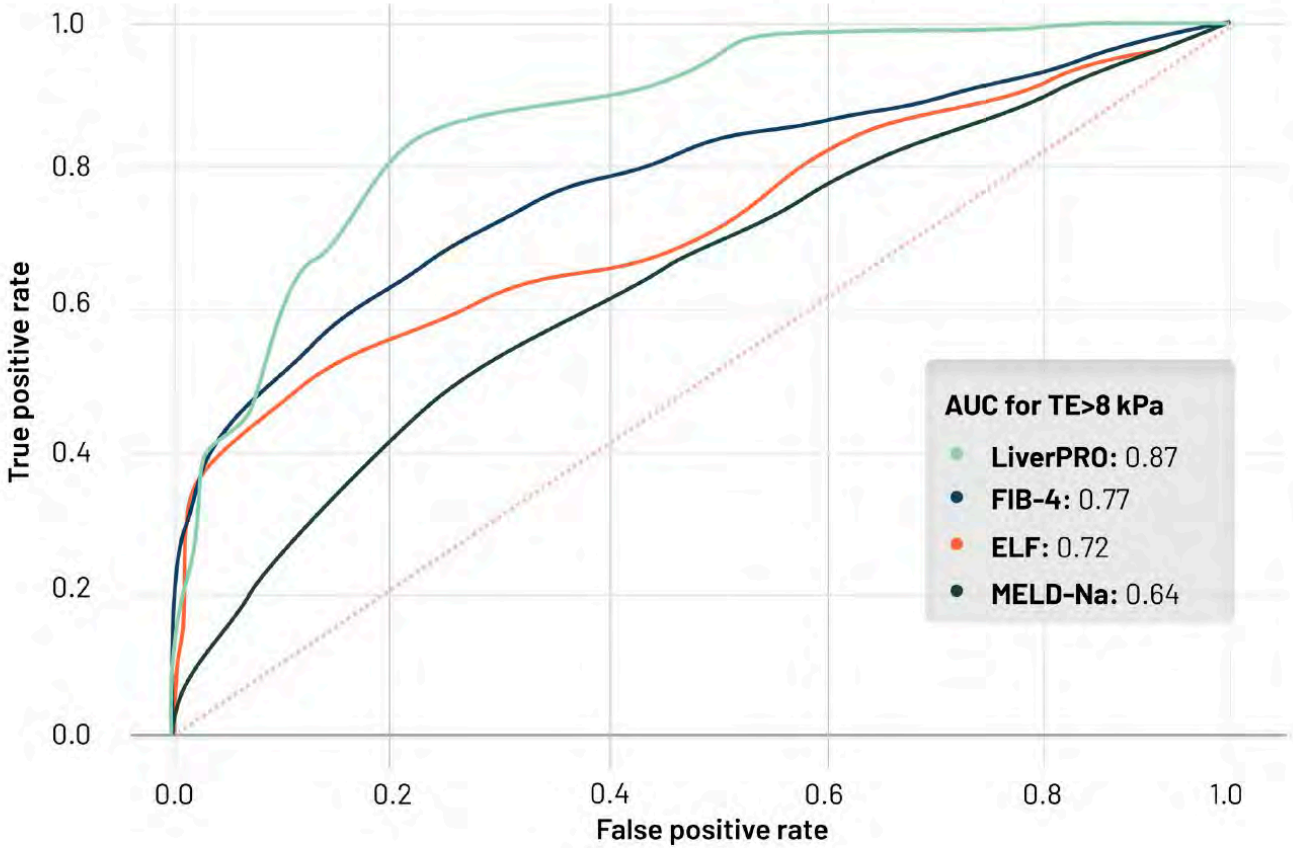
20 met endpoint 2



Original trial : Israelsen et al. Lancet Gas Hep 2024

MetALD/ALD recruitment

LiverPRO outperforms other NITs in detecting elevated liver stiffness in MetALD and ALD population.



evido.

Population characteristics

1,855	All alc risk factor	25% MetALD	11% ALD

Disease severity

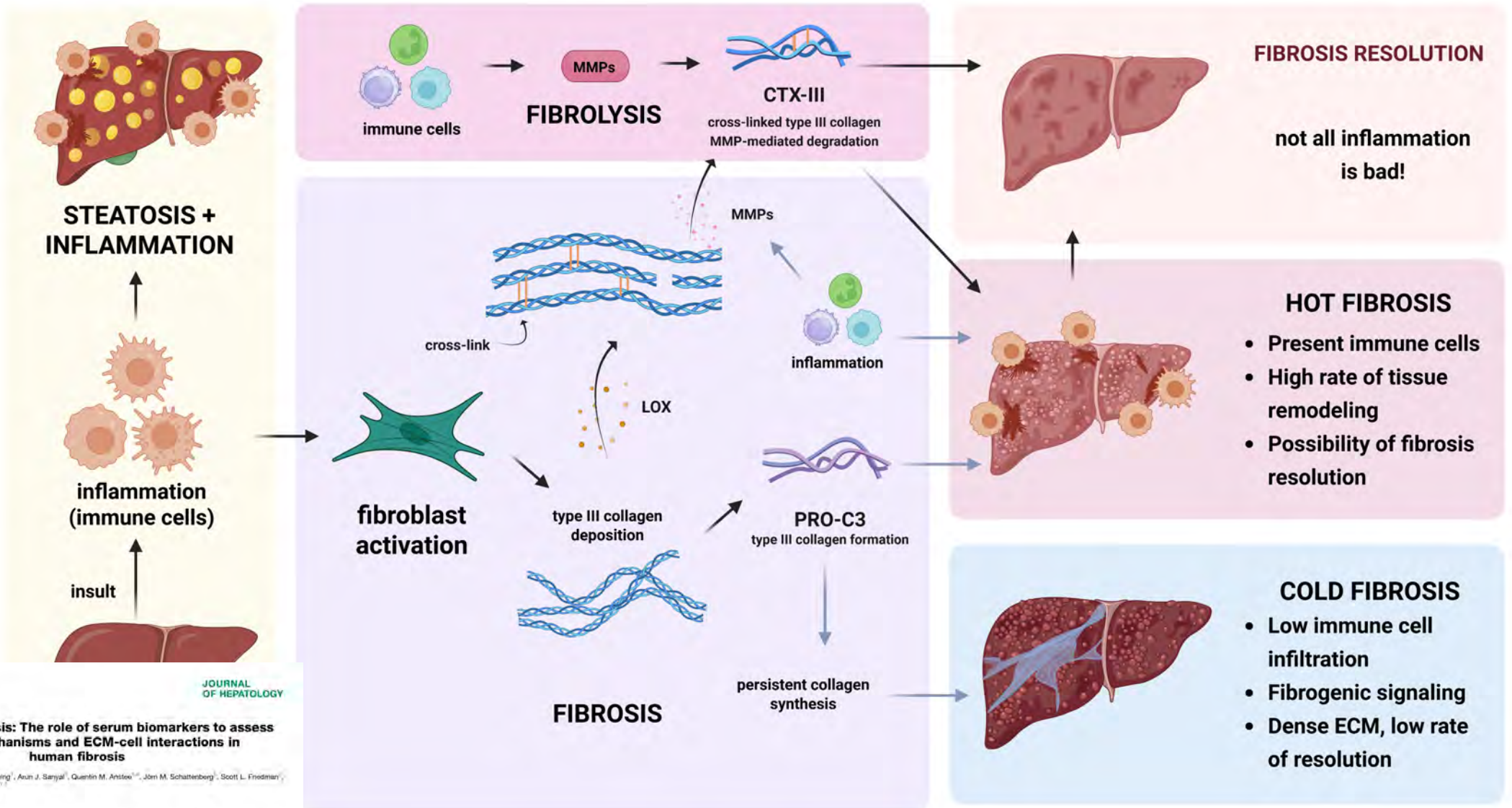
MetALD: 12% TE ≥8 kPa	ALD: 29% TE ≥8 kPa

Results

Performance comparison between NITs.

	LiverPRO	ELF	MELD-Na	FIB-4
AUC TE>8 kPa	0.87 [95% CI 0.83-0.91]	0.72 [95% CI 0.64-0.80]	0.64 [95% CI 0.56-0.71]	0.77 [95% CI 0.70-0.84]
Correct classification rate	85%	82%	74%	60%
False positive rate	8%	14%	20%	40%
False negative rate	50%	46%	55%	19%

Hot & cold fibrosis



Review

JOURNAL OF HEPATOLOGY

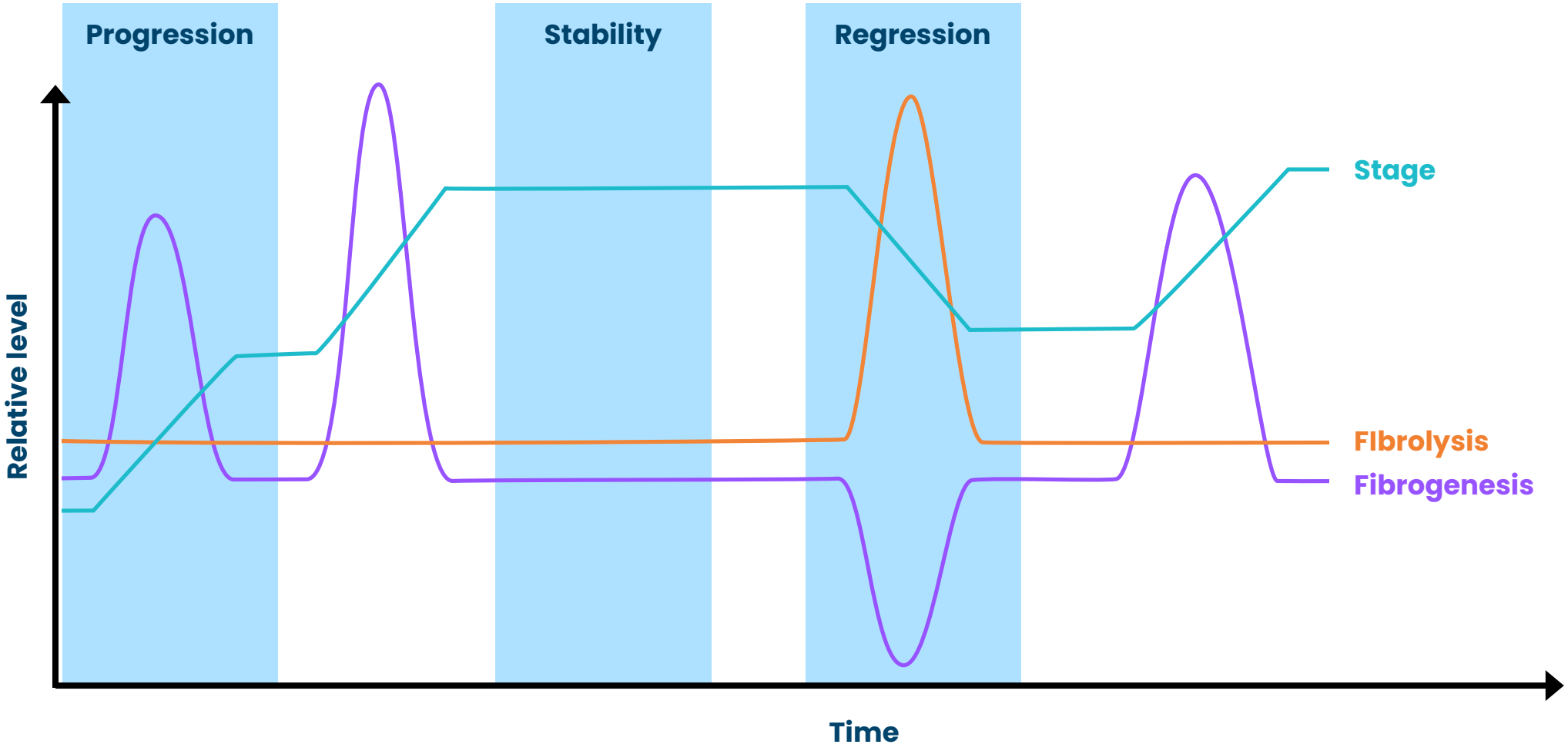
Hot and cold fibrosis: The role of serum biomarkers to assess immune mechanisms and ECM-cell interactions in human fibrosis

Andressa de Zawadzki[1,*], Diana J. Leeming[2], Arun J. Sanyal[3], Quentin M. Anstee[4,5], Jörn M. Schattenberg[6], Scott L. Friedman[7], Detlef Schuppan[8,9], Morten A. Karsdal[2]

Summary

Fibrosis is a pathological condition characterised by excessive accumulation of extracellular matrix (ECM) components, particularly collagens, leading to tissue scarring and organ dysfunction. In fibrosis, an imbalance between collagen synthesis (fibrogenesis) and degradation (fibrolysis) results in the deposition of fibrillar collagens disrupting the structural integrity of the ECM and, consequently, tissue architecture. Fibrosis is associated with a wide range of chronic diseases, including cirrhosis, kidney fibrosis, pulmonary fibrosis, and autoimmune diseases. Recently, the concept of "hot" and "cold" fibrosis has emerged, referring to the immune status within fibrotic tissues and the nature of fibrogenic signalling. Hot fibrosis is characterised by active immune cell

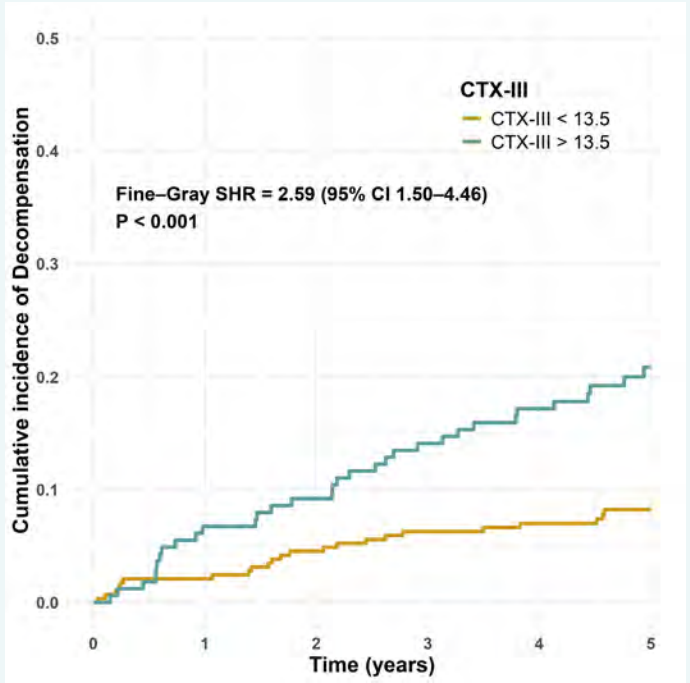
Fibrosis stage and activity are independent !



Fibrogenesis and fibrolysis is prognostic for liver decompensation

FLASH
• LIVER RESEARCH CENTRE

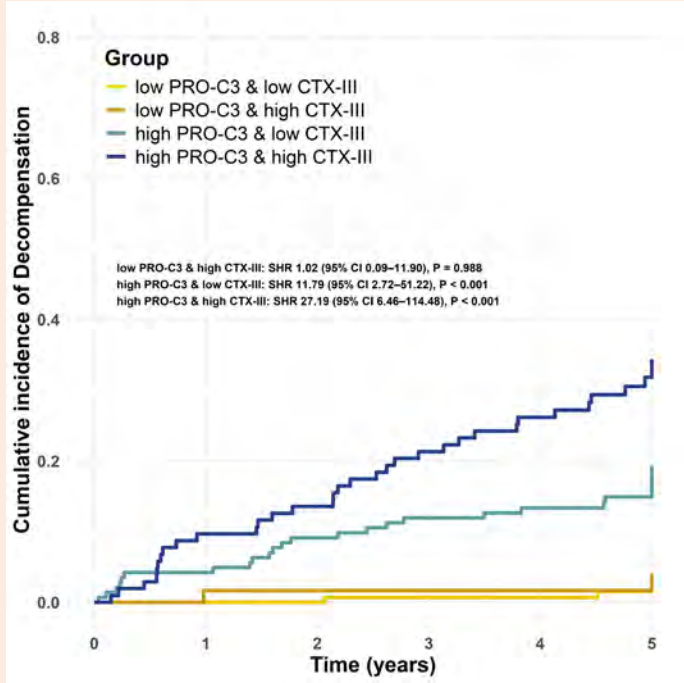
Fibrolysis by CTX-III is prognostic for decompensation at baseline HR: 2.6



HR: 2.6
[1.5- 4.46]

Non-Official cutoffs

High fibrogenesis & high fibrolysis is prognostic for decompensation at baseline HR: 27.2



High PRO-C3 & High CTX-III: **HR: 27.19** [6.46 – 114.48]
High PRO-C3 & low CTX-III: **HR: 11.79** [2.72 – 51.22]
Low PROC3 & High CTX-III: HR: 1.2 [0.09- 11.90]
Low PROC3 & low CTX-III: HR: 1

N= 450 steatotic liver disease (SLD) patients with alcohol overuse followed for up to 5 years.

Zadwadzki A et al AASDL 2025

Perspectum

Perspectum: Measuring Change in MASH

Marija Mavar
President, Pharma Solutions

Liver Forum 21, September 9, 2026, Paris

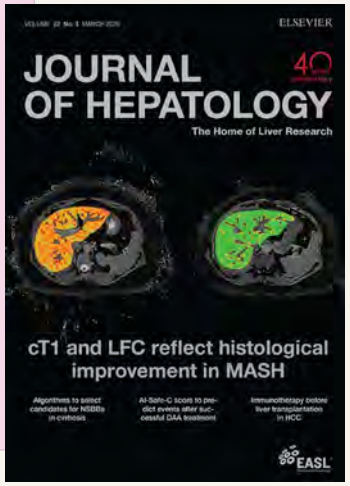
MASH TRIAL EXPERIENCE

Our Measurement Methods, Peer-reviewed and in Use

Imaging and Endoscopy

MRI-PDFF and cT1, with multi-organ MRI, MRE and DXA as required.

For advanced MASH and cirrhosis trials, our expert central readers provide assessment of varices through an integrated endoscopy workflow with standardized reading, rapid reporting and high-quality endpoint data.



J HEPATOL, MARCH 2025
cT1 and liver fat track histological response

Pathology

Central reading, end to end management: biopsy kit provision and sample collection, central laboratory processing, QC and digital central reading with AI-supported review.

Fifteen expert pathologists centrally report using our platform including Prof Bedossa and five NASH CRN pathologists.

J CLIN PATHOL, MARCH 2026
AI quantifies inflammation by region

TO DATE

70+

MASH studies delivered

25+

Late phase MASH trials supported, over half in Phase III

100+

Standardized metrics across imaging and histology

100K+

Datasets analyzed, paired with biochemistry and genetics

Abbreviations: AI: artificial intelligence; cT1: corrected T1; DXA: dual-energy X-ray absorptiometry; MASH: metabolic dysfunction-associated steatohepatitis; MRE: magnetic resonance elastography; MRI-PDFF: proton density fat fraction; NASH CRN: Nonalcoholic Steatohepatitis Clinical Research Network. Study, trial and dataset counts are Perspectum internal data.

REGULATORY PROGRESS

cT1: Monitoring, Outcomes, and the LIVO Study

Monitoring

Pooled placebo response was **0 ms** across 16 studies and 1,134 patients.[1]

In a systematic review, repeatability was **7%** for cT1 and **73%** for VCTE liver stiffness. Only cT1 and liver fat fell below the threshold for clinically meaningful change.[2]

More than **50 MASH trials** have used cT1, most recently SYNCHRONIZE-MASLD, published this year.[3]

FDA BQP: Letter of Intent accepted for **pharmacodynamic biomarker**, qualification plan in progress

Outcomes

In **28,841** UK Biobank participants, elevated cT1, but not liver fat, was associated with major liver and cardiovascular events, and all-cause mortality.[4]

LIVO: A retrospective outcomes study led by Prof. Arun Sanyal across six sites in the US and Asia, in more than **1,500 patients with MASLD** who already have a cT1 measurement.

FDA BQP: Letter of Intent in preparation for a **reasonably likely surrogate endpoint**.

References: 1. Andersson et al., 2026, *Clin Gastroenterol Hepatol.* 2. Ndaa et al., 2026, *Endocr Pract.* 3. Kaplan et al., 2026, *Nat Med.* 4. Jackson et al., 2025, *Nat Med.*

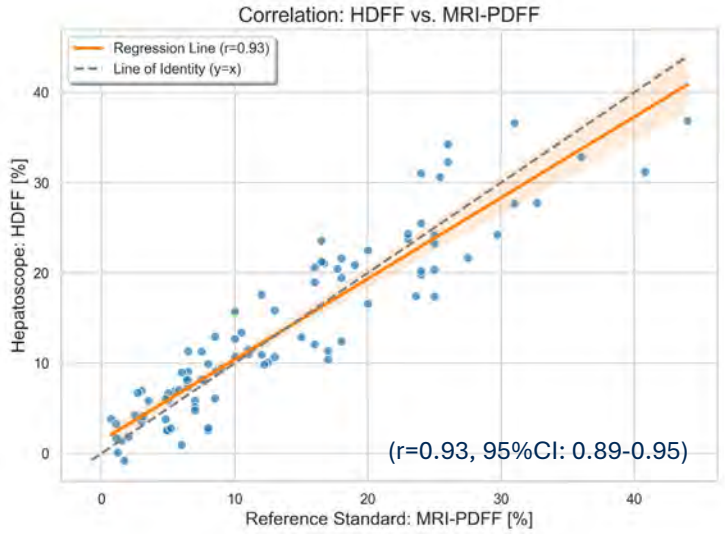
Abbreviations: cT1: corrected T1; FDA: US Food and Drug Administration; BQP: Biomarker Qualification Program; MASH: metabolic dysfunction-associated steatohepatitis; MASLD: metabolic dysfunction-associated steatotic liver disease; ms: milliseconds; VCTE: vibration-controlled transient elastography.

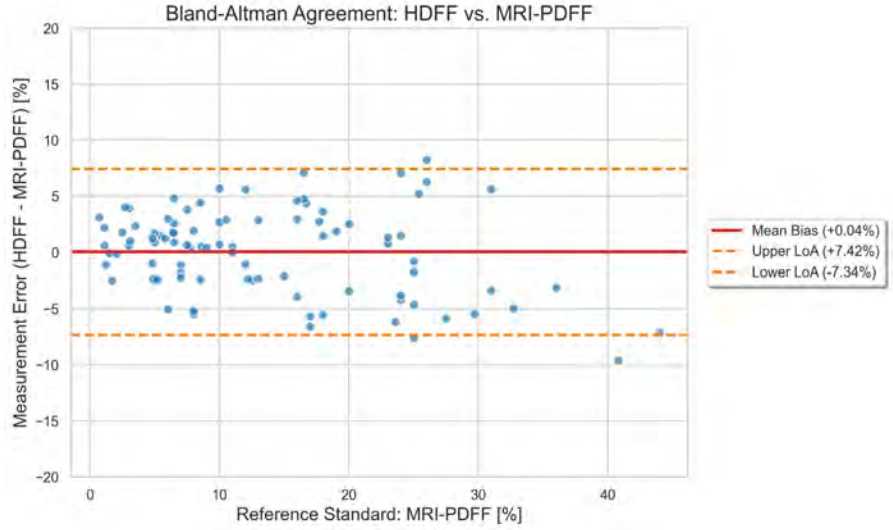
THE FORUM
For Collaborative Research℠
Berkeley's Hub for Regulatory Science

LabCorp Updates

UC Berkeley Public Health

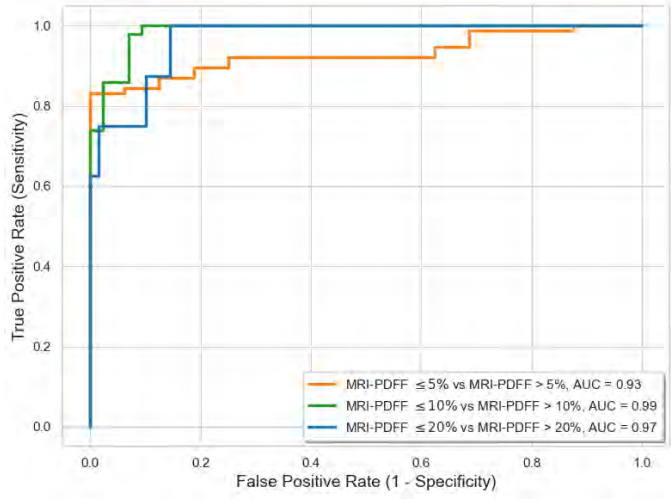
Hepatoscope now integrates a novel real-time quantitative ultrasound estimation of liver fat: Hepatoscope-derived fat fraction (HDFF)





Participants' characteristics:

- 3 clinical cohorts (American and European)
- N = 93 adults with MASLD or benign liver lesions
- Sex ratio (F, %): 47 (51%)
- Age: 58.7 ± 9.7 (27-78) years
- BMI: 32.0 ± 4.9 (18.4-42.3) kg/m^2, including 68% with BMI > 30.
- MRI-PDFF: 10.5 (6.0-20.0)



Liver Forum Update – September 9, 2026

Cindy Serdjebi,
Clinical Science

What is the impact for the Liver Forum Members?

- MRI-PDFF was shown as a potential biomarker of early response for MASH therapies (resmetirom and semaglutide).
  => Important for pharma and CRO members

- Detection of steatosis at the point-of-care is part of the solution for an earlier management.
  => Important for clinicians and patients' advocacy members.

- Hepatoscope has become the only ultrasound device with the following features:
  - 50 Hz (liver) / 100 Hz (spleen) transient elastography
  - Fat fraction estimation
  - Under anatomical real time image guidance
  - Point-of-care

Thank you for your attention !

Any questions?
Send me an email at cindy.serdjebi@e-scopics.com

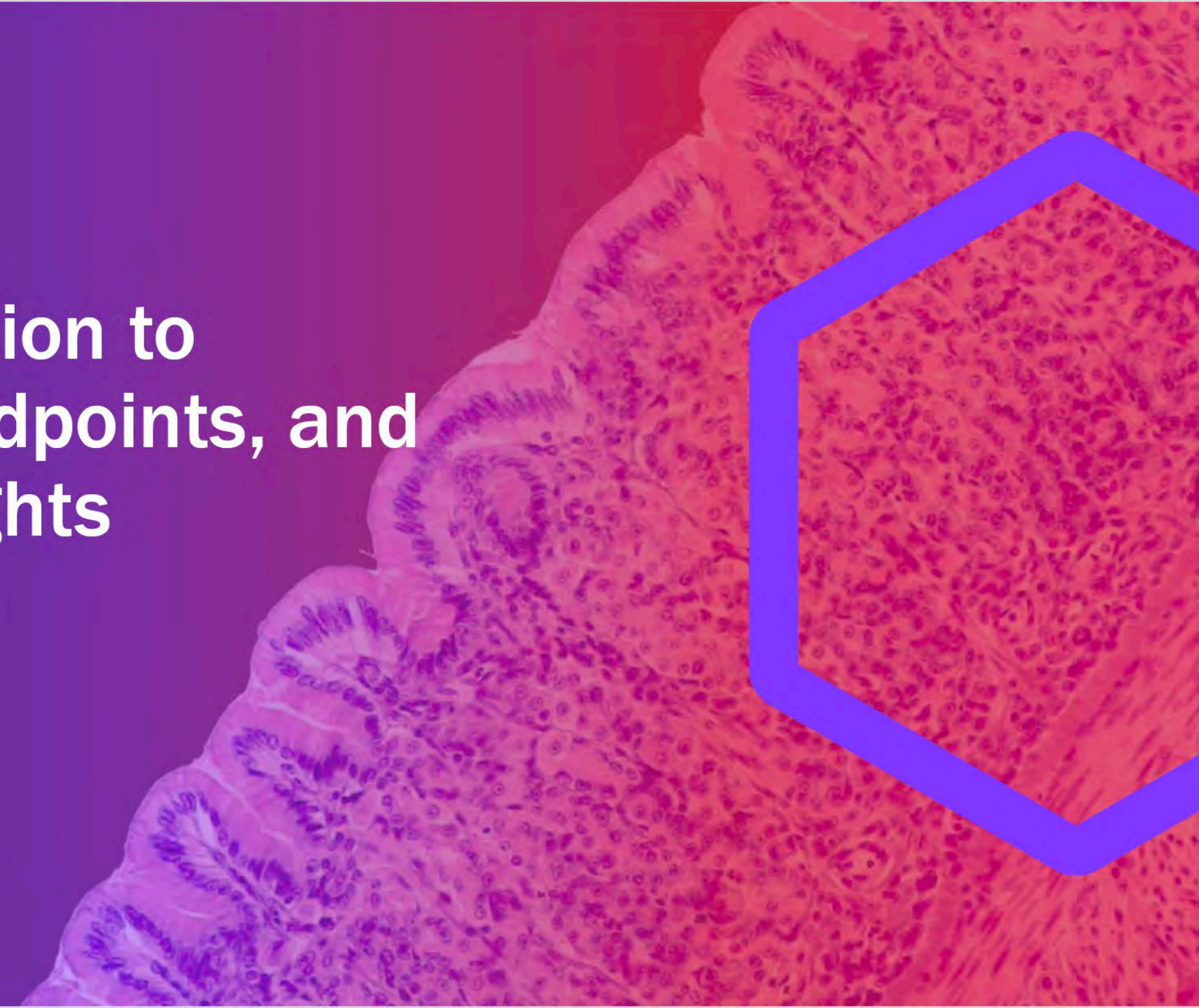
SCAN ME

PathAI

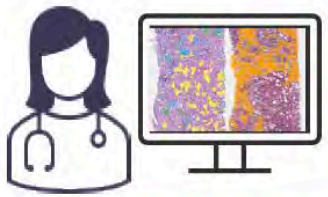
Bringing Precision to Enrollment, Endpoints, and Histologic Insights

Liver Forum, Paris
Sept 9, 2026

Katy Wack, PhD
SVP, Clinical Science, PathAI
A Division of Roche Diagnostics



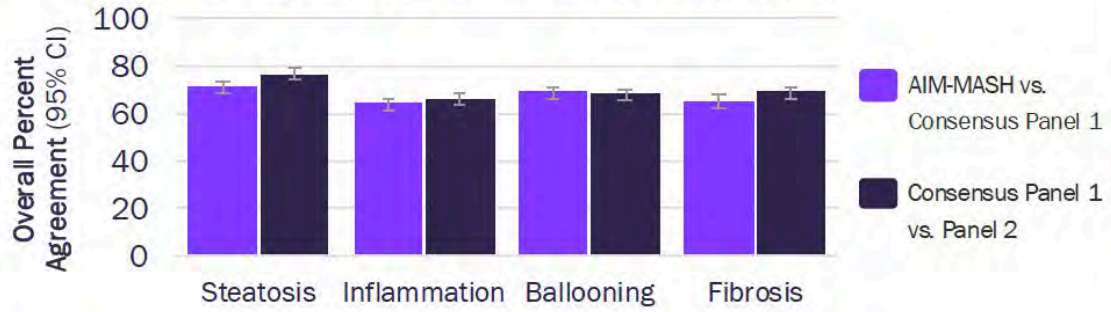
FDA and EMA Qualified, AIM MASH AI Assist now being prospectively used in a ph3 trial for enrollment and primary endpoints



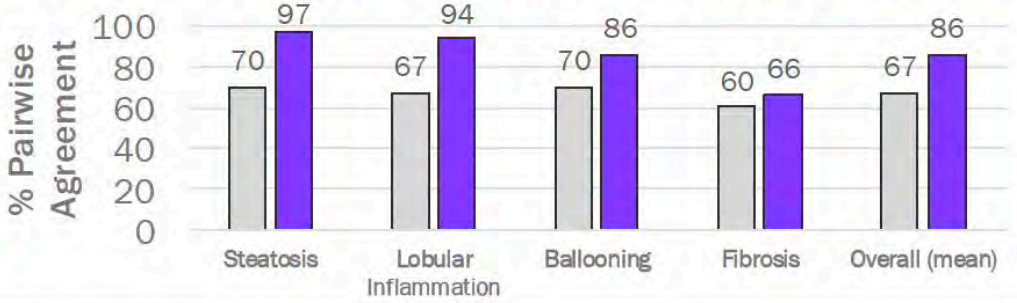
Milestone: AIM-MASH AI Assist is now being prospectively utilized in the phase 3 PERFORMA (Pemvidutide) trial by consensus pathologists to enroll patients. Multiple phase 2b trials are also utilizing the qualified tool for enrollment and primary endpoints!!!

The only AI-based pathology tool qualified for use by pathologists for enrollment, 1º Endpoint, AIM-MASH Algorithm is:

Non-inferior Accuracy to Gold Standard Consensus [5,6]



Reader Precision Superior to Manual Reads w/ FDA Qualified Workflow

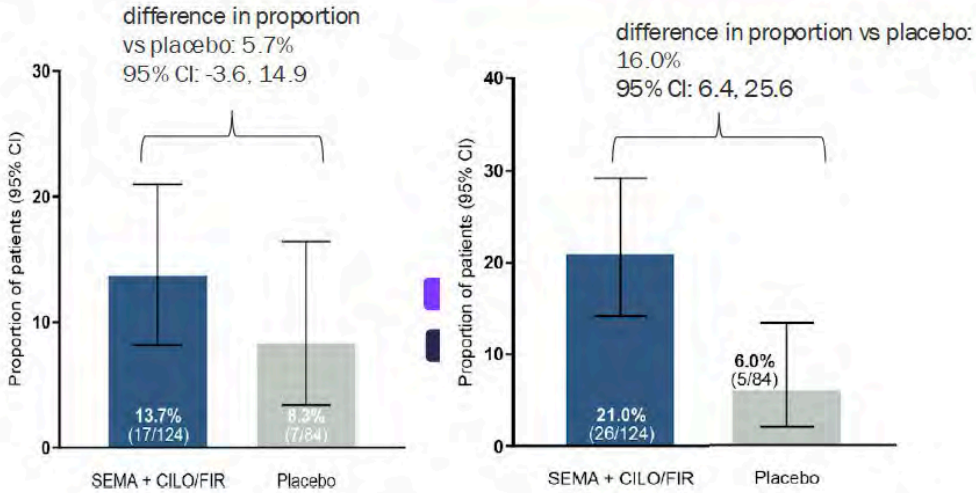


1. FDA Draft Guidance for Industry 2018. 2. Kleiner DE JAMA Network Open 2019; 3. Iyer Nature Medicine 2024. 4. Davidson J. Heptol. 2020. 5. Pulaski Nature Medicine 2025. 6. FDA FQP DDT-BMQ-000105

AIM-MASH AI Assist is qualified as a tool in the EU and as a DDT in the US for use in MASH clinical trials; not for use in diagnostic procedures.

Wayfind Cirrhosis Trial: Fibrosis Improvement Without MASH Worsening at Week 52

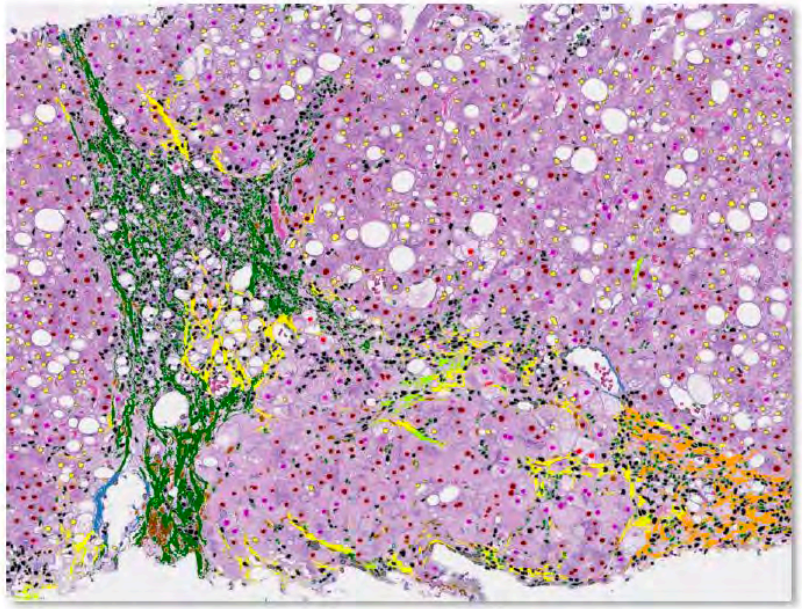
Central Pathologists	AIM-MASH AI Assist
$p = 0.2289$ ✗	$p = 0.0011$ ✓
Primary Endpoint Failed	Primary Endpoint Achieved

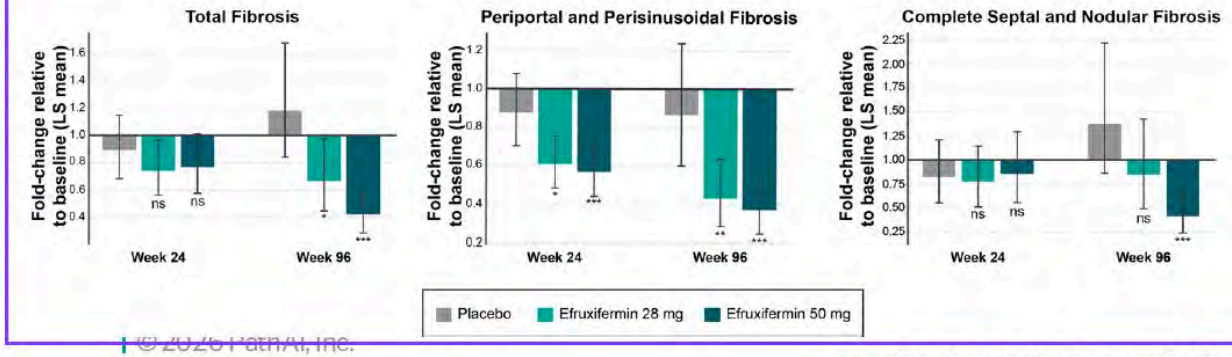


Retrospective analysis of WAYFIND, a Ph2 study of the safety and efficacy of combination treatment of Semaglutide, Cilofexor, and Firsocostat in patients with Compensated Cirrhosis due to MASH (Gilead, Novo Nordisk)[1]

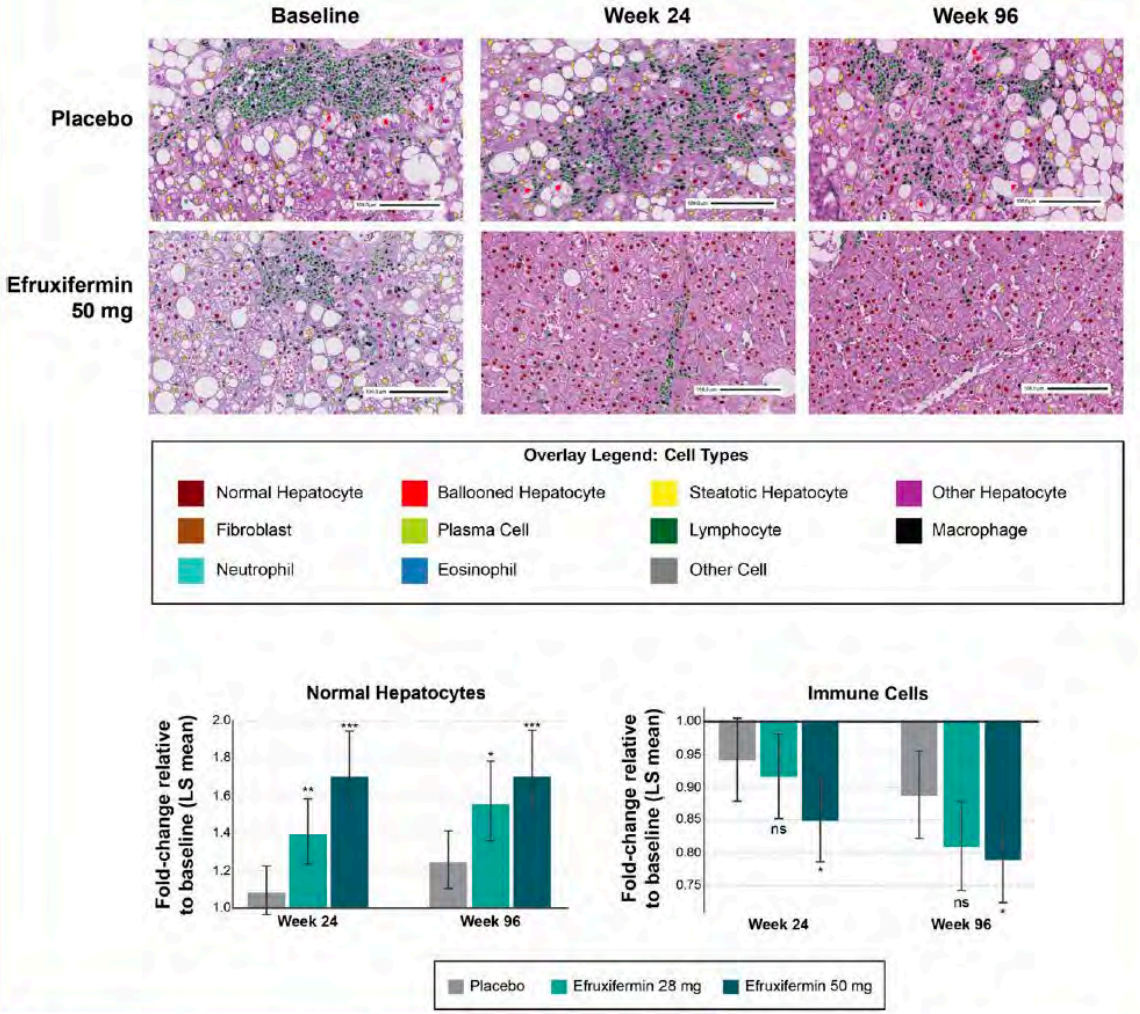
LiverExplore enables spatially-resolved quantification of fibrosis and cellular changes with treatment over time beyond ordinal scores

Fibrosis sub-type and Cellular Quantification:





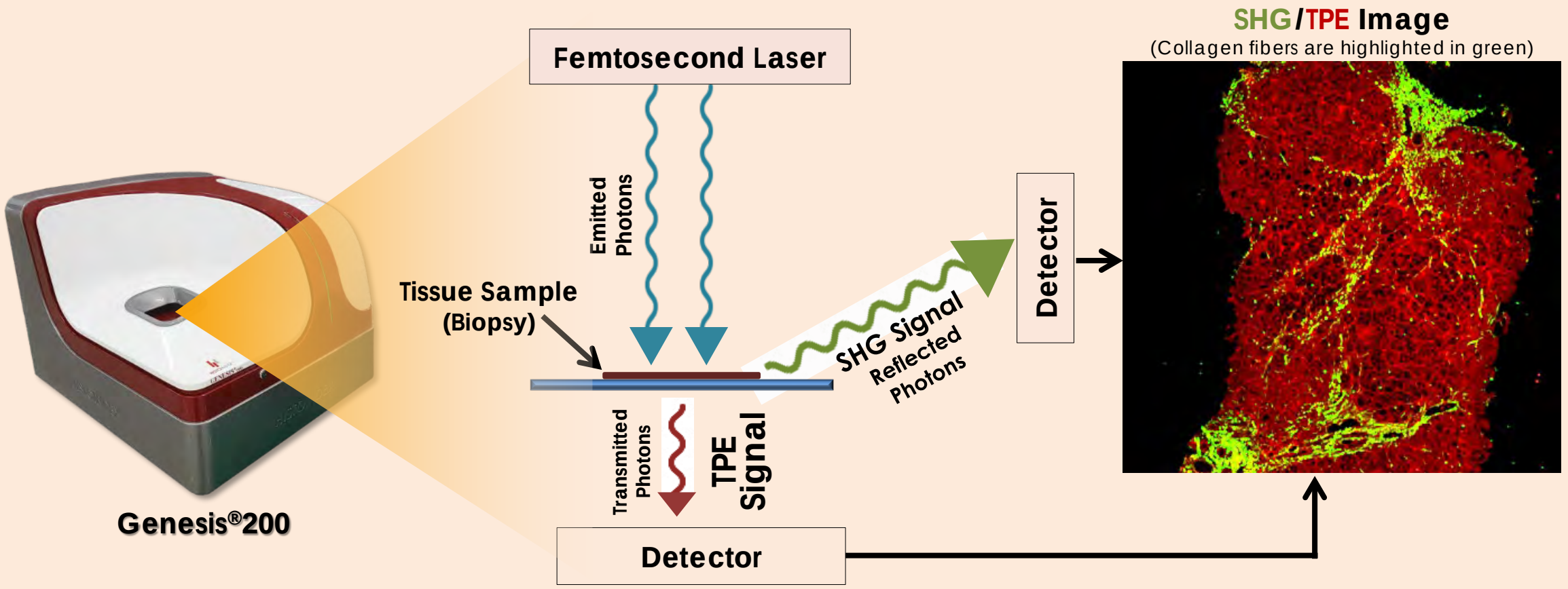
Cell Quantification:



LiverExplore is for Research Use Only. Not for use in diagnostic procedures

Schattenberg et al. AASLD 2025

qFibrosis using stain-free digital pathology - highly reproducible quantitative assessment



Sun W, Chang S, Tai D C, et al. Nonlinear Optical Microscopy: Use of Second Harmonic Generation and Two-photon Microscopy for Automated Quantitative Liver Fibrosis Studies[J]. Journal of Biomedical Optics, 2008, 13(6):7-0.

Septa quantification for cirrhotic trials

- In participants with F4c MASH, qFibrosis confirmed fibrosis improvement with Efruxifermin at Week 96
- Treatment with Efruxifermin reduced septa area consistently across all participants
- Quantitative septa area change showed dose-dependent reduction patterns

Rinella et.al. Poster, AASLD 2025

Connecting septa changes to non-invasive test (NIT) measurements

Combined individuals with MASH and advanced fibrosis (F3) or compensated cirrhosis (F4c), who are at high risk of disease progression

Schattenberg et.al. Poster, EASL 2026

Continuous reduction patterns in septa area detected

- Reduction in septa area and collagen burden were detected are consistent with NIT measurements
- Zonal fibrosis assessment indicates matrix remodeling, with the greatest reductions observed in periportal and zone 2
- qSepta revealed further septa remodeling and provides a sensitive measurement for cirrhotic trials

Schattenberg et.al. Poster, EASL 2026

HEPQuant®
Transforming Liver Health

Industry Update for Liver Forum

Joanne Imperial, MD
Chief Medical Officer

Liver Forum September 8, 2026

Milestone: HepQuant SHUNT® Liver Diagnostic Test is FDA approved as of June 18, 2026

- The HepQuant SHUNT® Liver Diagnostic Test quantitatively detects concentration of 13C-cholate and d4-cholate in human serum.
- Blood samples collected after intravenous administration of 13C-cholate and oral ingestion of d4-cholate.
- **A DSI score below the validated threshold (≤18.3) essentially rules out the presence of large esophageal varices (LEV).**

Other HepQuant Major Achievements

HepQuant has also achieved the following commercial milestones that facilitate implementation in global pharmaceutical trials:

- **CAP Accreditation – June 2026**
- **ISO 13485 Certification – June 2025**
- **Global Privacy Framework Certification – November 2025**
- **Oral presentations related to functional heterogeneity and risk for varices and portal hypertension in CPA cirrhosis at major meetings:**
  - **SOLAR - June 2026, DDW – May 2026, MASH TAG – January 2026**
- **29 publications since 2024 – vast majority related to HepQuant DuO®**
  - **Publications in high impact journals – *Nature Medicine* and *American Journal of Transplantation***

Noureddin M *et al*. Understanding the Functional and Physiologic Heterogeneity of Advanced MASH as Defined by the Oral Cholate Challenge Test May Enhance Clinical Trial Design**.** Presented at MASH TAG 2026.
Shiffman M *et. al.* The Disease Severity Index (DSI) from the Oral Cholate Challenge Test Defines Varices Risk Across Child-Pugh A5 and A6 and MASH Versus Non-MASH Etiologies. Presented at DDW 2026.
Chalasani *et al*. Noninvasive Quantification of Liver Function and Portal-Systemic Shunting Distinguishes Differences between Child-Pugh A5 and A6, Presented at SOLAR 2026**.** Presented by Imperial JC.

Potential Use Cases for Pharma Trials

In our research, we have shown that the DSI from the HepQuant DuO® test is equivalent to the DSI from HepQuant SHUNT and that DSI from HepQuant DuO is reproducible.[1] [2] [3] These attributes of HepQuant DuO favor its use in trials to:

- **Screen/enrich to characterize the baseline heterogeneity of a cohort**
  - MASH compensated cirrhosis patients have a mean DSI=22[4]
  - For DSI >22, the estimated probability of liver related event at 2 yr=29%[5]
  - For DSI <22, the estimated probability of liver related event at 2 yr=3%[5]
- **Determine precisely the functional and physiologic response to treatment**
  - On treatment decisions
  - Enable efficient adaptive design strategies
- **Predict potential clinical benefit**
  - Measure effect of drug therapy on liver-related events

1. McRae M et al .*Basic Clin Pharmacol* Ther. 2024;*doi 10.1111/bcpt.13980..*
2. McRae M et al. *Clin Transl Sci*. 2024. *doi 10.1111/cts.13786.*
3. McRae M et al. *Trans Res* 2023; doi:*10.1016/j.trsl.2022.08.002*
4. Imperial JC et al. Presented at *EASL* 2026.
5. Kittelson J et al. *Eur J Int Med* 2024;*doi 10.1016/jejim.2024.11.029*

HepQuant to Submit LOI for DSI as a Monitoring Biomarker

Joanne Imperial MD
joanne.imperial@hepquant.com

PDGFRβ-PET Imaging of Human Fibrogenesis

Especially well suited for:

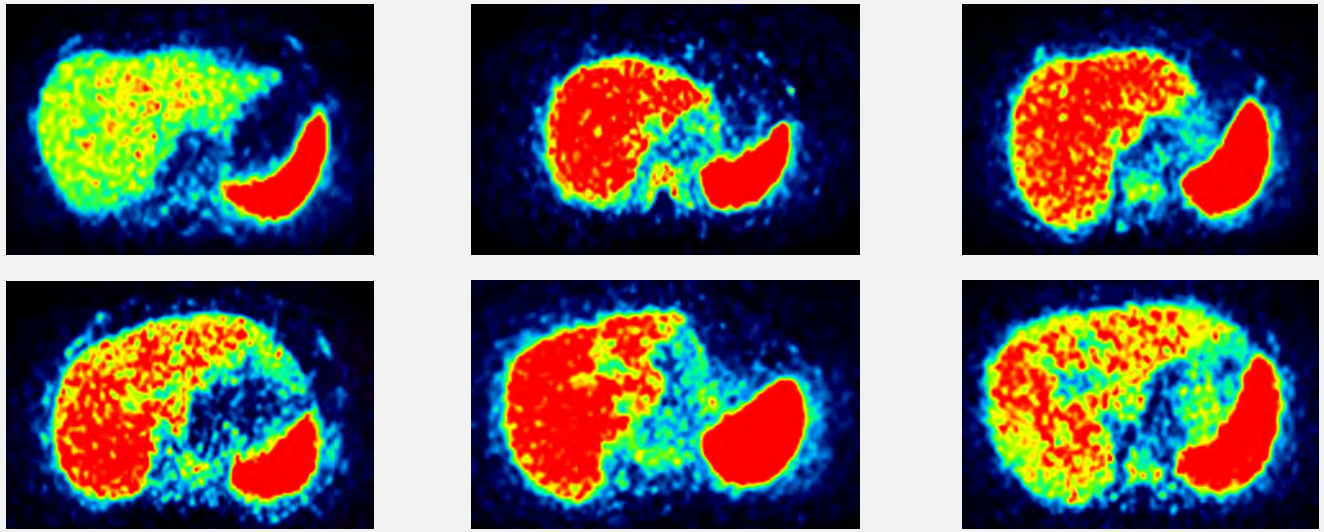
-Mechanistic Trials
-Combination Therapies

With shorter readout time

Antaros Medical

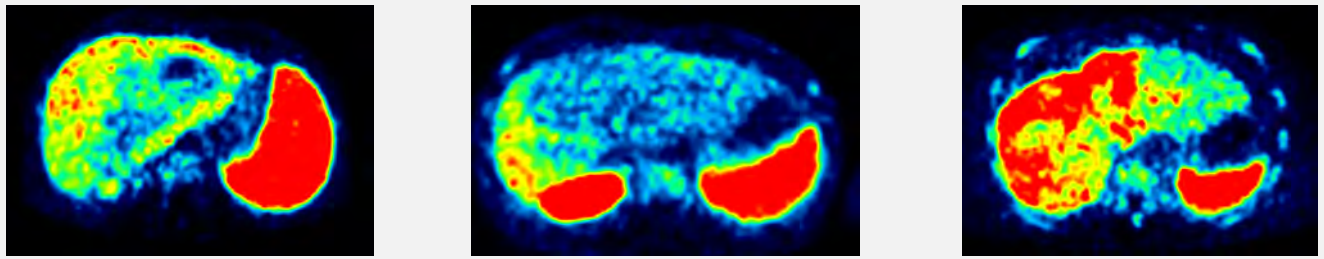
PDGFRβ-PET in MASH-F4 versus PSC

MASH-F4



Heterogeneity within group

PSC



Heterogeneity within liver

Antaros Medical