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

Company Updates

UC Berkeley Public Health

MASH Pipeline Evolution

David Soergel, MD
Chief Medical Officer

*For Educational Purposes Only upon request of Liver Forum

Madrigal is Uniquely Positioned to Extend its Leadership in MASH

Our R&D strategy is to build the **industry-leading MASH pipeline** through targeted business development and internal innovation, **leveraging Rezdiffra as the foundational therapy**

Deliver transformational **outcomes** data, securing full approval from F2-F4c

Advance **combination therapies** anchored by Rezdiffra

Invest in **new modalities**, including those that enable patient-specific care

Execute **disciplined, capital-efficient** clinical development (quick go/no-go)

We’re Building Our Pipeline with the Most Promising Targets

MASH Disease Pathways and Potential Mechanisms

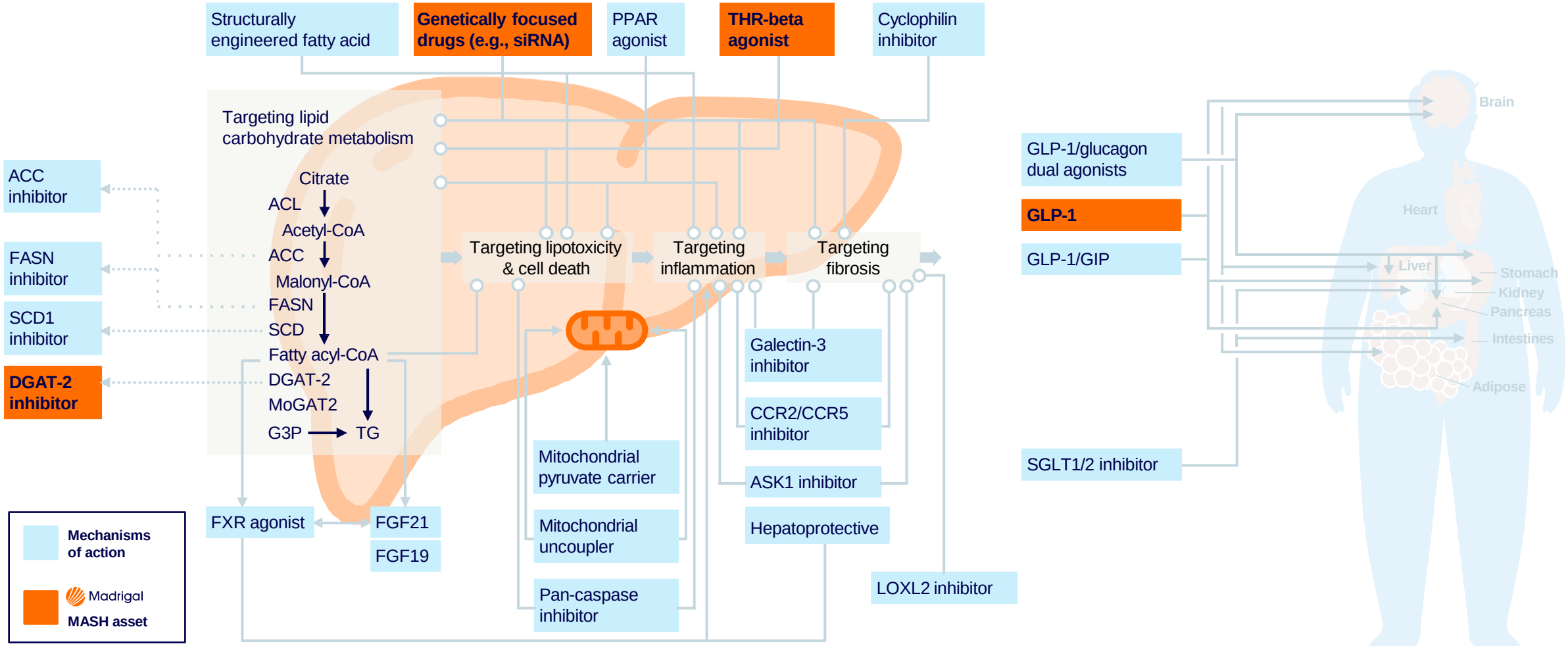


Image adapted from: Noureddin M. MASH clinical trials and drugs pipeline: An impending tsunami. *Hepatology*. 2025;82(5):1325-1340.

Advancing an Industry-Leading MASH Pipeline to Transform Patient Care

	MOA	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Accelerated approval
Resmetirom	**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					
siRNA combo/resmetirom combo	**siRNA (6)**	MASH					
Additional MASH Assets in varying stages of development	**Exploratory oral assets (3)**	MASH					

1. Ervogastat monotherapy Phase 2b study completed by Pfizer; drug-drug (resmetirom/ervogastat) interaction (DDI) study expected to initiate in 2026; Phase 2 combination study expected to initiate in 2027 following regulatory discussions; 2. MGL-2086 Phase 1 single ascending dose (SAD) study expected to initiate in 2Q26; **MOA**: Mechanism of action.

akero
a Novo Nordisk company

Restoring Balance. Renewing Life.

Akero Therapeutics

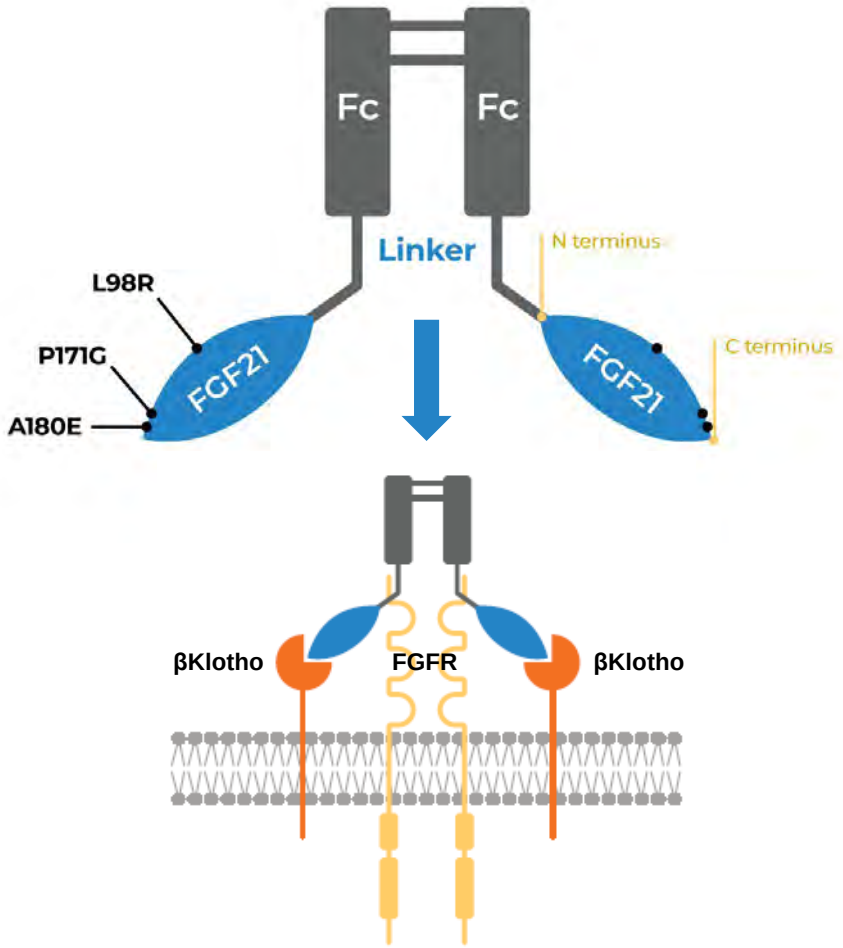
a Novo Nordisk Company

Reshma Shringarpure, PhD

VP, Clinical Research & Medical Affairs

Akero Therapeutics, a Novo Nordisk Company

Efruxifermin: Bivalent Structure Optimized for MASH Efficacy with Convenient Once-Weekly Dosing



Bivalent FGF21 Analog Properties

- High β-Klotho affinity
- High systemic exposure
- Maintained agonism of FGFRs throughout weekly dosing
- Sustained pharmacodynamic effect through Week 96

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

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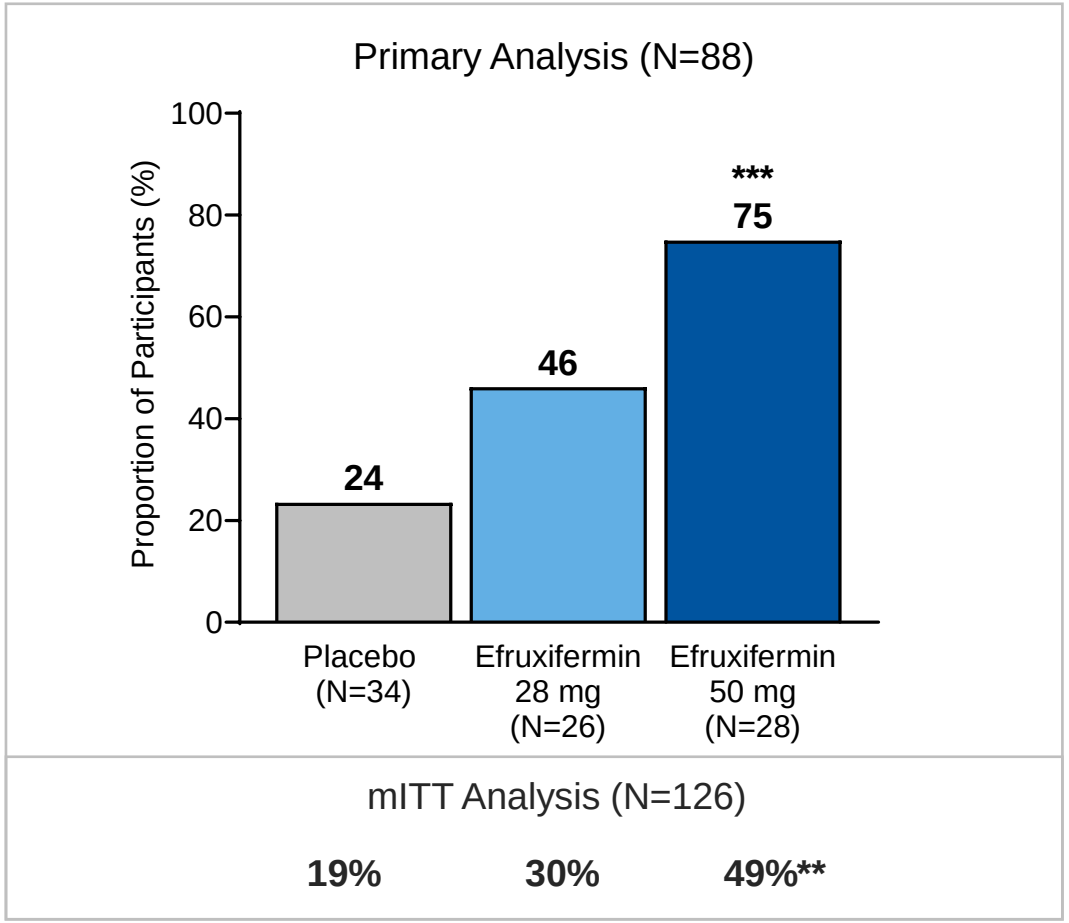
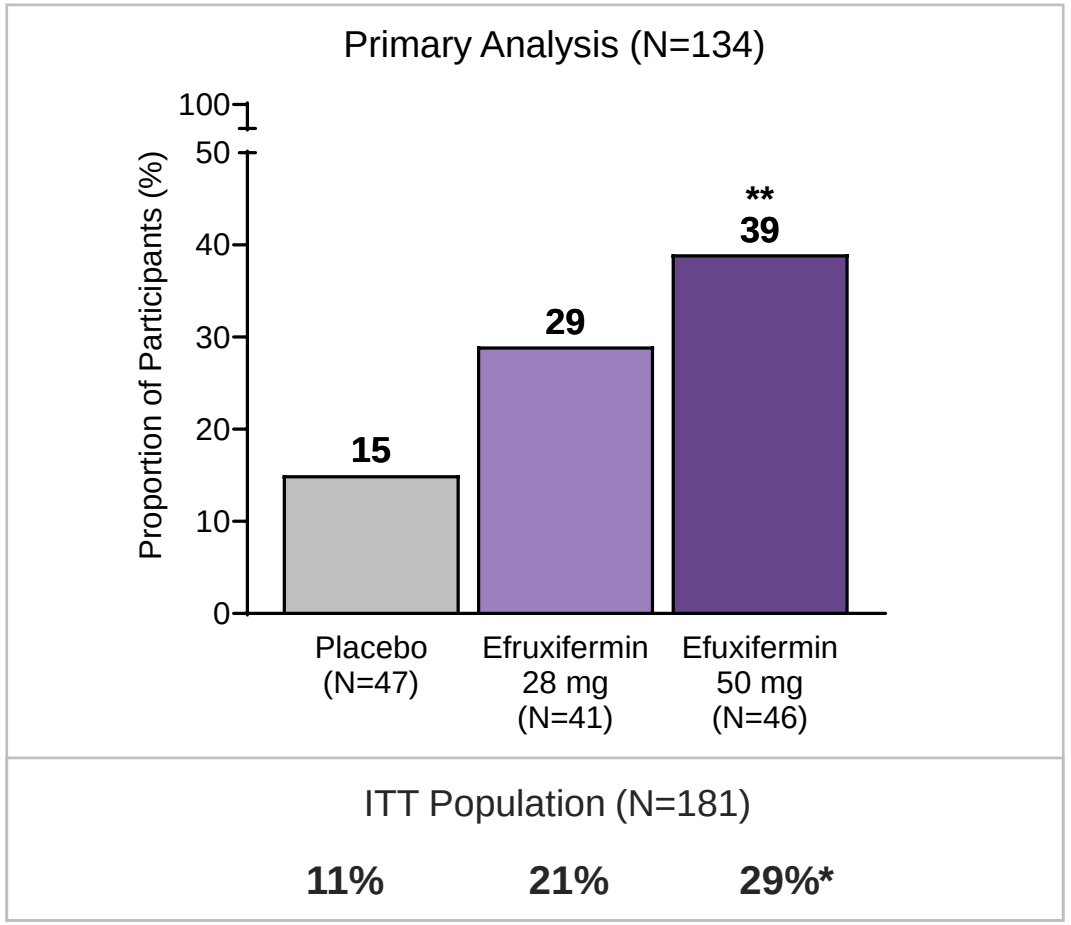
Fibrosis Improvement & No Worsening of MASH with 50 mg Efruxifermin at Week 96 in F2-F3 and F4c MASH

≥1-Stage Fibrosis Improvement & No Worsening of MASH at Week 96 (F2-F3 MASH)



≥1-Stage Fibrosis Improvement & No Worsening of MASH at Week 96 (F4c MASH)



**p<0.01, ***p<0.001 vs placebo (Cochran-Mantel-Haenszel test).
The primary analysis included all participants with baseline and Week 96 liver biopsies. The mITT analysis included all randomized participants that received ≥1 dose of study drug; missing biopsy imputed as non-response. Fibrosis improvement was defined as ≥1-stage fibrosis decrease without MASH worsening.

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Publications: Key Phase 2b Clinical Trials of Efruxifermin

Efruxifermin improved fibrosis, resolved MASH and demonstrated consistent improvements in noninvasive markers of fibrosis, liver injury, lipid metabolism and insulin sensitivity

TRIAL	CITATION
HARMONY *Efruxifermin vs placebo for 96 weeks[1,2]* *N=128*	**Harrison et al. *Lancet Gastroenterol Hepatol.*** 2023;8(12):1080–1093. DOI: 10.1016/S2468-1253(23)00272-8. **Noureddin et al. *Lancet.*** 2025;406(10504):719–730. DOI: 10.1016/S0140-6736(25)01073-6.
symmetry FOR CIRRHOTIC NASH *Efruxifermin vs placebo for 96 weeks[3]* *N=182*	**Noureddin et al. *N Engl J Med*** 2025;392(24):2413–2424. DOI: 10.1056/NEJMoa2502242.
Cohort D **(expansion of SYMMETRY)** *Efruxifermin vs placebo in GLP-1 RA users for 12 weeks[4;] N=31*	**Harrison et al. *Clin Gastroenterol Hepatol*** 2025;23(1):103–113. DOI: 10.1016/j.cgh.2024.02.022.

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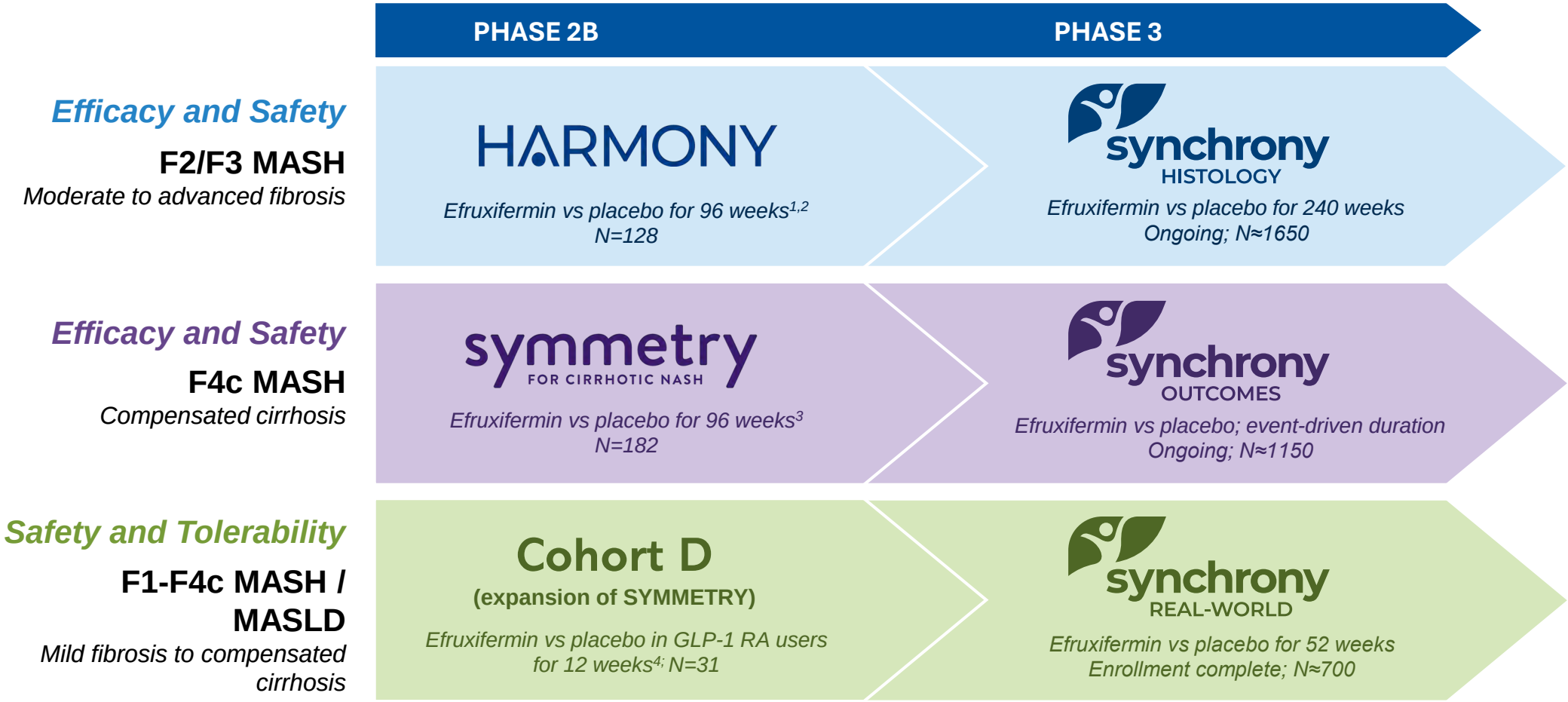
Efruxifermin for MASH Late-Stage Clinical Program

Phase 3 SYNCHRONY program consists of 2 efficacy trials evaluating outcomes of liver histology and clinical events and a third trial evaluating safety and tolerability.



[1] Harrison (2023) *Lancet Gastroenterol Hepatol;* [2] Noureddin (2025) *Lancet;* [3] Noureddin (2025) *N Engl J Med.* [4] Harrison (2025) *Clin Gastroenterol Hepatol.*

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Corporate Update: Akero, A Novo Nordisk Company

- Akero was acquired by Novo Nordisk in Q4 2025
- Akero, a Novo Nordisk Company, continues to execute on the Phase 3 program in MASH fibrosis and MASH cirrhosis
- Akero and Novo Nordisk continue to work together towards the goal of bringing efruxifermin to patients with MASH and advanced fibrosis or cirrhosis

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Lanifibranor: Balanced pan-PPAR Designed to Address the Biology of MASH

A new chemical entity engineered to deliver coordinated metabolic, anti-inflammatory and antifibrotic effects

Tom Capozza, MD
SVP, Clinical Development
Inventiva

Property of Inventiva

Striking the PPAR Balance

LIVER

Steatosis

PPARγ

- ↓ Fatty acid uptake
- ↑ Fatty acid breakdown (catabolism)
- ↓ Fat creation (lipogenesis)

Inflammation and Ballooning

PPARγ, PPARα, PPARδ

- ↓ NFkB-dependent gene activation
- ↓ Inflammasome
- ↓ Ballooning

Fibrosis

PPARγ, PPARα

- ↓ Stellate cell proliferation and activation
- ↓ Collagen and fibronectin production

Vascular

PPARγ, PPARδ

- ↓ Portal pressure
- ↓ LSEC capillarization
- ↓ Intrahepatic vascular resistance

WHOLE BODY

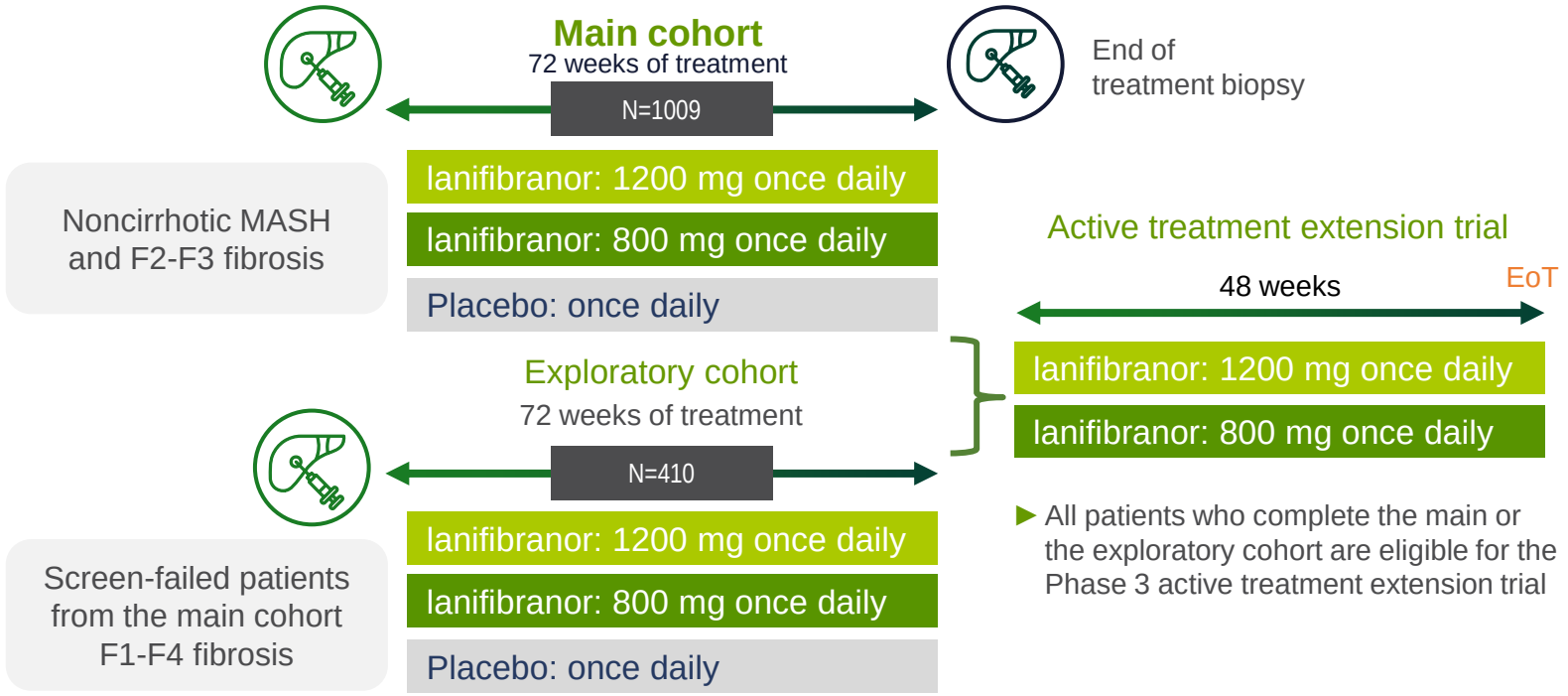
Metabolism

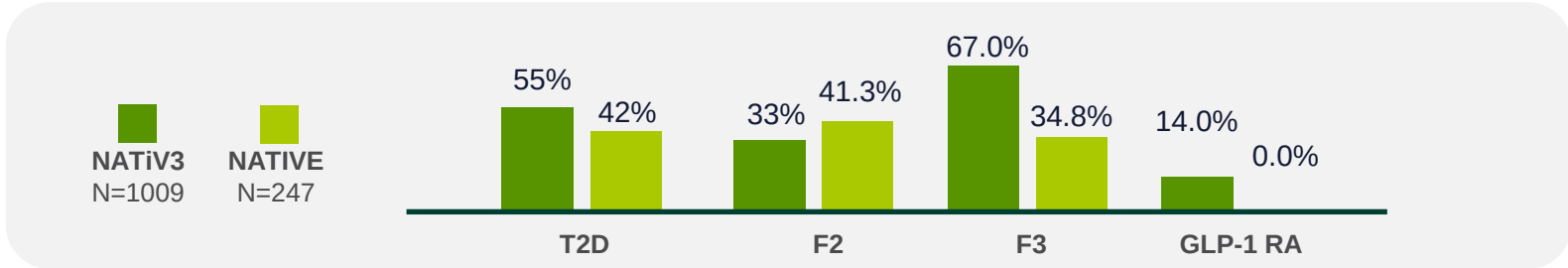
PPARγ, PPARα, PPARδ

- ↑ Insulin sensitivity
- ↑ HDL-C
- ↓ Triglycerides

Phase 3 NATiV3 fully recruited

Trial design mirrors the successful Phase 2b study





EoT, end of treatment; GLP-1, glucagon-like peptide-1; GLP-1-RA, glucagon-like peptide-1 receptor agonist; MASH, metabolic dysfunction-associated steatohepatitis.
* As of October 2025.

Phase 3 NATiV3 Clinical Trial

Primary Endpoint
Composite end point of patients having both MASH resolution and 1 stage of fibrosis improvement.

Key Secondary Endpoints
MASH resolution and no worsening of fibrosis, fibrosis improvement, and no worsening of MASH.

GLP-1 Inclusion
Patients under a stable dose of GLP-1-RA for at least 3 months prior to screening can be included.

Statistical Powering
- 90% considered for sample size calculations.
- Stratification by fibrosis stage and diabetic status.
- NATiV3 fully recruited with 1,009 patients in the main cohort and 410 in the exploratory cohort.

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Zydus Updates

UC Berkeley Public Health

Wave Life Sciences Update

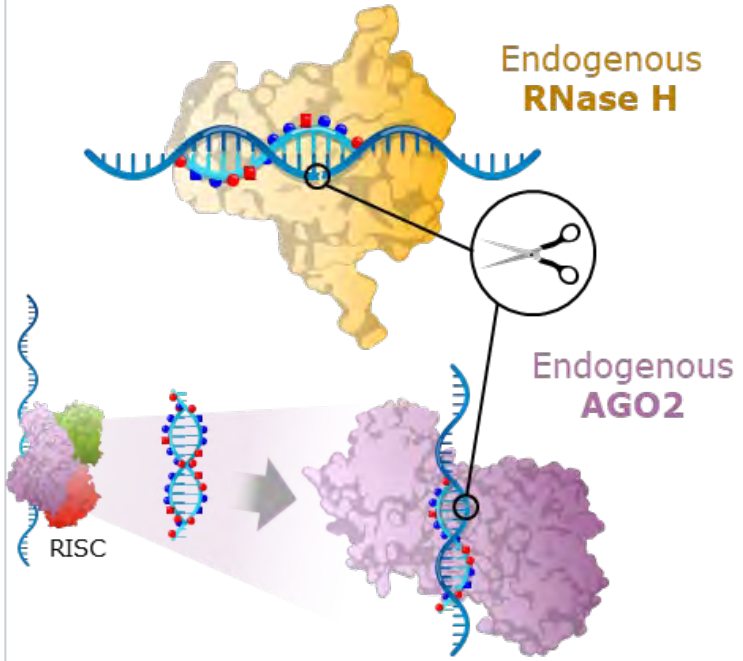
Presenter: Daniel Paulson, MD

March 6, 2026

Three major RNA medicine modalities at Wave

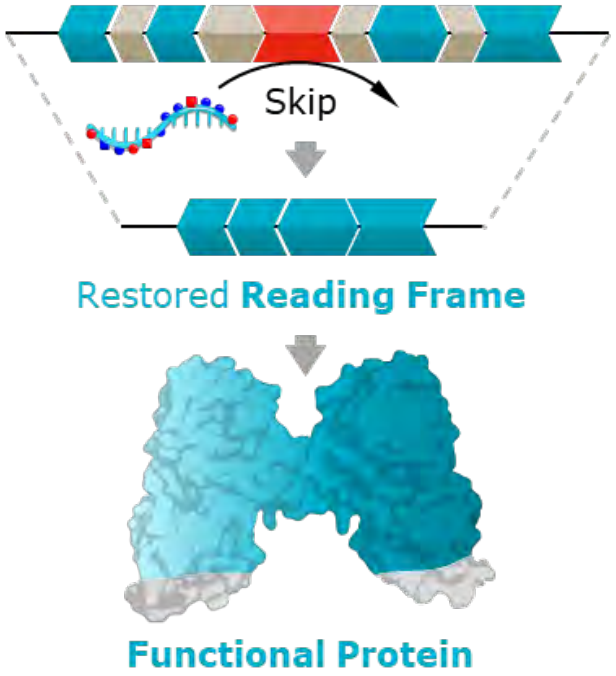
Silencing (**siRNA**)

Clinically validated with WVE-007, Obesity program



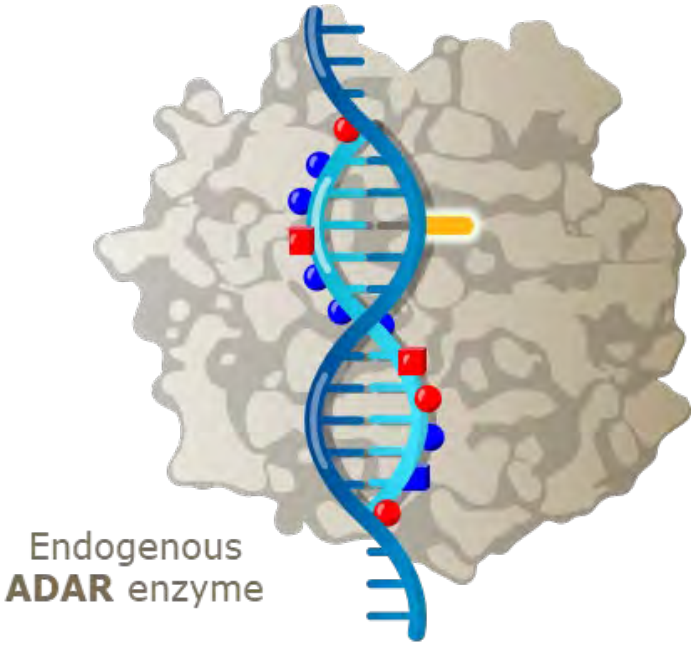
Splicing

Clinically validated with WVE-N531, DMD exon53 program



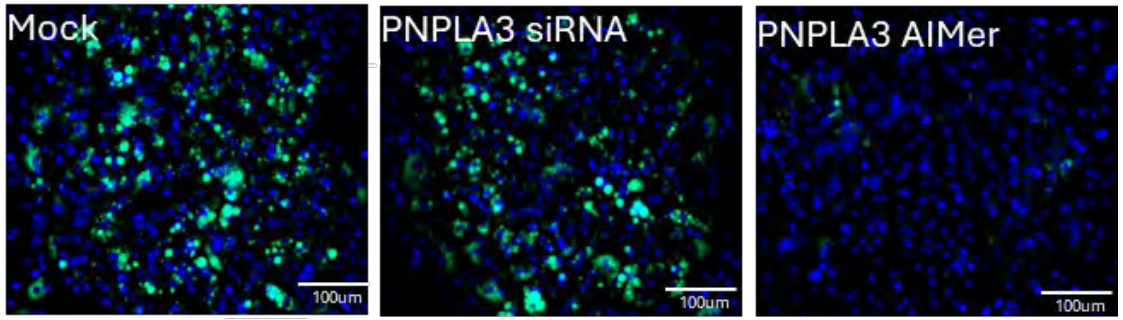
RNA base editing (**AIMer**)

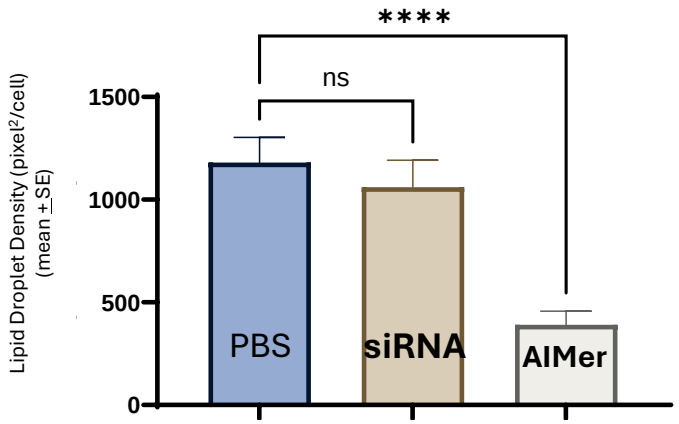
Clinically validated with WVE-006, AATD program



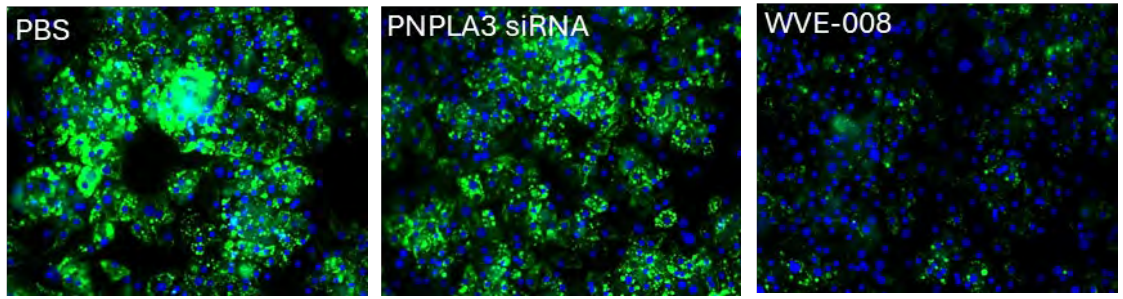
RNA editing through AIMer corrects I148M mutation and restores PNPLA3 function, leading to reduction of lipid accumulation in hepatocytes, higher than that induced by siRNA

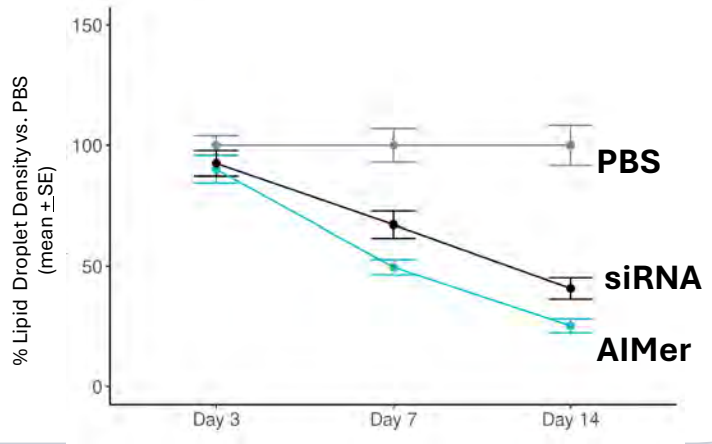
Significant decrease in liver fat with PNPLA3 editing in human HEPATOPAC® model with homozygous I148M





Decrease in liver fat with WVE-008 in monolayer culture





One-way ANOVA with Dunnett post hoc test comparisons to Mock **** P< 0.0001

REGENERON

MASH Program

PNPLA3, HSD17B13, CIDEB

Fady Tanios, PhD

March 2026

Fady is an employee and shareholder of Regeneron Pharmaceuticals, Inc.

Phase I randomized double-blind study of Rapirosiran (an RNA interference therapeutic) targeting HSD17B13 for MASH

Background

Loss of function in *HSD17B13* is associated with reduced risk of chronic liver disease

Rapirosiran, an investigational RNA interference therapeutic, targets liver-expressed *HSD17B13* mRNA

Methods

Participants

- 18-65 years old
- **Part A**: Healthy adults (N = 58)
- **Part B**: MASH (N = 46)

Treatments

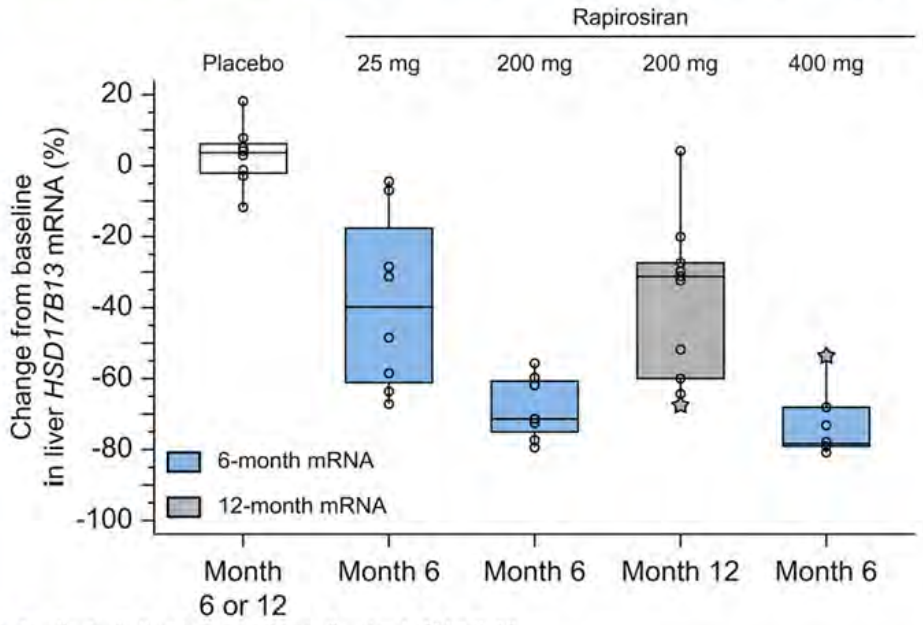
- Rapirosiran
- Placebo

Endpoints

- **Part A:** AEs, PK
- **Part B:** AEs, change in liver *HSD17B13* mRNA, NAFLD Activity Score

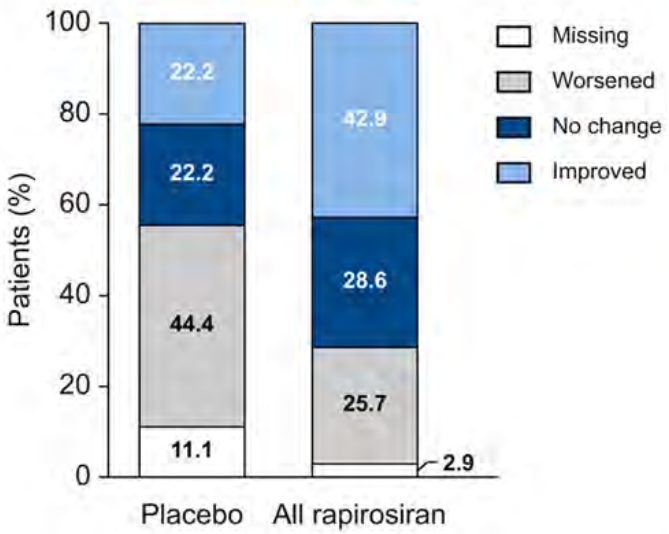
Results

Percentage change from baseline in *HSD17B13* mRNA



☆ 1 patient with liver biopsy at Month 6 instead of Month 12
☆ 1 patient who received only 1 rapirosiran dose due to hepatitis E infection

Change from baseline in NAFLD activity total score



Part A: Healthy participants	Placebo (n = 14)	Rapirosiran (n = 44)
TEAE Serious AE	3(21) 0(0)	17(39) 1(2)
Injection Site Reaction	0(0)	5(11)
Part B: Patients with MASH	**Placebo (n=9)**	**Rapirosiran (n=36)**
TEAE Serious TEAE	7(78) 0(0)	29(81) 1(3)

Sanyal, Taubel, Badri, *et al.* (2025)

PNPLA3 mRNA silencing with ALN-PNP (800 mg single dose) reduces liver fat by 55% at 24 week in patients with MASLD homozygous for the *PNPLA3* p.I148M risk allele

REGENERON®

Presented at the American Association for the Study of Liver Diseases (AASLD), Washington, DC, USA, November 7–11, 2025. - Selin Somersan-Karakaya et.al

Summary

Genetic Variants Impact Risk

PNPLA3, HSD17B13, CIDEB influence MASLD/MASH risk

Variants impact disease progression and treatment response

Target Genes & Their Effects

Allele-specific targeting supports liver protection

Regeneron–Alnylam siRNA Program

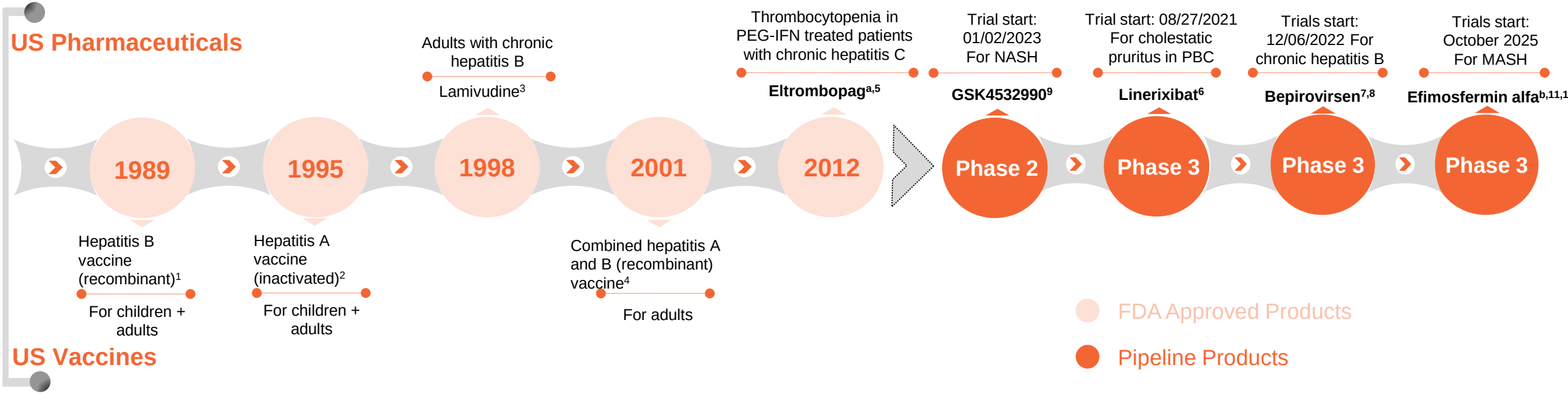
Liver-targeted siRNAs reduce mRNA expression

Targets: HSD17B13, CIDEB, PNPLA3

Hepatology Heritage at GSK

Presented by Meej Kim, Sr. Director, GSK Clinical Development

GSK



Over 4.5 million US adults have been diagnosed with liver disease and over 50,000 die each year, making chronic liver disease and cirrhosis the 9th leading cause of death in the US[10]

[a] Divested to Novartis in 2015. [b] Acquired July 2025 from Boston Pharmaceuticals.

MASH = metabolic dysfunction-associated steatohepatitis; NASH = non-alcoholic steatohepatitis; PBC = primary biliary cholangitis; PEG-IFN = pegylated interferon

1. Prescribing Information for *Energix-B*. 2. Prescribing Information for *Havrix*. 3. Drugs@FDA: FDA-Approved Drugs. Accessed October 29, 2025. 4. Prescribing Information for *Twinrix*. 5. Drugs@FDA: FDA-Approved Drugs. Accessed October 29, 2025. 6. Clinicaltrials.gov identifier NCT04950127. Accessed October 29, 2025. 7. Clinicaltrials.gov identifier NCT05630807. Accessed October 29, 2025. 8. Clinicaltrials.gov. Identifier NCT05630820. Accessed October 29, 2025. 9. Clinicaltrials.gov identifier NCT05583344. Accessed October 29, 2025. 10. Centers for Disease Control and Prevention. Mortality in the United States, 2023. Accessed October 29, 2025. 11. ClinicalTrials.gov identifier NCT07221227. Accessed October 29, 2025. 12. ClinicalTrials.gov identifier NCT07221188. Accessed October 29, 2025.

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MED--US-14754 | March 2026

Ongoing Steatotic Liver Disease Clinical Trials

Investigational Compound	Study Population	Identifier/Status	Design	Study Phase	Study Information on ClinicalTrials.gov
Metabolic Dysfunction-Associated Steatohepatitis/Nonalcoholic Steatohepatitis (MASH*/NASH)					
GSK4532990	Adults with MASH/ NASH and advanced fibrosis (F3/F4)	HORIZON NCT05583344 Active, not recruiting	Randomized, double-blind, placebo-controlled	2b	
efimosfermin alfa† GSK6519754	Adults with MASH and biopsy-confirmed F2- or F3-stage fibrosis	ZENITH-1 NCT07221227 Recruiting	Randomized, double-blind, placebo-controlled	3	
	Adults with known or suspected MASH with fibrosis consistent with stage F2 or F3	ZENITH-2 NCT07221188 Recruiting	Randomized, double-blind, placebo-controlled	3	
	Adults with MASH and compensated cirrhosis (F4)	NCT06920043 Recruiting	Randomized, double-blind, placebo-controlled	2	
Alcohol-Related Liver Disease (ALD)					
GSK4532990	Adults living with advanced ALD and MetALD	STARLIGHT NCT06613698 Recruiting	Randomized, dose-finding, double-blind, placebo-controlled	2	

Interested in learning more?

Please contact us at GSKClinicalSupportHD@gsk.com or call +1 (877) 379-3718

*Under new nomenclature consensus MASH replaces the term NASH (Rinella ME, et al. *J Hepatol*. 2023;79[6]:1542-1556); † Efimosfermin alfa has been acquired by GSK as of July 7, 2025

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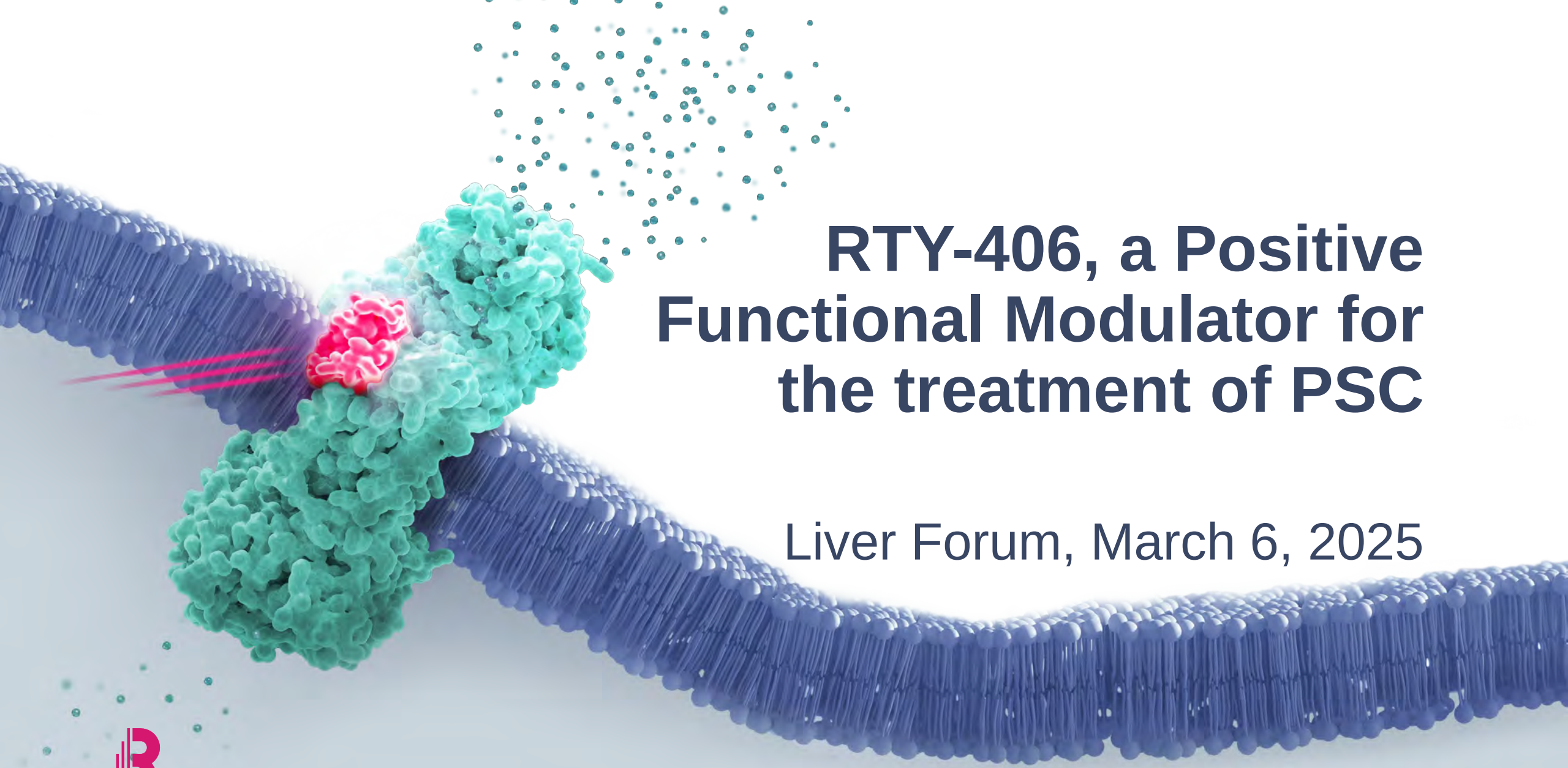
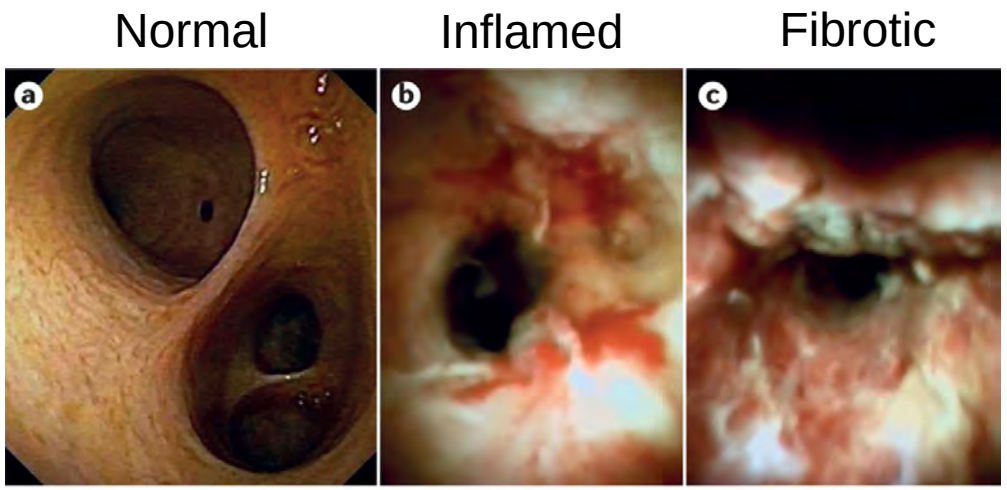


RTY-406, a Positive Functional Modulator for the treatment of PSC

Liver Forum, March 6, 2025

RECTIFY PHARMA

PSC is a debilitating orphan bile duct disease leading to cholangitis, biliary cancers, and liver failure



[4]

Abnormal Bile Composition

Reduced Bile Flow

→ **Bile Duct Injury** →

Inflammation

Cholestasis

Fibrosis

CCA >580X
Increased risk[1]

Bile Stones
Frequent ≥25%[2]

50%
Patients require liver transplant

Bile PL Deficit
50% decrease[3]

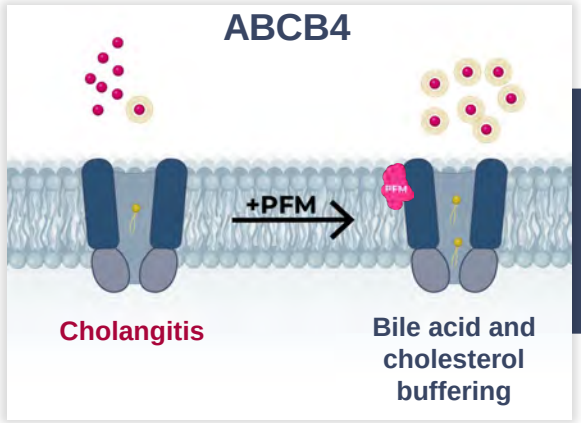
0
FDA / EMA approved drugs

Targeting abnormal bile composition may offer a new mechanism to address the disease

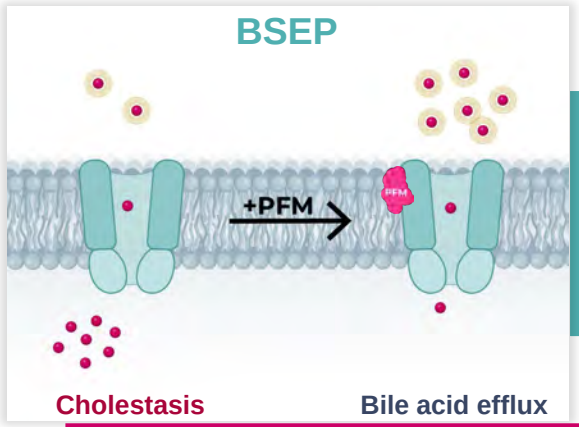
[1] Aune D, et al. PSC and the risk of cancer. Sci Rep. 2021 May 20;11(1):10646 [2] Said K et al. Gallbladder disease in patients with PSC. J Hepatol 2008 [3] Mohajeri S et al. In vivo 1H MRS of human gallbladder bile in understanding the pathophysiology of PSC. NMR Biomed 2019 [4] Jiang, X, et al. 2017;14;279 CCA Cholangiocarcinoma PL Phospholipids

ABCB4/BSEP PFM RTY-406 improves bile composition and enhances bile flow, a novel MOA to treat PSC

ABCB4/BSEP dual-targeted PFM



Enhanced phospholipid efflux → Improved bile composition → Neutralization of bile acids and free cholesterol (restore mixed micelles)



Enhanced bile acid efflux → Improved bile flow → Reduced bile stasis and liver parenchyma damage

Reduced cholangitis and cholestasis

& Improved biliary & liver health

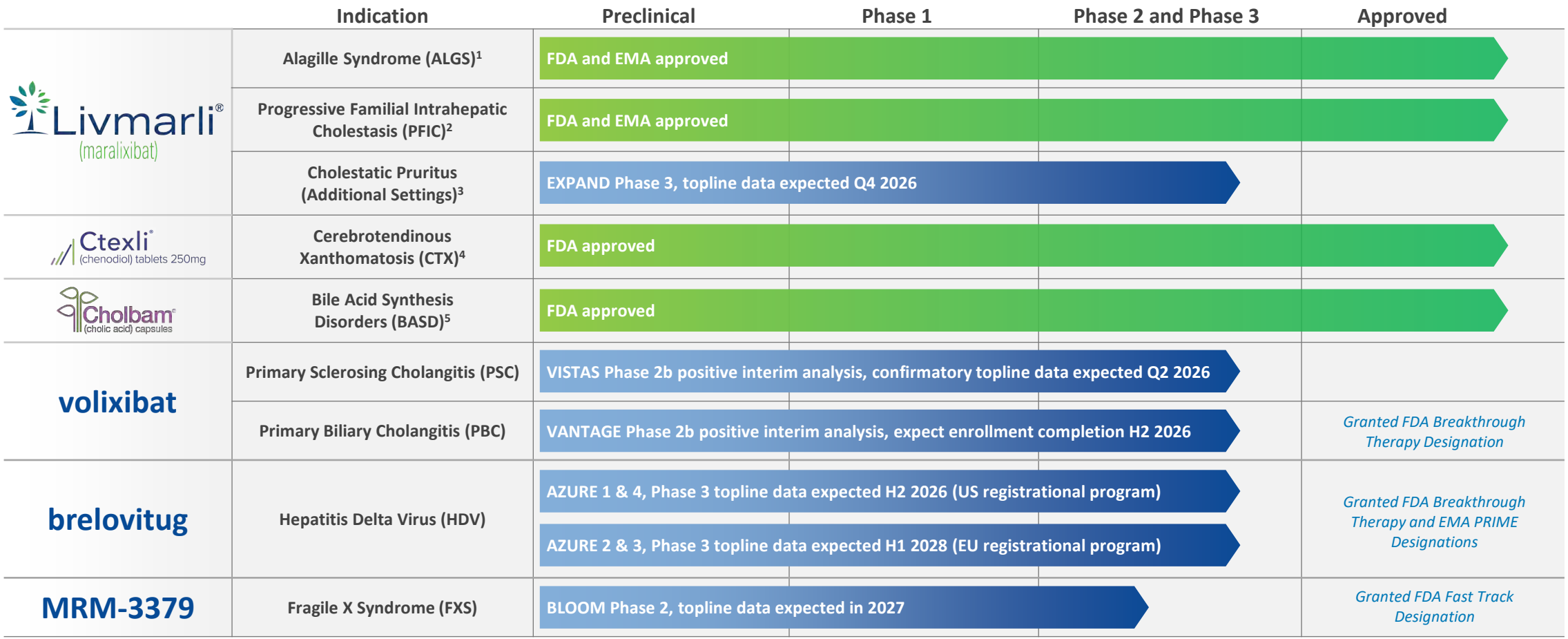
Reduced symptoms burden

Altered disease progression

Proof of concept achieve in animal model of PSC, Clinical program to be Initiated soon

Commercial Portfolio with Pipeline of Growth Opportunities

3 APPROVED RARE DISEASE MEDICINES, 5 ADDITIONAL INDICATIONS IN DEVELOPMENT IN HIGH-NEED ORPHAN INDICATIONS



[1]Received U.S. FDA approval for cholestatic pruritus in patients with Alagille syndrome 3 months of age and older. European Commission has granted marketing authorization for LIVMARLI® (maralixibat) for the treatment of cholestatic pruritus in patients with Alagille syndrome 2 months of age and older

[2] Received U.S. FDA approval for cholestatic pruritus in patients with PFIC 12 months of age and older. European Commission has granted marketing authorization for LIVMARLI® (maralixibat) for the treatment of PFIC in patients 3 months of age and older

[3]Using liquid oral formulation for the EXPAND study looking at patients with additional settings of ultra-rare cholestatic pruritus, excluding PSC, PBC, ICP, ALGS and PFIC

[4] Received U.S. FDA approval for the treatment of adults with cerebrotendinous xanthomatosis (CTX)

[5]Bile acid synthesis disorders include Peroxisome biogenesis disorder-Zellweger Spectrum Disorder (PBD-ZSD)

Phase 2b Study of Volixibat in PSC Patients with Cholestatic Pruritus

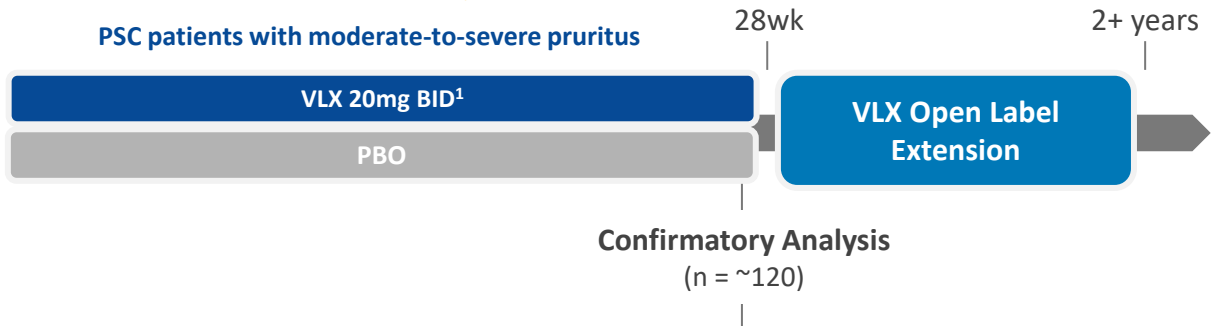
Positive Interim Analysis

Exceeded prespecified efficacy and safety thresholds for continuation

20 mg BID dose selected

VISTAS continues with no changes

vistas
EFFICACY & SAFETY OF VOLIXIBAT IN THE TREATMENT OF CHOLESTATIC PRURITUS IN PATIENTS WITH PSC



Primary Endpoint
Change in pruritus from baseline to 28wk

Confirmatory Topline Data Expected Q2 2026

[1] Participants are randomized 1:1 between Volixibat 20mg and Placebo. BID, twice daily

Resolution Therapeutics

Pioneering Regenerative Macrophage Therapy in Inflammatory and Fibrotic Diseases

PLATFORM:

Regenerative Macrophage Therapy (RMT)

IN THE CLINIC

First indication **End Stage Liver Disease (ESLD)**, opportunity to transform outcomes in a growing patient population

TRANSFORMATIVE TREATMENT

Engineered macrophages with **enhanced anti-inflammatory and anti-fibrotic efficacy**

ROBUST SCIENCE & CLINICAL EVIDENCE

15 years of pre-clinical research and two proof of concept clinical studies **demonstrating safety and efficacy** in patients with cirrhosis

FOCUSED PIPELINE

Two engineered regenerative macrophage therapies being evaluated in **lung fibrosis and GvHD**

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Macrophages have a dual anti-inflammatory and anti-fibrotic effect

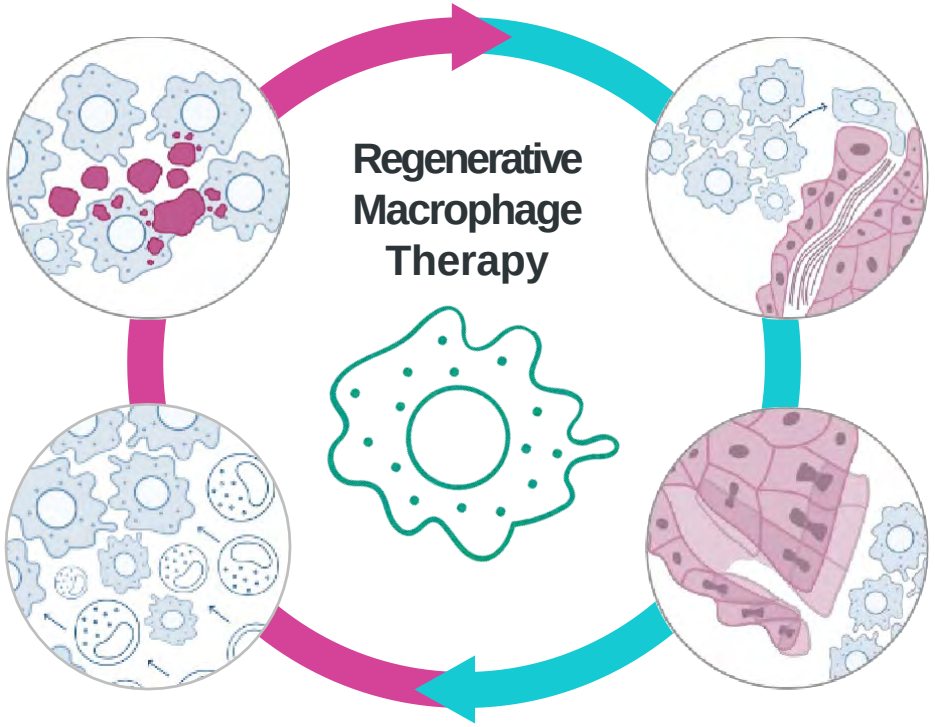
15+ years preclinical research unveils mechanism of action of pro-regenerative macrophages in liver fibrosis

Phagocytosis
Engulfment and removal of bacteria and necrotic tissue, preventing activation of downstream inflammatory cascade.

A

Monocyte recruitment & polarisation
Endogenous monocytes are recruited and polarized to pro-regenerative macrophages, creating an anti-inflammatory environment.

B



C

Fibrosis breakdown
Degradation of the extracellular matrix (ECM) including the removal of fibrotic scar tissue.

D

Fibrogenesis suppression
Suppression of new scar formation by down-regulation of myofibroblast activation.

Anti-Inflammatory **Anti-Fibrotic**

Thomas *et al.*, Hepatology, 2011; Ramachandran P *et al.*, PNAS, 2012; Moore *et al.*, Cytotherapy, 2015; Fraser *et al.*, Cytotherapy, 2017; Thomas *et al.*, J Hepatology 2018; Stuart Forbes., EASL, 2018; Ramachandra *et al.*, Nature, 2020.

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MATCH clinical program designed to demonstrate clinical PoC

MATCH 2 builds on MATCH 1 safety results with a larger, randomised controlled study of well-matched patients

MATCH I (University of Edinburgh)

Non-engineered macrophages shown to be safe in 3x3 dose escalation study

FIH Ph1 open-label dose escalation study ; ISRCTN 10368050
N=9, single ascending dose, peripheral infusion 10^7, 10^8 or 10^9 cells

Primary outcomes for safety and feasibility met

- ✓ All patients alive and transplant-free after 1 year.
- ✓ No transfusion reactions.
- ✓ No dose-limiting toxicities.
- ✓ No macrophage activation syndrome.
- ✓ Only one clinical event recorded as mild ascites.

nature medicine

Moroni, Francesca, *et al*. "Safety profile of autologous macrophage therapy for liver cirrhosis." *Nature Medicine* 25.10 (2019): 1560-1565

MATCH II (University of Edinburgh)

Non-engineered macrophages show dramatic clinical effect in randomised controlled study

Open-label, parallel-group, phase 2, RCT ; ISRCTN10368050 ; Brennan PN, *et al*., BMJ Open, 2021
N=50, single dose up to 10^9 cells, peripheral infusion, 3 patients with 3x doses

nature medicine

Brennan PN, *et al.,* Nature Medicine, 2025

Baseline Demographics		Treatment (1x infusion)	Treatment (3x infusion)	Control	All
Total		23	3	24	**50**
Gender	Male	16	2	14	**32**
	Female	7	1	10	**18**
Age	*Mean*	57.83	58.00	60.67	**59.20**
Dominant Aetiology	ALD	12	2	12	**26**
	NAFLD	7	1	8	**16**
	Prev. Hep C	1	-	-	**1**
	PBC	1	-	3	**4**
	Other	2	-	1	**3**
Decomp. events	*Patients*	14/23	2/3	14/24	**30**
MELD day 0	*Mean*	11.87	12.00	11.96	**11.92**

Note: Treatment = "as treated". Table excludes one patient originally assigned to treatment after screening but who failed apheresis and withdrew. Liver decomp. events prior to study enrollment based on medical history.

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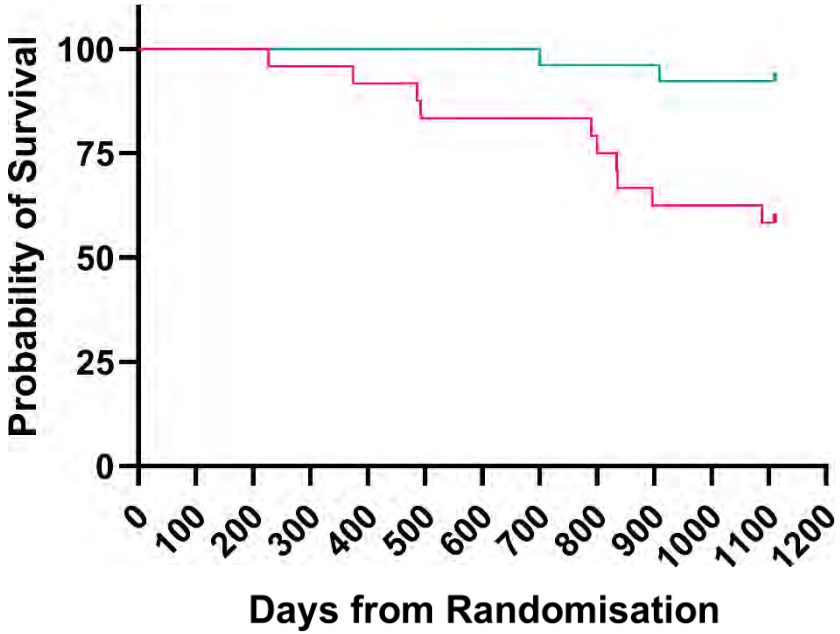
Strong clinical evidence supporting macrophage cell therapy in ESLD

MATCH II Kaplan-Meier curves show clear cut risk reduction and survival benefit in advanced cirrhosis

Prof. Stuart Forbes
THE UNIVERSITY of EDINBURGH

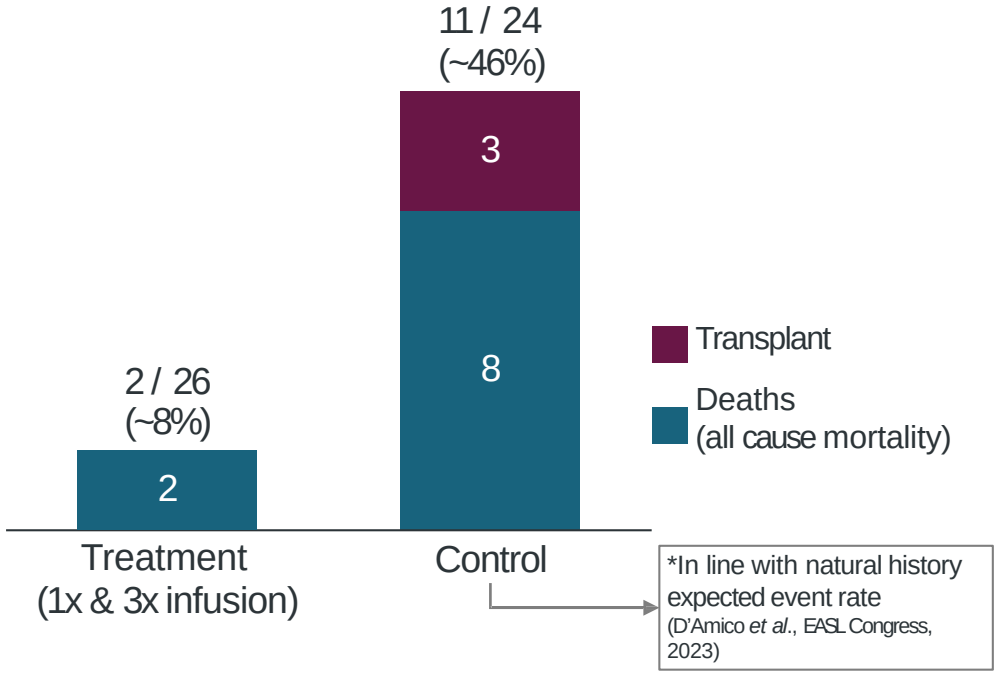
Non-Engineered Regenerative Macrophages

3 Year Transplant Free Survival
(Time to Death or Transplant)



Mortality or Transplant:
Hazard Ratio of 0.19
[95% CI 0.05, 0.75; **p=0.0015**]

3 Year Patient Deaths & Transplants



AASLD The Liver Meeting® Nov. 15-19, 2024

Forbes S*et al*., Hepatol., 2024
AASLD Abstract #0095

Source: Data on file, University of Edinburgh

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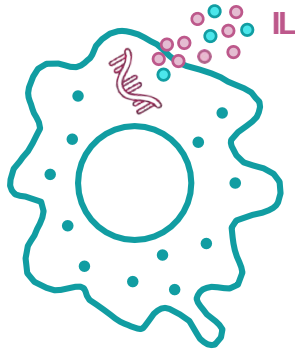
RTX001 demonstrates compelling efficacy *in vitro* and *in vivo*

IL-10 + MMP9 engineering drives greater anti-inflammatory and anti-fibrotic effects than non-engineered

Core Program: RTX001

Our optimised **engineered macrophage** product developed for commercialisation



> Autologous engineered monocyte-derived pro-regenerative macrophages.

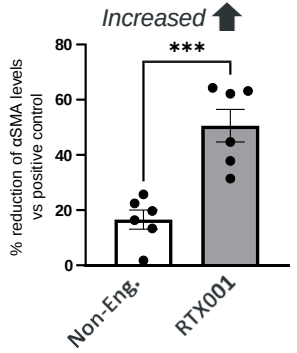
> Engineered with IL-10 + MMP9 to have a more potent and durable clinical effect.

> The best chance for a macrophage therapy product to achieve clinical efficacy and commercial success.

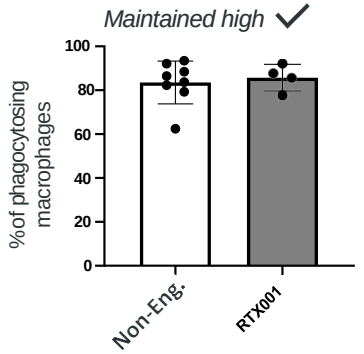
in vitro

RTX001 improves on non-engineered RMTs across MoA

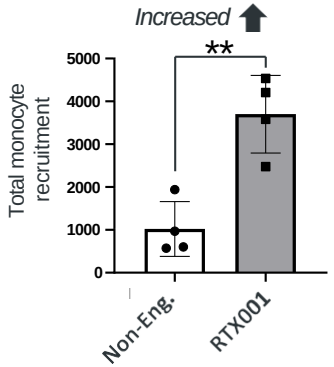
Fibrogenesis suppression



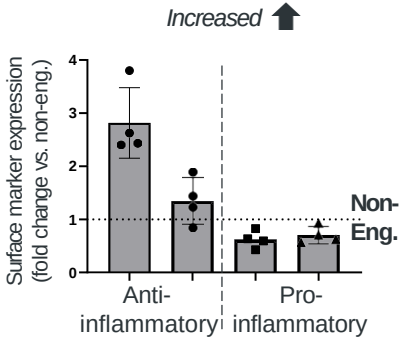
Phagocytosis



Monocyte recruitment



Polarisation



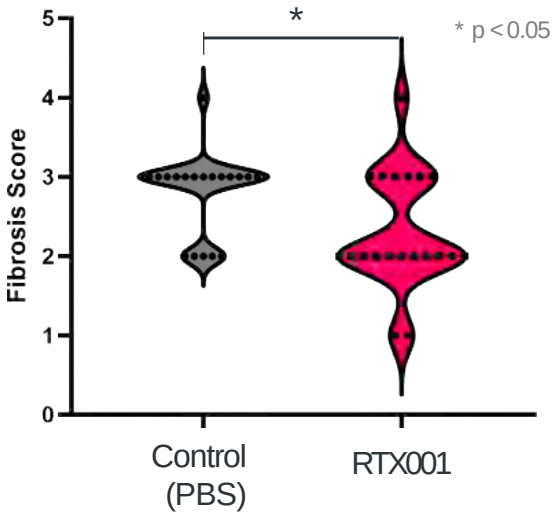
in vivo

RTX001 shows fibrosis regression *in vivo*

Fibrosis Resolution

Reduction in histo fibrosis score

5 doses of RTX001 in CCl_4 fibrosis model NSG



Safety

✅ No findings from GLP-toxicology study

Campana L *et al.*, Hepatology, 2024, AASLD TLM Abstract #3556

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

Takeda Updates

UC Berkeley Public Health

New Challenges in the Evolving MASH Drug Development Landscape

Special Focus in Patients' Perspective **Claudia Filozof, Fortrea**

Reduced biopsies, but higher screening failure burden

Incorporation of non-invasive (NI) biomarkers decreases reliance on liver biopsy, which is positive for patients. However, stricter composite eligibility criteria increase overall SFR, excluding many patients who may still have significant disease and unmet need.

Expanded use of imaging biomarkers increases patient burden

Multiple imaging modalities (e.g., VCTE, MRI-PDFF, cT1) add logistical complexity, and time commitment for patients, while also increasing operational burden at sites.

Prolonged and fragmented screening experience

Requirement for multiple appointments and sequential biomarker panels extends screening duration with impact in motivation

Retention challenges in long-term outcome trials

Accelerated approval pathways and real-world access to incretin-based therapies for obesity and T2DM create strong incentives for patients to discontinue participation, particularly during the long-term portion of marketing authorization trials.

Regulatory emphasis on meaningful patient involvement

Regulators explicitly state that sponsors are responsible for ensuring appropriate patient and public involvement in trial design. Early patient input can reduce unnecessary complexity, improve feasibility, and increase the likelihood of clinically meaningful and patient-relevant outcomes.

Need to focus on patient feasibility

Future MASH development must better align biomarker strategy, visit schedules, and trial duration with real-world patient capacity to participate and remain engaged.

Implications for MASH Drug Development

Patient-centric design is no longer optional
Increasing complexity in screening and follow-up directly threatens enrollment speed, representativeness, and retention. Trials that are not designed around patient feasibility risk delayed timelines and limited generalizability.

Non-invasive does not automatically mean patient-friendly
While NI biomarkers reduce biopsy burden, cumulative testing, imaging, and visits may offset this benefit. Simplification and prioritization of biomarker strategies are critical to avoid excluding patients with true unmet need.

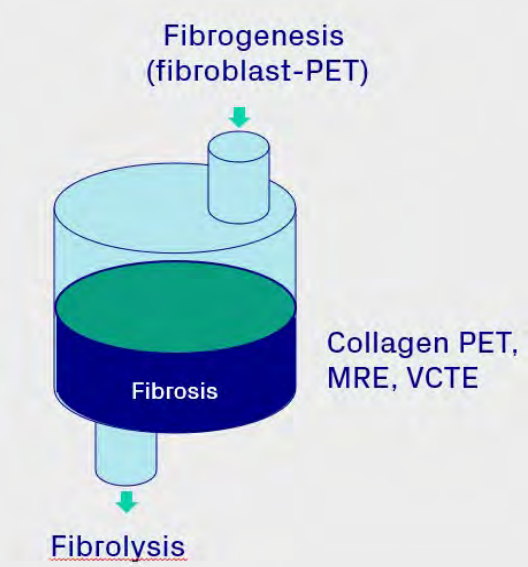
Retention is the new rate-limiting step
Availability of approved incretin therapies raises the bar for long-term participation. Sponsors must proactively address patient motivation, perceived value, and burden to protect the integrity of outcome trials.

Early patient input de-risks development
Meaningful patient involvement can identify unnecessary complexity, optimize visit schedules, and improve acceptance of endpoints—supporting both regulatory success and trial execution.

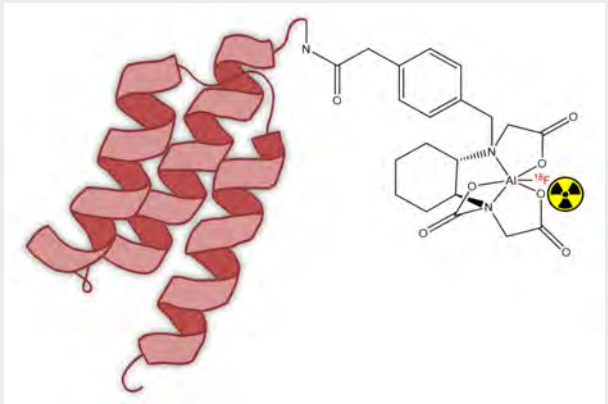
Competitive differentiation will include trial experience
Beyond efficacy and safety, the *patient experience* of participating in a MASH trial will increasingly influence recruitment, retention, and site engagement.

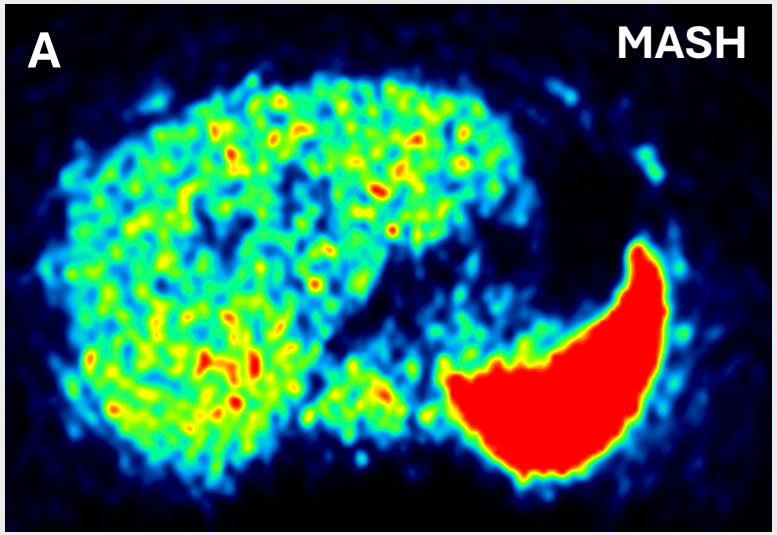
Bottom line:
Successful MASH programs will balance scientific rigor with operational simplicity—designing trials that patients can enter, stay in, and complete, while still meeting regulatory expectations.

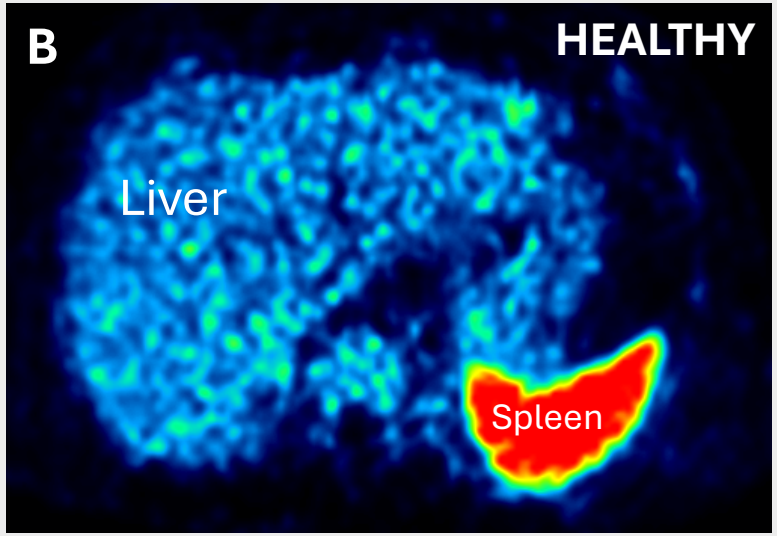
Update from Antaros Medical: Imaging of Fibrogenesis



ATH001: PDGFRb binding PET tracer



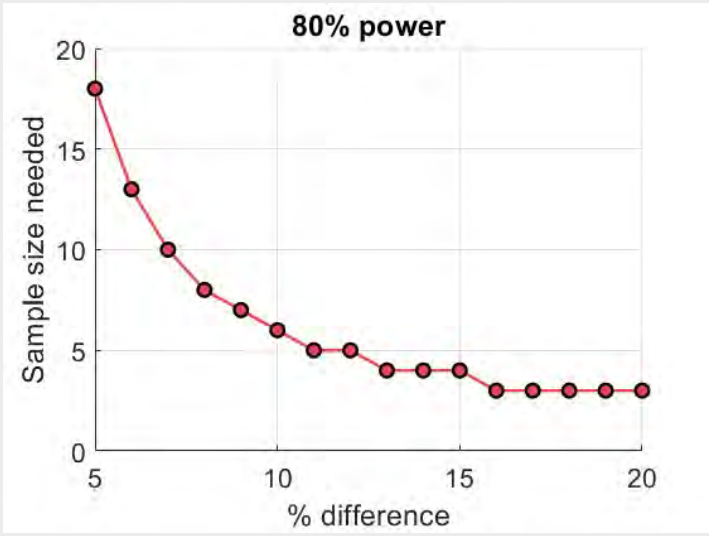




C

D

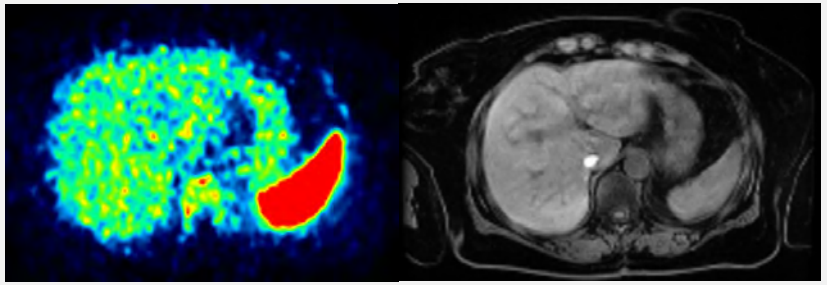
E



Antaros Medical

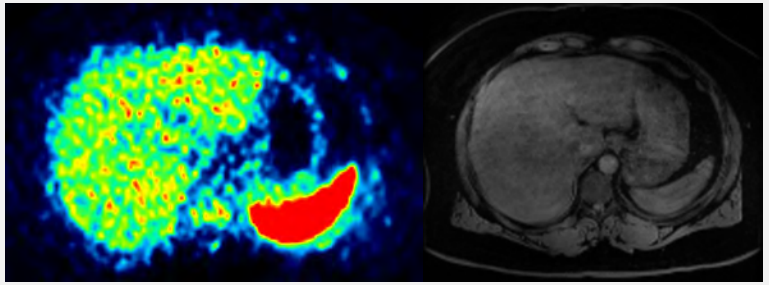
PDGFRb Imaging in Healthy, presumed MASH and advanced MASH

104-S0018, **Cohort 1**



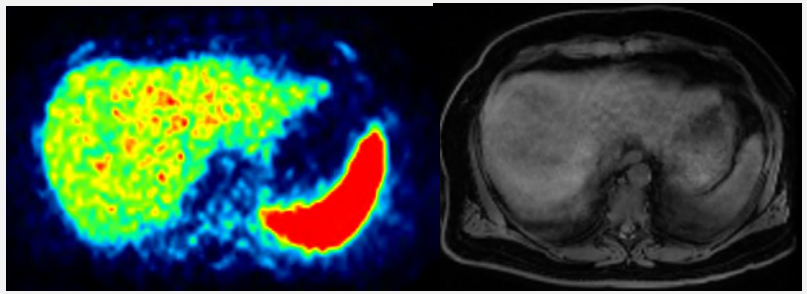
Healthy

205-S0015, **Cohort 2** 8.9 kPA



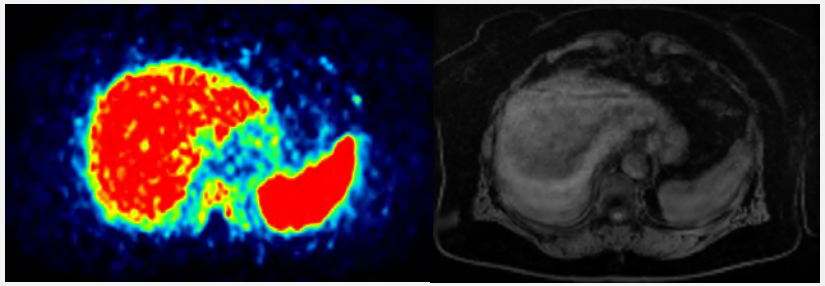
FIB-4 Score: 0.83 F2-MASH

301-S0029, **Cohort 3** 12.9 kPa



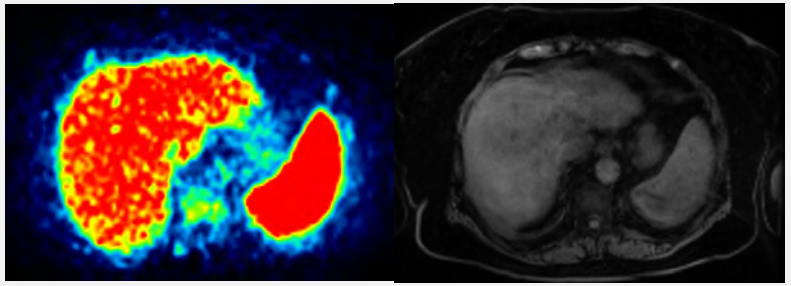
FIB-4 Score: 2.16 F4-MASH

302-S0030, **Cohort 3** 15.4 kPa



FIB-4 Score: 3.72 F4-MASH

303-S0033, **Cohort 3** 19.1 kPa



FIB-4 Score: 5.72 F4-MASH

Antaros Medical

hepatoscope by escopics

Liver Forum Update – March 6, 2026

1. GOOD TO **EXCELLENT** REPEATABILITY AND **REPRODUCIBILITY** FOR EXPERT AND **NOVICE** USERS FOR **LSM** BY 2DTE AND **STEATOSIS**-RELATED PARAMETERS

- NCT04782050
- Monocenter prospective study in outpatient hepatology clinic
- Patients with various chronic liver diseases (n = 96)
- LSM ICC: **0.79 - 0.87**
- ATT ICC: **0.90 - 0.96**
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Besson et al. WFUMB Ultra Open 2, 2024
Serdjebi et al. ClinResGastroHep, 2025

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Heriard-Dubreuil et al. WFUMB Ultra Open, 2024.

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Heriard-Dubreuil et al. WFUMB Ultra Open, 2024.

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3. STRONG **CORRELATION** OF HEPATOSCOPE QUANTITATIVE **ULTRASOUND** PARAMETERS WITH **MRI-PDFF FAT** CONTENT ASSESSMENT

- Patients with MASLD and obesity /diabetes in diabetology (n = 294)
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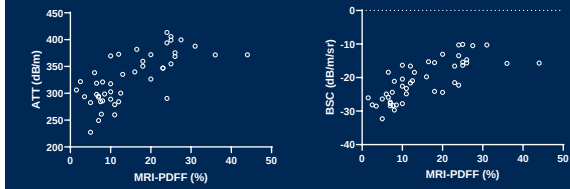

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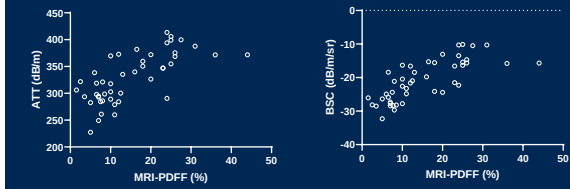

Caussy et al. EASL, 2024

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- Patients with MASLD in gastro-enterology unit (n = 193)
- **r = 0.61 - 0.63**

Serdjebi et al. ClinResGastroHep, 2025
Caussy et al., EASL 2025, manuscript under review 2026
Lescalleet et al. ACG 2025, manuscript in preparation

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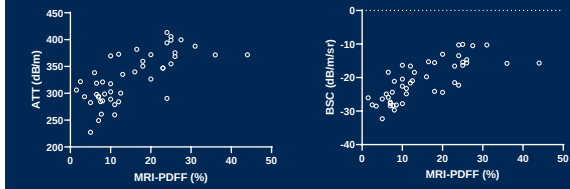

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5. **GOOD DIAGNOSTIC** PERFORMANCE OF LSM BY **2DTE** TO **TRIAGE** PATIENTS AT RISK FOR **ADVANCED FIBROSIS**

- Screening of patients with MASLD and obesity or diabetes in diabetology (n = 294)
- Use of a composite score as reference liver biopsy > MRE > FibroScan VCTE
- **AUROC = 0.81** [95%CI: 0.73 – 0.89] for patients to be referred to liver specialist
- **AUROC = 0.84** [95%CI: 0.73 – 0.95] for patients at high risk for advanced fibrosis

Caussy et al., EASL 2025, manuscript under review 2026

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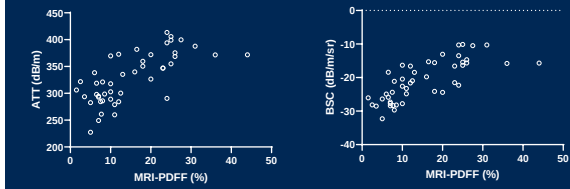
  ATT = 0.98 [95%CI: 0.92–1.0]
  BSC = 0.99 [95%CI: 0.96–1.0]

Heriard-Dubreuil et al. WFUMB Ultra Open, 2024.

hepatoscope by escopics

3. STRONG **CORRELATION** OF HEPATOSCOPE QUANTITATIVE **ULTRASOUND** PARAMETERS WITH **MRI-PDFF FAT** CONTENT ASSESSMENT

- Patients with MASLD and obesity /diabetes in diabetology (n = 294)
- Ultrasound attenuation ATT
  r = 0.71 [95%CI: 0.52 – 0.83]****
- Backscattering coefficient BSC
  r = 0.80 [95%CI: 0.66- 0.89]****



Caussy et al. EASL, 2024

4. **CONSISTENT** AND **STRONG** CORRELATION BETWEEN LSM BY **2DTE** AND LSM BY **VCTE**, WITH **NO BIAS**

- Patients with chronic liver diseases in outpatient hepatology clinic (n = 96)
- Patients with MASLD and obesity or diabetes in diabetology for risk stratification (n = 294)
- Patients with MASLD in gastro-enterology unit (n = 193)
- **r = 0.61 - 0.63**

Serdjebi et al. ClinResGastroHep, 2025
Caussy et al., EASL 2025, manuscript under review 2026
Lescalleet et al. ACG 2025, manuscript in preparation

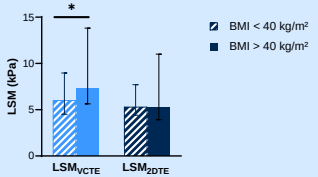
5. **GOOD DIAGNOSTIC** PERFORMANCE OF LSM BY **2DTE** TO **TRIAGE** PATIENTS AT RISK FOR **ADVANCED FIBROSIS**

- Screening of patients with MASLD and obesity or diabetes in diabetology (n = 294)
- Use of a composite score as reference liver biopsy > MRE > FibroScan VCTE
- **AUROC = 0.81** [95%CI: 0.73 – 0.89] for patients to be referred to liver specialist
- **AUROC = 0.84** [95%CI: 0.73 – 0.95] for patients at high risk for advanced fibrosis

Caussy et al., EASL 2025, manuscript under review 2026

6. **BMI** DOES NOT AFFECT **LSM** BY **2DTE**

- Patients with MASLD in outpatient gastro-enterology clinic (n = 193)
- Patients with BMI < 40 or > 40 kg/m^2 had similar liver health phenotypes based on blood biochemistry.
- LSM 2DTE with a single probe does not correlate with BMI
  r = 0.009 [95%CI: -0.06 – 0.24]



Lescalleet et al. ACG 2025, manuscript in preparation

1. GOOD TO **EXCELLENT** REPEATABILITY AND **REPRODUCIBILITY** FOR EXPERT AND **NOVICE** USERS FOR **LSM** BY 2DTE AND **STEATOSIS**-RELATED PARAMETERS

- NCT04782050
- Monocenter prospective study in outpatient hepatology clinic
- Patients with various chronic liver diseases (n = 96)
- LSM ICC: **0.79 - 0.87**
- ATT ICC: **0.90 - 0.96**
- BSC ICC: **0.91 - 0.93**

Besson et al. WFUMB Ultra Open 2, 2024
Serdjebi et al. ClinResGastroHep, 2025

2. **IMPROVEMENT** OF **CONSISTENCY** OF MEASUREMENTS OF QUANTITATIVE **ULTRASOUND** PARAMETERS IN **LARGER REGIONS OF INTEREST**

- Monocenter prospective study in outpatient hepatology clinic
- Patients with various chronic liver diseases (n = 96)
- Excellent agreement across ROI depths:
  ATT = 0.99 [95%CI: 0.95–1.0]
  BSC = 1.0 [95%CI 0.98–1.0]
- Excellent agreement across ROI sizes:
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Heriard-Dubreuil et al. WFUMB Ultra Open, 2024.

hepatoscope by escopics

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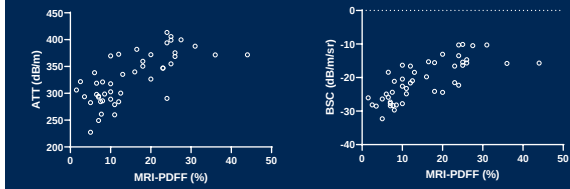

Caussy et al. EASL, 2024

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Caussy et al., EASL 2025, manuscript under review 2026

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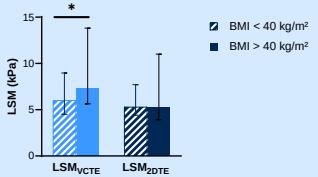


Lescalleet et al. ACG 2025, manuscript in preparation

7. HEPATOSCOPE IS USED IN A **VARIETY** OF **CONTEXTS OF USE**

- Clinical investigations/ routine clinical care
- Screening
  - community-care centers or mobile units (n = approx. 2200)
- Risk stratification
  - diabetology / endocrinology (n = 294)
  - Community-care centers (n = 193)
- Fibrosis assessment
  - Hepatology (n = approx 300)
  - Gastro-enterology (n=193)

Villavicencio et al. ClinResGastroHep, 2025
Serdjebi et al. ClinResGastroHep, 2025
Caussy et al., EASL 2025, manuscript under review 2026
Lescalleet et al. ACG 2025, manuscript in preparation
Moriariu-Barb et al. UEG 2025, manuscript submitted

Thank you for your attention !

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

SCAN ME

Magnetic Resonance Elastography (MRE)

BQP Update

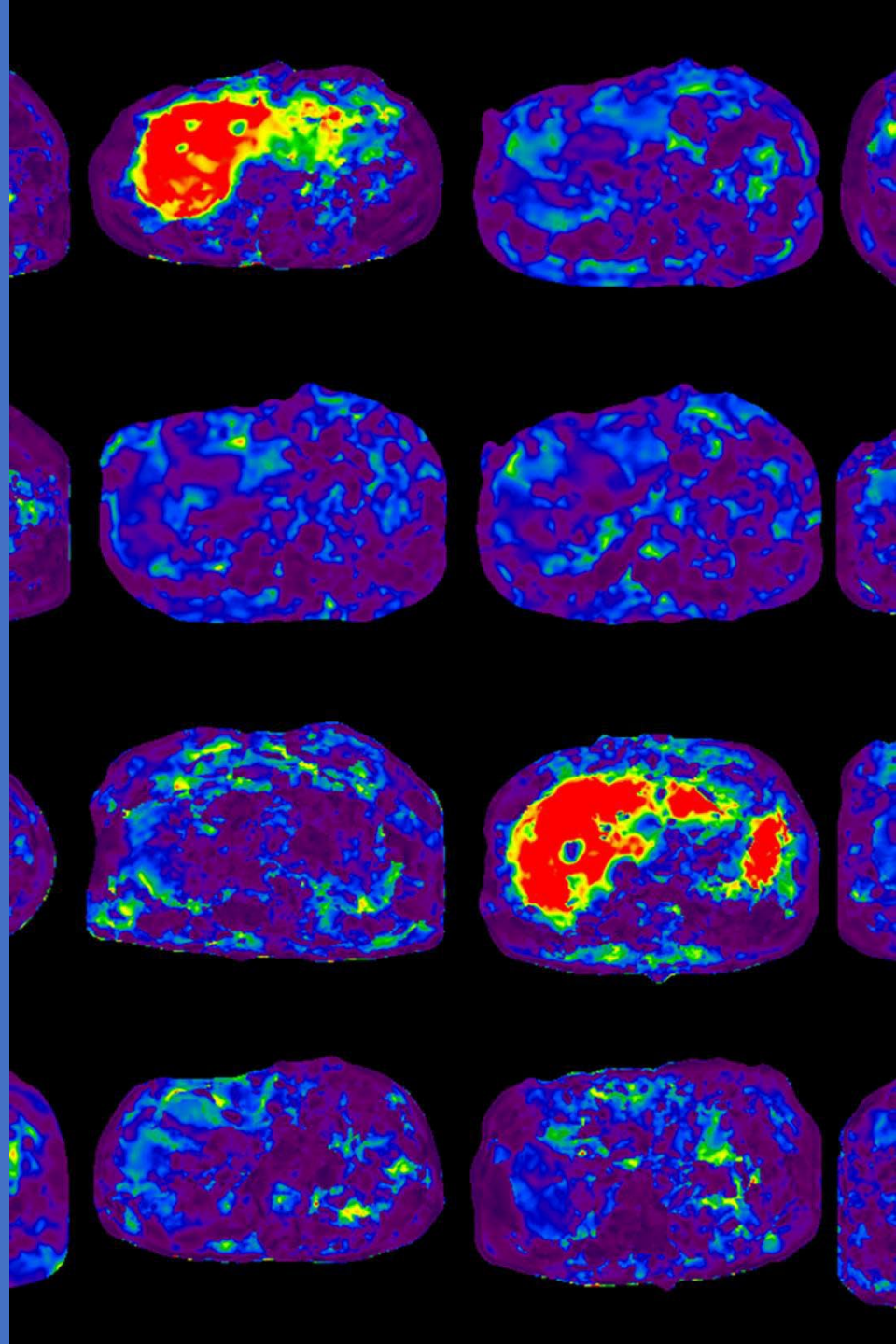
- **FDA accepted LOI for MRE as an RLSE in MASH F2-F3 trials.**
- QP in progress – existing outcomes evidence base is strong. Many ongoing or planned trials using MRE will help complete the evidence base.

MRE in Cirrhosis

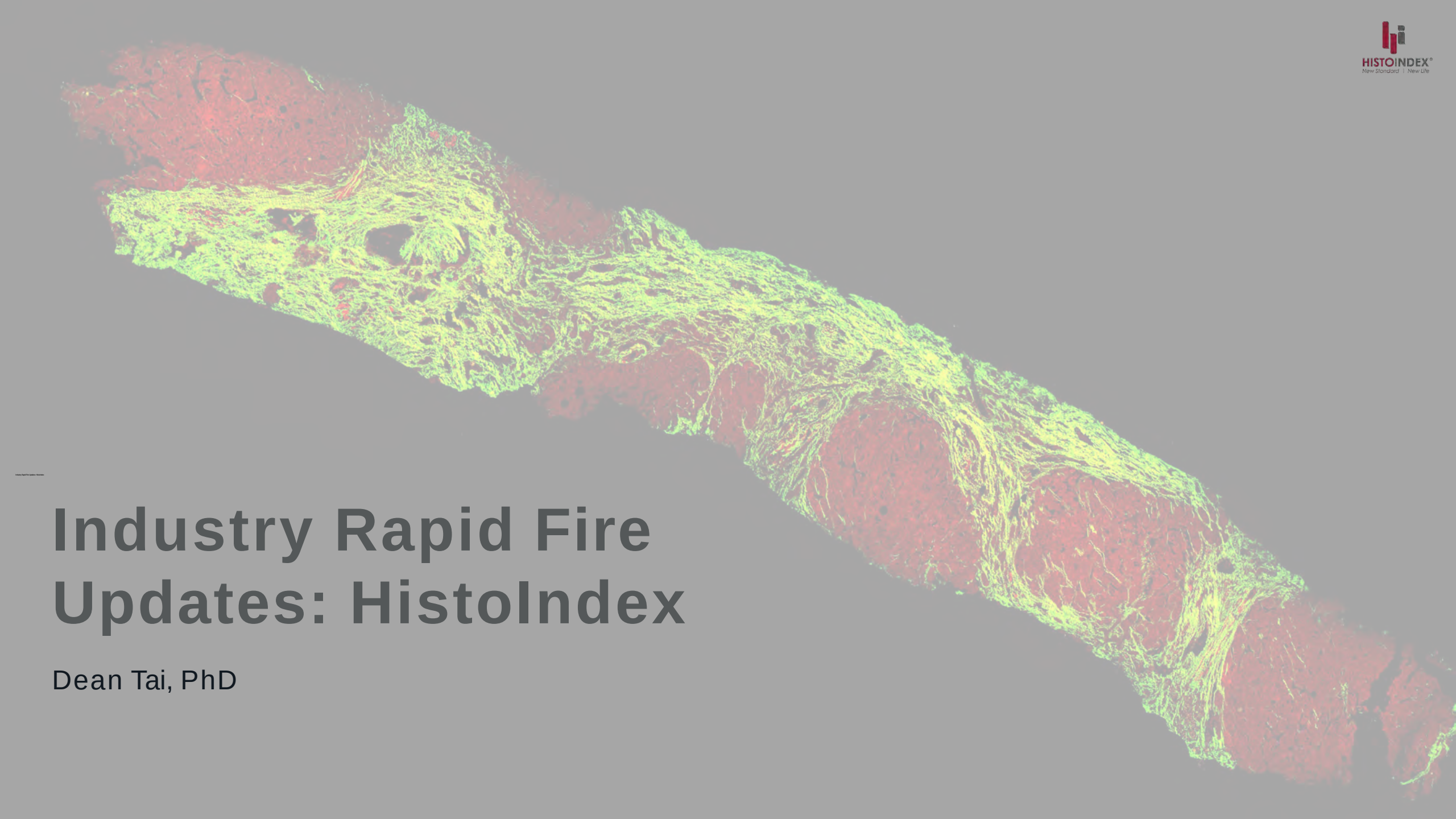
- Considering second LOI for cirrhosis and possibly other indications based on requests from sponsors

Availability

- 3000 systems globally
- Currently exploring system lease model to improve availability for clinical trials



RESOUNDANT



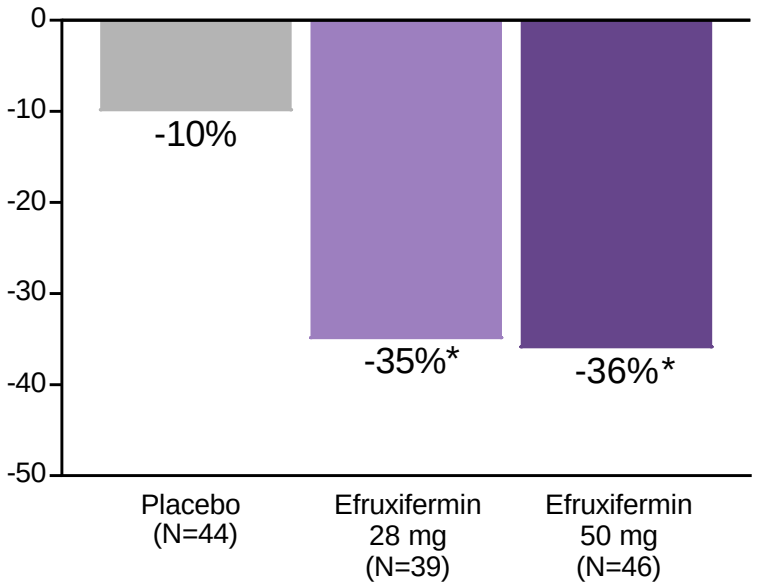
Industry Rapid Fire Updates: HistoIndex

Dean Tai, PhD

qSepta Detects Antifibrotic Response Beyond NASH CRN Responder Status

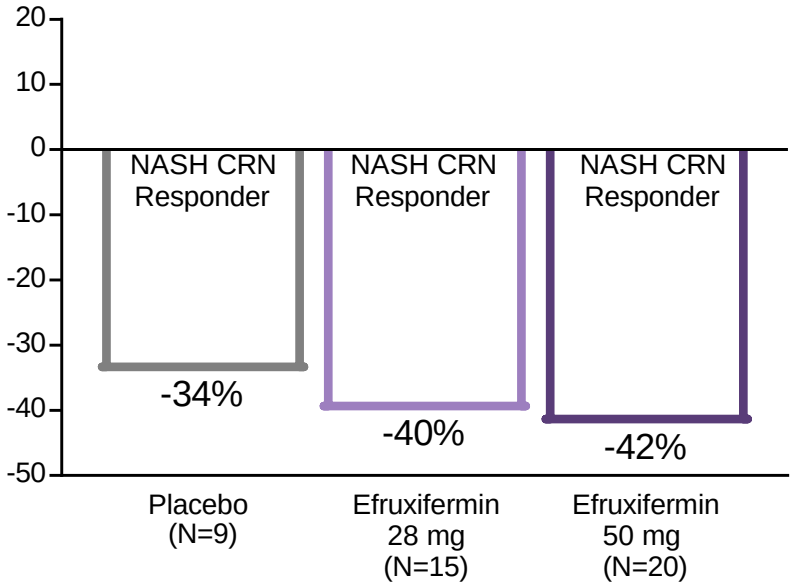
Septa Area was Reduced in Participants treated with Efruxifermin

Relative Change in Septa Area at Week 96

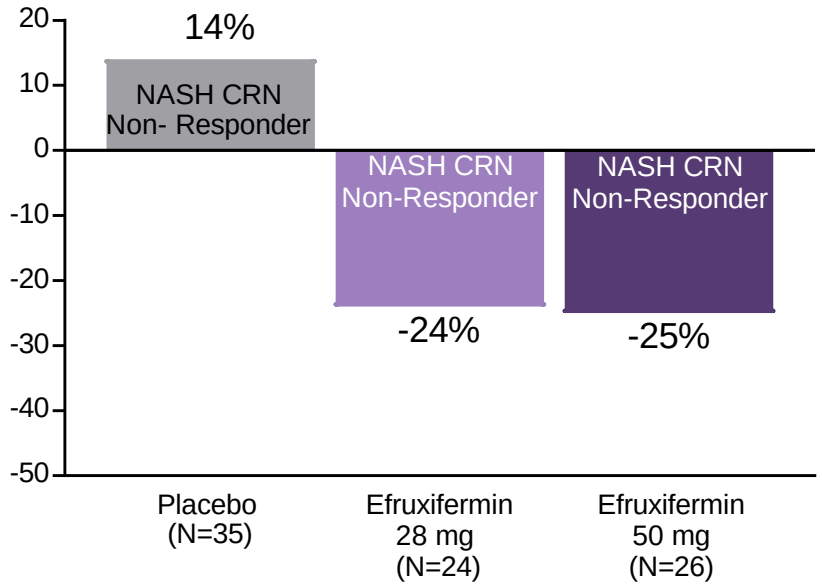


Septa Area was Reduced with Efruxifermin Regardless of NASH CRN Responder Status

Relative Change in Septa Area at Week 96 in NASH CRN Responders



Relative Change in Septa Area at Week 96 in NASH CRN Non-Responders



- Digital analysis of septa area also revealed subtle changes in fibrosis with efruxifermin.
- Treatment with efruxifermin reduced septa area consistently across all participants, including participants with CSPH/probable CSPH at baseline, NASH CRN fibrosis non-responders, and participants that did not improve CSPH risk category

Rinella M et al, Hepatology. 2025; AASLD The Liver Meeting 2025 Late Breaking Abstracts (Abstract 5024)

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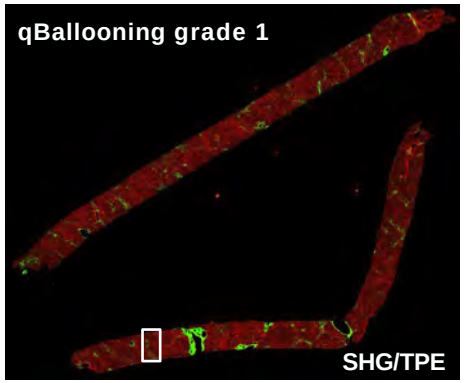
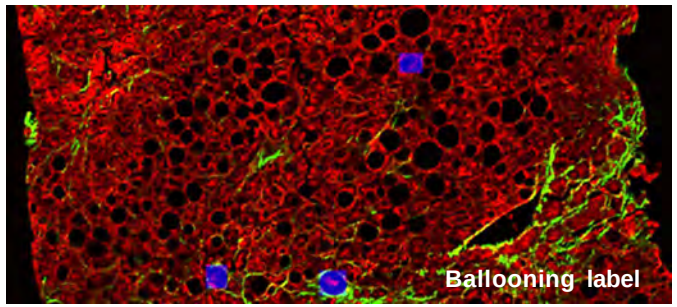
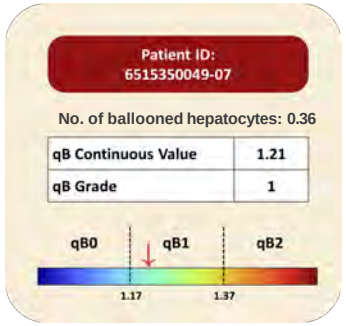
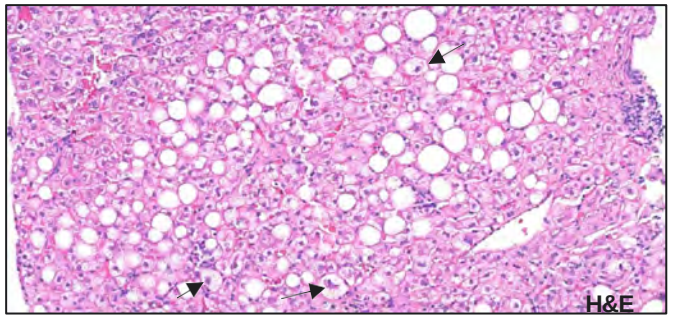
AI-aiding: qBallooning and qInflammation

qBallooning

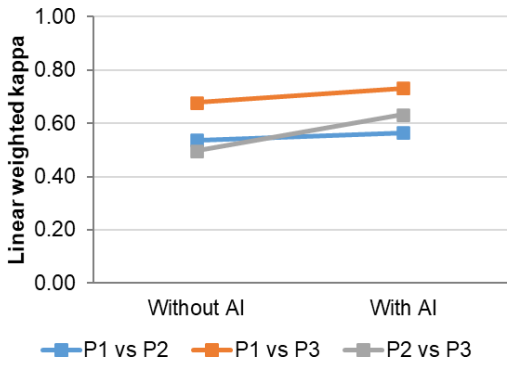








Internal validation (n=60)

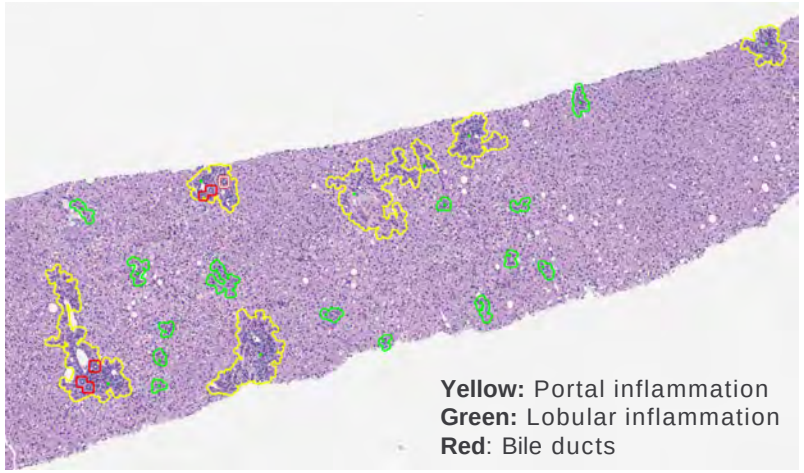


Mean Kappa

0.57 (without AI) → **0.64 (with AI)**

Linear weighted kappa	Without AI	With AI
P1 vs P2	0.54	0.57
P1 vs P3	0.68	0.73
P2 vs P3	0.50	0.63

qInflammation



- Portal inflammation foci and lobular inflammation foci were identified by AI from H&E images
- The accuracy was 92% and 83% for portal foci and lobular foci, respectively. (agreed upon by at least 2 pathologists)

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NORDIC BIOSCIENCE

What is more important for outcome - Disease activty or disease status?

Strictly private & confidential

Fibrosis activity *vs.* disease stage: Complementary and independent predictors of outcomes in alcohol-related liver disease☆

Stine Johansen[1,2], Mads Israelsen[1,2], Katrine Holtz Thorhauge[1,2], Johanne Kragh Hansen[1,2], Camilla Dalby Hansen[1,2], Helle Lindholm Schnefeld[1,2], Peter Andersen[1,2], Ida Villesen[1,2], Katrine Tholstrup Bech[1,2], Sönke Detlefsen[2,3], Nikolaj Torp[1,2], Diana Leeming[4], Maja Thiele[1,2], Aleksander Krag[1,2,*], Morten Karsdal[4,5], on behalf of the GALAXY consortia

JHEP Reports **2026**. vol. 8 | 1–5

Check for updates

Background & Aims: Excessive alcohol consumption accelerates fibrosis progression in steatotic liver disease. Disease activity can be described by fibrogenic activity, of which collagen formation is a central process. Type III collagen formation (PRO-C3) is a biomarker of fibrosis activity. We aimed to evaluate whether PRO-C3 predicts clinical outcomes in alcohol-related liver disease (ALD) independent of fibrosis stage.

Methods: We conducted a prospective cohort study including patients with prior or current excessive alcohol intake (men: ≥36 g/day; women: ≥24 g/day for >1 year) and no prior decompensation. At baseline, liver biopsies, clinical investigations, and non-invasive blood tests were performed. During follow-up, patients' electronic healthcare records were manually reviewed for decompensation events and all-cause mortality. Decompensation was defined according to Baveno VII recommendations.

Results: We followed 458 patients with ALD (76% male; mean age 57 ± 10 years) for a median of 5.9 years (IQR 4.5–7.8). At baseline, fibrosis stages were F0–1 (n = 260), F2 (n = 107), and F3-4 (n = 91). During follow-up, 67 patients experienced decompensation and 100 died. PRO-C3 provided prognostic value beyond fibrosis stage as a predictor of decompensation, both in patients with no to moderate fibrosis (F0-2; subhazard ratio per unit increase in PRO-C3 1.05; 95% CI 1.03–1.07; p <0.001) and in patients with cirrhosis (F4; subhazard ratio 1.01; 95% CI 1.00–1.03; p = 0.048).

Conclusions: In ALD, prognosis is determined by both baseline fibrosis stage and markers of fibrosis activity. PRO-C3, a biomarker of fibrosis activity, was more strongly associated with the risk of decompensation than Kleiner fibrosis stage and predicted decompensation across fibrosis stages.

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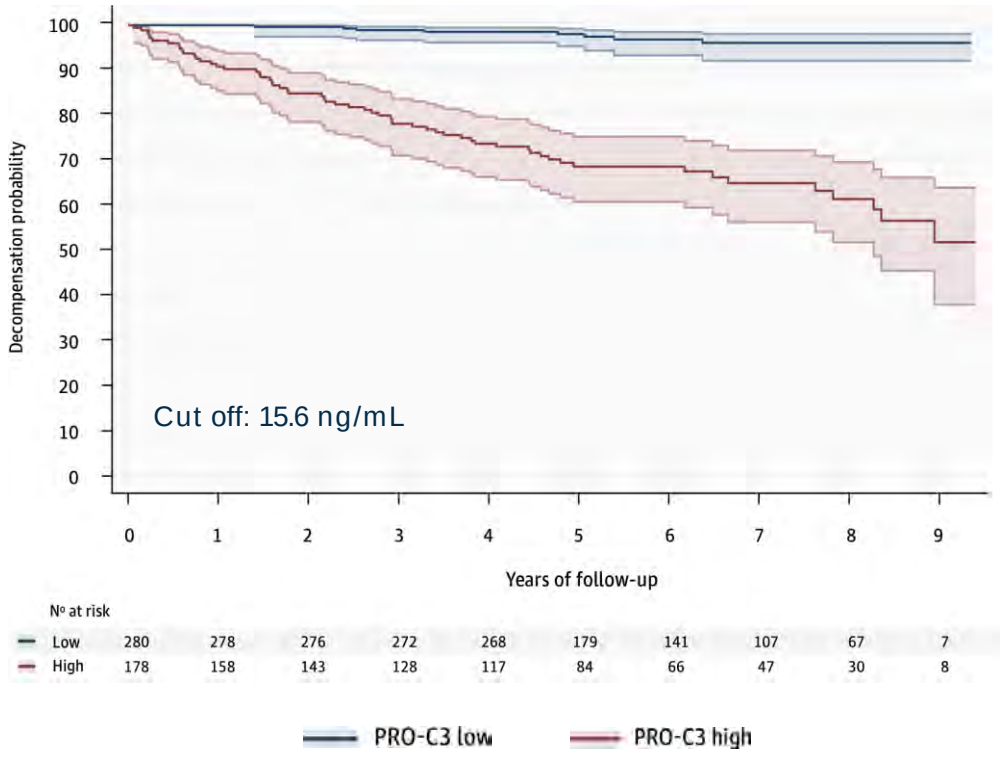
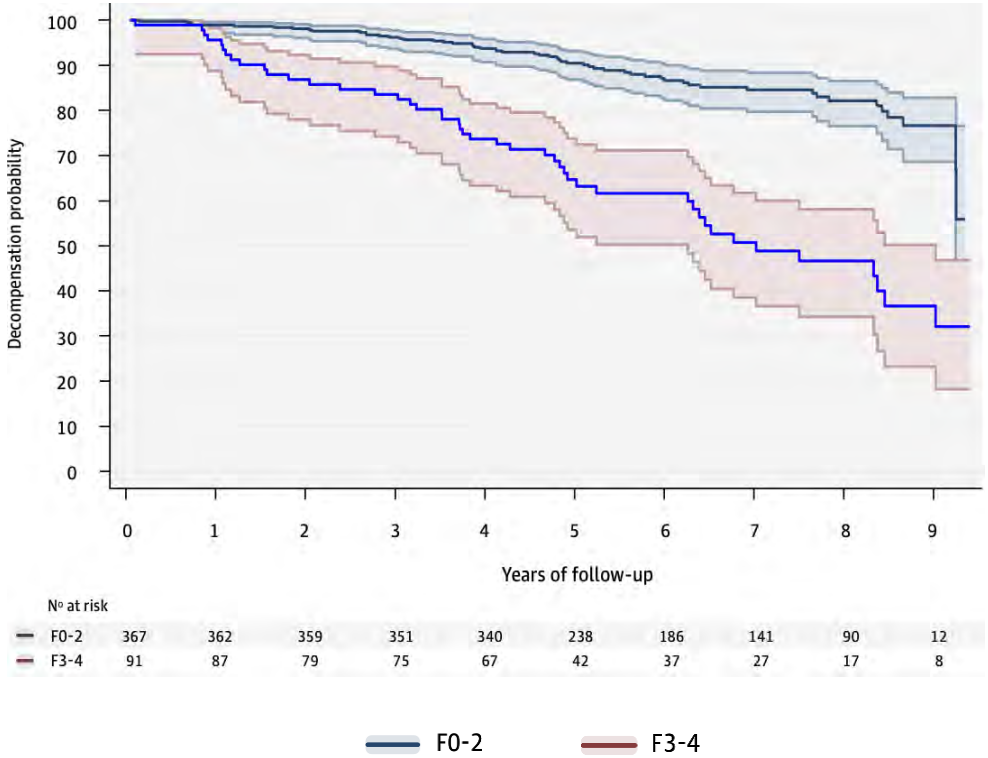
Risk of decompensation – PRO-C3 outperforms biopsy Activity outperforms stage

PRO-C3



Kleiner fibrosis stage



Predictors of decompensation

Variable	Hazard ratio (95% CI)	p
PRO-C3 <15.6 vs ≥15.6	7.09 (3.21-15.68)	<0.001
Fibrosis stage F0-2 vs F3-4	5.16 (2.98-8.94)	<0.001

Strictly private & confidential

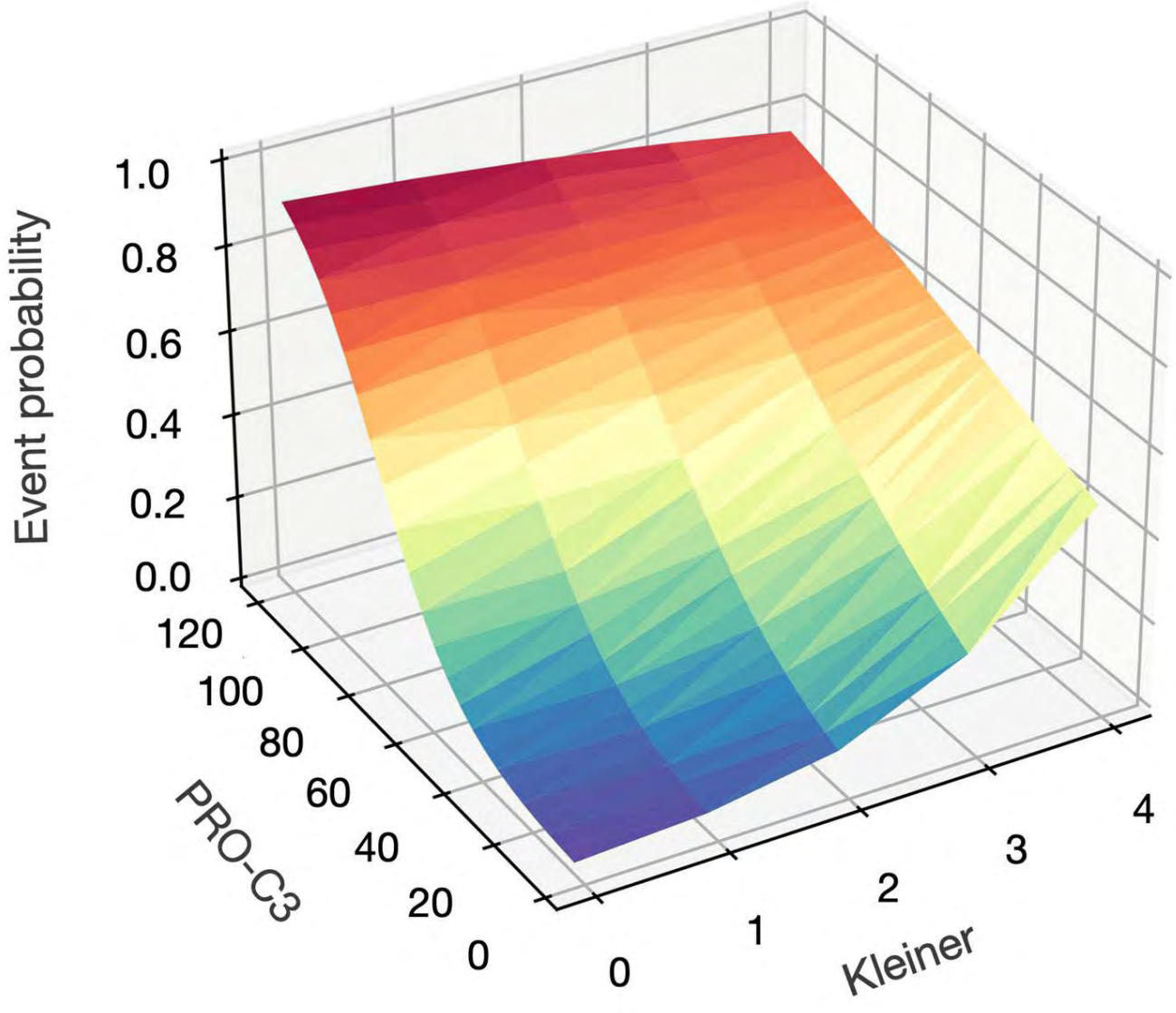
PRO-C3 is prognostic of outcome in all stages

Disease stage (Kleiner)	Patients, n	Events, n	Hazard ratio Per ng/mL change in PRO-C3	p
F2-4	196	61	1.02 (1.01-1.02)	<0.001
F3-4	90	44	1.01 (1.00-1.02)	0.027
F4	63	35	1.02 (1.01-1.04)	0.004
F0-2	361	22	1.05 (1.03-1.07)	<0.001

Johansen S & FLASH, Confidential

Strictly private & confidential

Probability of decompensation
High activity in F3 is worse than low in F4



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

LabCorp Updates

UC Berkeley Public Health

LEADING THE BRIGHT FUTURE OF LIVER HEALTH

25

YEARS STRONG

echosens

Liver Forum 20 - Reston, VA - March 2026

Echosens at a glance

A complete portfolio of solutions for a healthier liver

FibroScan® by echosens

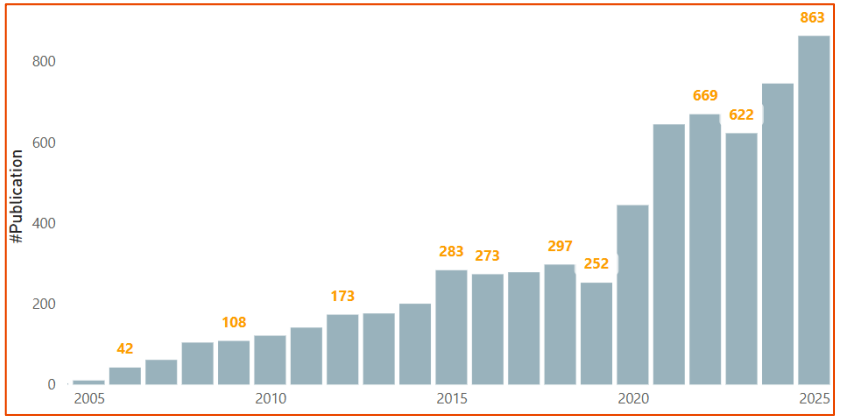
Liver Health MANAGEMENT

Scores
FibroScan based
Fast
Agile 3+
Agile 4

myFibroScan

FibroScan® gateway by echosens

10,500+
Installed base



>6,500+
Peer-reviewed publications

60+
Pharma-sponsored trials

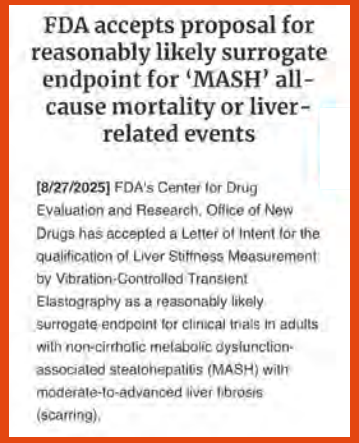
Therapeutic Area	Phase 2	Phase 3	TOTAL
MASH F2-F3	20	10	30
MASH F4	3	5	8
Portal Hypertension	3		3
ALD	4		4
HCV	2		2
PBC/PSC	2	6	8
ALPHA-1	1	3	4
Others	2		2
TOTAL	**37**	**24**	**61**

Updates for the Liver Forum

LSM by VCTE as RLSE

Aug 2025: FDA acceptance of the first LOI proposing LSM by VCTE as a non-invasive RLSE alternative to liver biopsy in non-cirrhotic MASH trials

➔ **Actively working on the preparation of the Qualification Plan**



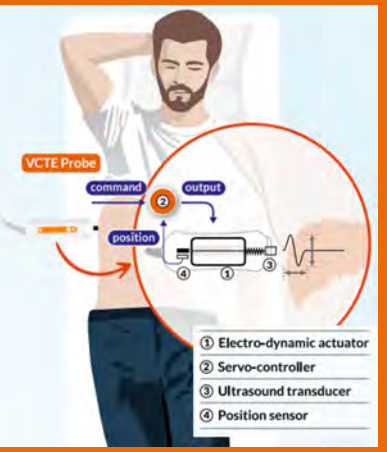
FDA accepts proposal for reasonably likely surrogate endpoint for 'MASH' all-cause mortality or liver-related events

[8/27/2025] FDA's Center for Drug Evaluation and Research, Office of New Drugs has accepted a Letter of Intent for the qualification of Liver Stiffness Measurement by Vibration-Controlled Transient Elastography as a reasonably likely surrogate endpoint for clinical trials in adults with non-cirrhotic metabolic dysfunction-associated steatohepatitis (MASH) with moderate-to-advanced liver fibrosis (scarring).

White paper on VCTE

Several ultrasound-based transient elastography technologies have emerged over the past few years and are currently under clinical validation

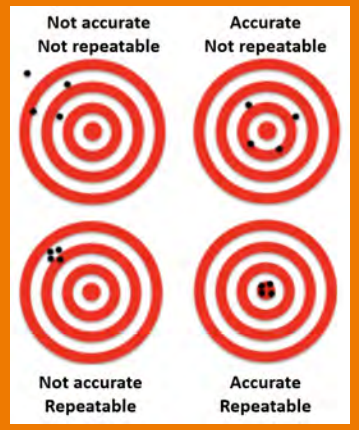
➔ **White paper highlighting the four key features making VCTE unique and specific to FibroScan**



NITs variability

Different-day different-operator variability assessed on Pfizer Phase 2b MASH study screening data presented by Q. Anstee at the LF 18

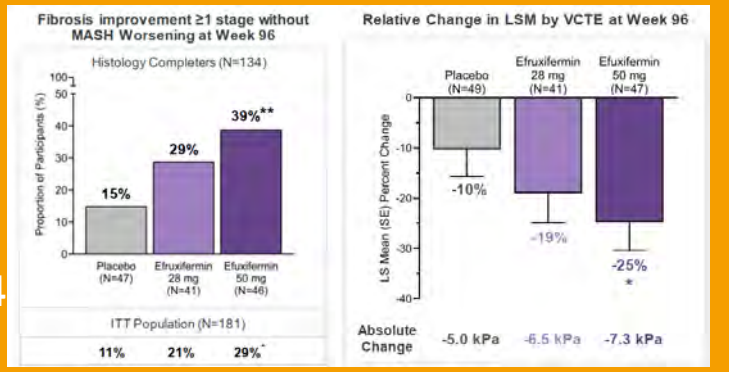
➔ **Publication under revision following reviewers' suggestions**



Latest readouts from pharma trials

Growing number of clinical trials reporting results using LSM by VCTE

➔ **Example of EFX SYMMETRY trial in cF4 at week 96**



Ratziu – AASLD TLM 2025 – O007

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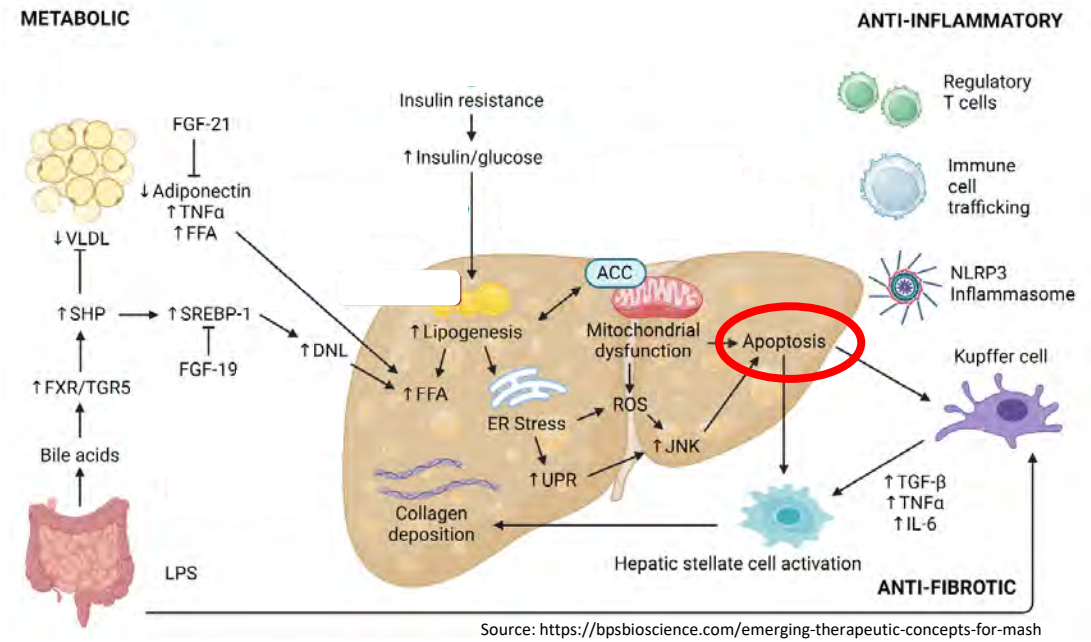
CK18 Biomarkers (M30® Apoptosense)



Source: https://bpsbioscience.com/emerging-therapeutic-concepts-for-mash

- CK18-M30® is a blood-based biomarker (NIT) of **hepatocyte apoptosis**
- Hepatocyte apoptosis is an underlying processes involved in the progression of MASLD/MASH **> Mechanistic Disease Activity Marker**
- Hepatocyte apoptosis is a central node in MASH pathogenesis
- CK18-M30® levels correlate with the NAS grade and fibrosis stage
- **Changes in CK18-M30® correlate with changes in liver histology: NAS (ballooning and inflammation) and fibrosis stage**

- **Value of CK18-M30® as a biomarker in MASH clinical trials:**
  - **MOA "agnostic" biomarker – ideal for combination trials**
  - **Early treatment response marker (12 weeks or sooner)**
  - Early changes in CK18-M30® have been associated with **subsequent histological changes**.
  - In the MAESTRO-NASH trial, **change in CK18-M30® at week 52 was one of the strongest predictors of fibrosis improvement**
  - **Low assay and intraindividual variability** (~10%)

- Ongoing collaborations: **pediatric MASH, MetALD/ALD,** and CK18 as a **prescreening tool to reduce the SFR** in biopsy MASH trials
- CK18-M30® Apoptosense is not currently approved for IVD use in the U.S.

For research use only. Not for use in diagnostic procedures

What's new for ELF?

Matt Gee
Director, Collaborations and External Engagement
Siemens Healthineers

March 6, 2026

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Disclosures and disclaimers

Matt Gee is an employee of Siemens Healthineers

For educational and scientific exchange only. Not for sales or promotional use.

The information presented herein reflects a potential context of use (COU)
for monitoring in clinical trials and drug development.
In the U.S., the ELF Test is currently limited to prognostic use for clinical practice.

U.S. Intended Use:
The ELF Test is indicated as a prognostic marker in conjunction with other laboratory findings and clinical assessments in patients with advanced fibrosis (F3 or F4) due to non-alcoholic steatohepatitis (NASH) to assess the likelihood of progression to cirrhosis and liver-related clinical events.

Outside U.S. Intended Use:
The ELF Test is indicated, in conjunction with other laboratory findings and clinical assessments, for the assessment of severity of liver fibrosis in patients with signs, symptoms, or risk factors of chronic liver disease. The ELF Test may be used diagnostically for fibrosis staging or prognostically to assess the likelihood of progression to cirrhosis and liver-related clinical events.

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Recent Posters / Manuscripts

1. Meta-analysis of the performance of the Enhanced Liver Fibrosis (ELF) Test to identify significant fibrosis, advanced fibrosis and cirrhosis in patients with MASLD
   Presented at The Liver Meeting (AASLD) 2025
2. 1-year change in Enhanced Liver Fibrosis (ELF) predicts liver-related clinical events in patients with metabolic dysfunction-associated steatohepatitis ELF
   Presented at The Liver Meeting (AASLD) 2025 – Late Breaker
3. Multi-threshold analysis of the ELF Test versus histology for prognostication of disease progression and regression in MASH
   In press (*Hepatology Communications*)
4. Parallel combination of FIB-4 and Enhance Liver Fibrosis Test improves prognostication in metabolic dysfunction-associated steatohepatitis Submitted to EASL Congress 2026

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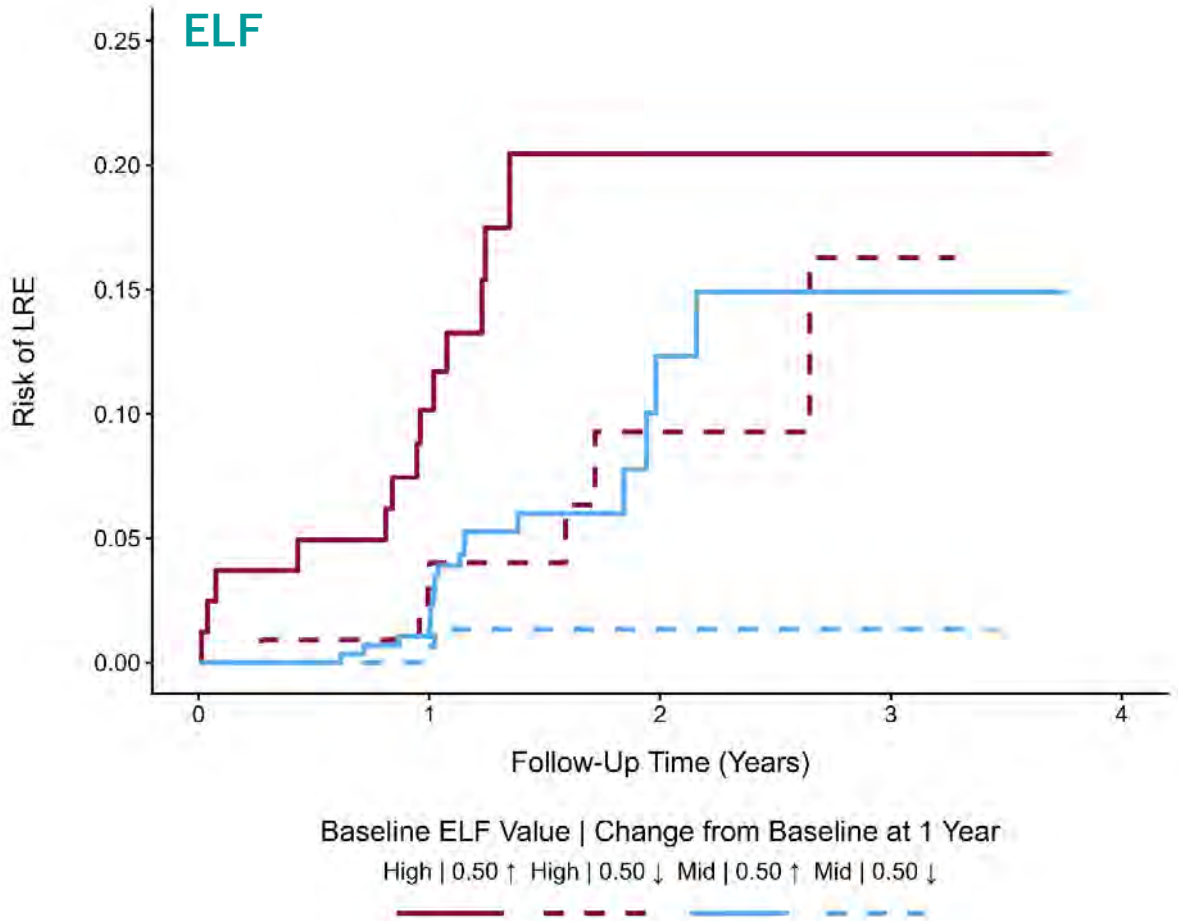
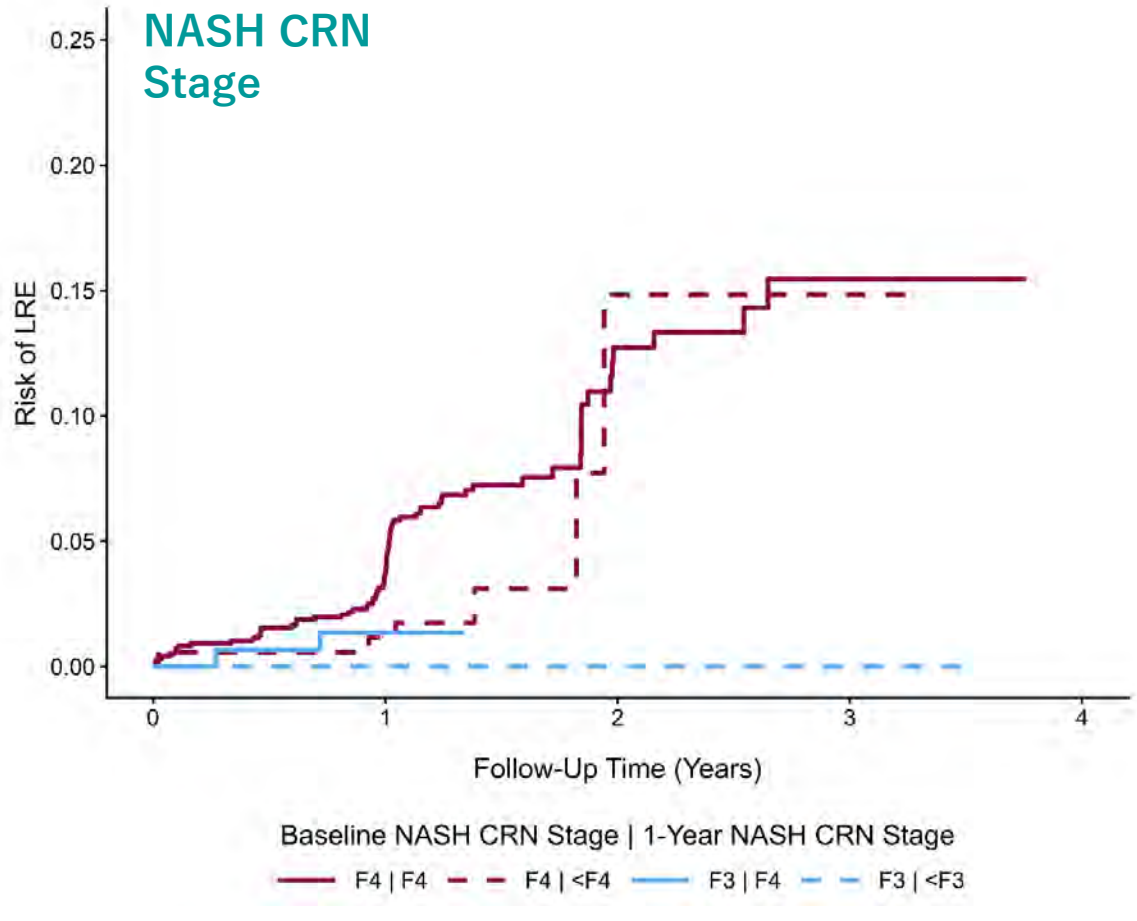
Serial ELF change & differential LRE risk

1-year change in Enhanced Liver Fibrosis (ELF) predicts liver-related clinical events in patients with metabolic dysfunction-associated steatohepatitis





Conclusion: Serial change in ELF is a strong and consistent predictor of near-term LRE risk, outperforming histology.

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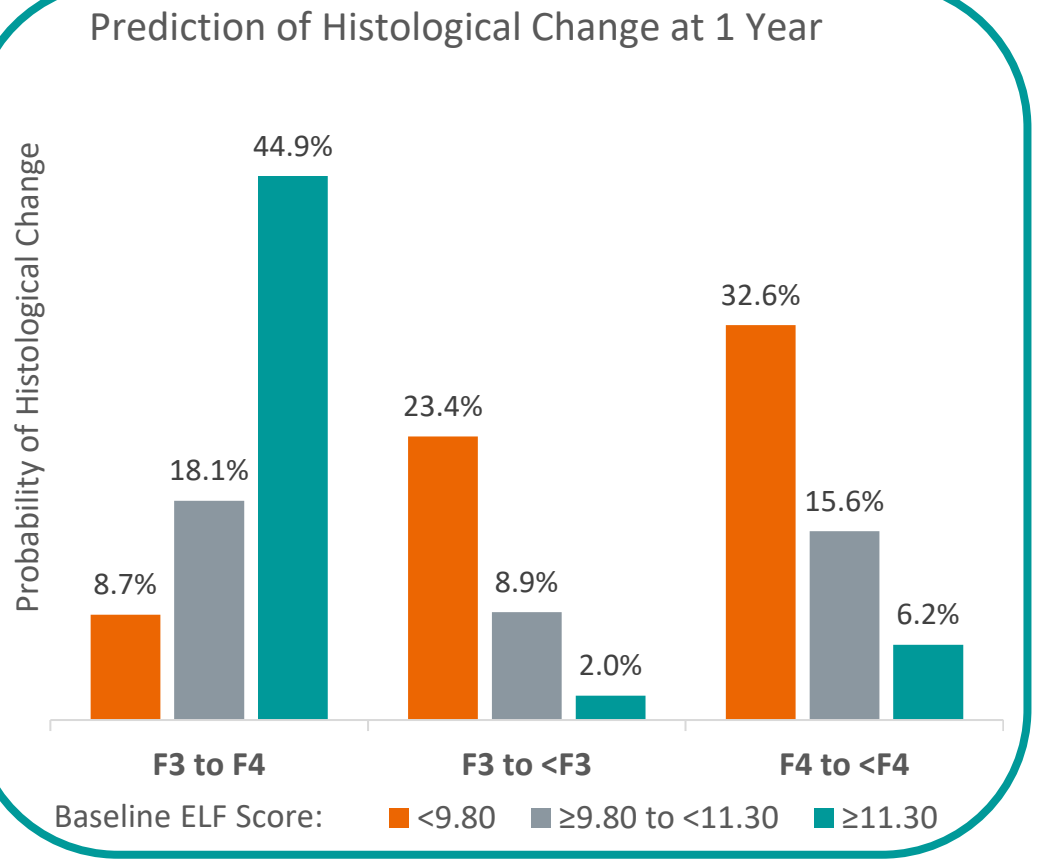
ELF & prognosis – *in press* at Hepatology Communications

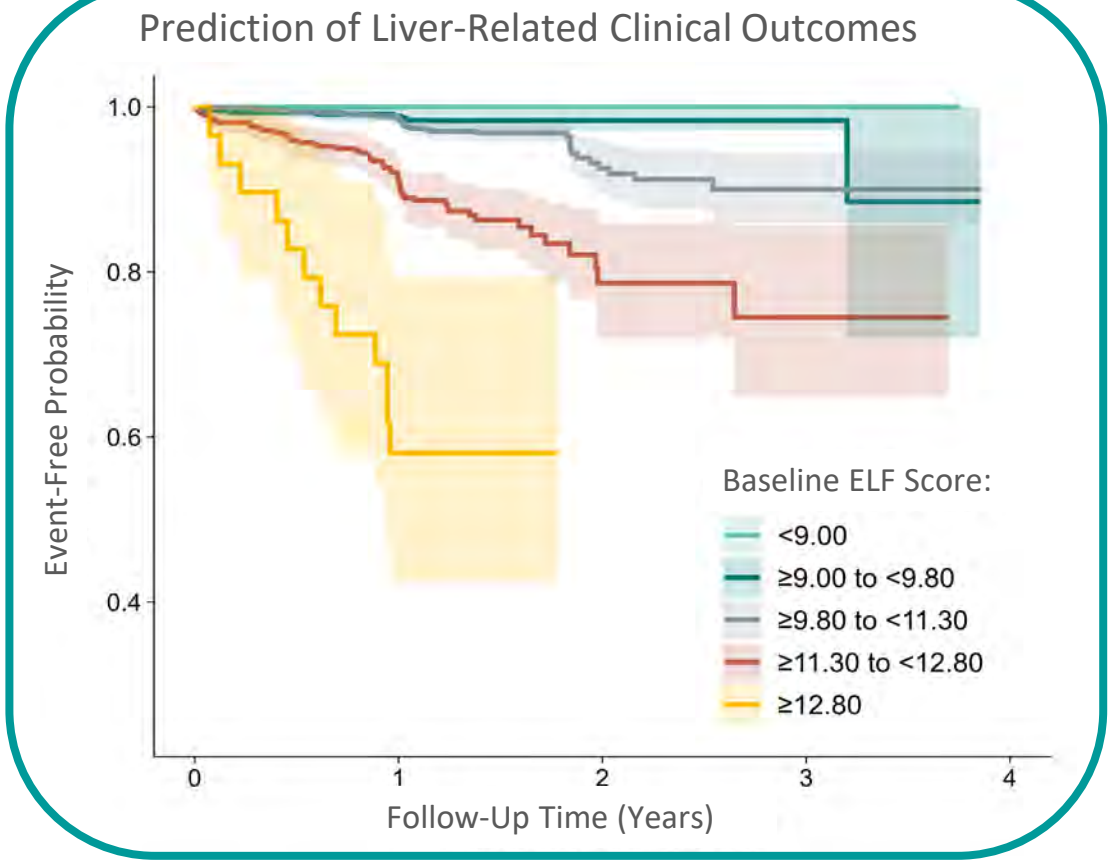
Multi-threshold analysis of the ELF Test versus histology for prognostication of disease progression and regression in MASH



F3/F4 cohort
- N = 2304
- Clinical outcomes

F3 cohort
- N = 1072
- Histology at 1 year

F4 cohort
- N = 1351
- Histology at 1 year



Conclusion: Among patients with MASH and advanced fibrosis, the ELF Test identifies distinct risk strata with differing probabilities of progression to cirrhosis, clinical outcomes, and spontaneous regression.

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Thank You

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