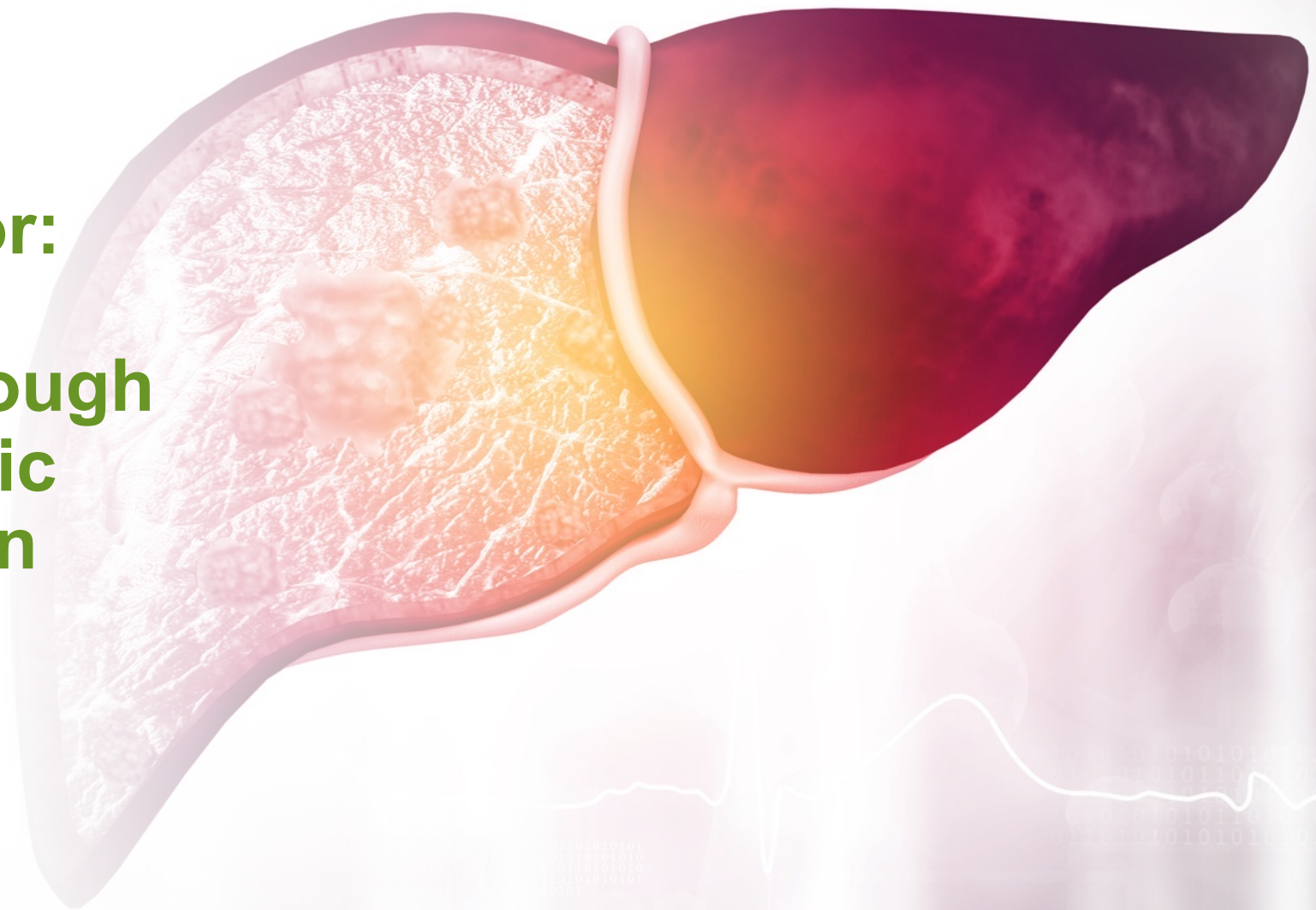


# The Comprehensive Impact of Lanifibranor: Addressing the Full MASH Spectrum Through Intra- and Extrahepatic Mechanisms of Action

October 8, 2025



# Forward Looking Statement

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This presentation contains forward-looking statements within the meaning of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Statements that are not historical facts, included in this presentation are forward-looking statements. Certain of these statements, forecasts and estimates can be recognized by the use of words such as, without limitation, “believes”, “anticipates”, “expects”, “intends”, “plans”, “seeks”, “estimates”, “may”, “will”, “would”, “could”, “might”, “should”, “designed”, “hopefully”, “target”, “potential”, “opportunity”, “possible”, “aim”, and “continue” and similar expressions. Such statements are based on management's beliefs. These statements reflect such views and assumptions prevailing as of the date of the statements and involve known and unknown risks and uncertainties that could cause future results, performance, or future events to differ materially from those expressed or implied in such statements. No representations are made as to the accuracy or fairness of such forward-looking statements, forecasts, and estimates. Furthermore, forward-looking statements, forecasts and estimates only speak as of the date of this presentation. Readers are cautioned not to place undue reliance on any of these forward-looking statements.

Please refer to the Universal Registration Document for the year ended December 31, 2024, filed with the *Autorité des Marchés Financiers* on April 15, 2025, and the Annual Report on Form 20-F for the year ended December 31, 2024, filed with the Securities and Exchange Commission (the “SEC”) on April 15, 2025 for risks and uncertainties affecting Inventiva, and in future filings with the SEC. Other risks and uncertainties of which Inventiva is not currently aware may also affect its forward-looking statements. Except as required by law, Inventiva has no intention and is under no obligation to update or review the forward-looking statements referred to above. Consequently, Inventiva accepts no liability for any consequences arising from the use of any of the above statements.

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# Investor & Analyst Day - Agenda

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- ▶ A Year in Review

**Mark Pruzanski, MD**

- ▶ Leading the Next Chapter of Growth

**Andrew Obenshain**

- ▶ Reimagining PPAR Modulation: The Power of Lanifibranor's pan-PPAR Mechanism of Action

**Prof. William Alazawi**

- ▶ A Foundational Asset for MASH- The Case for Lanifibranor

**Prof. Arun Sanyal**

- ▶ Real World Management of MASLD

**Prof. Nezam Afdhal**

- ▶ Panel Discussion

**Jason Campagna, President R&D and CMO, Henry Chang, Prof. Alazawi, Prof. Afdhal, Prof. Sanyal**

- ▶ Q&A

**All speakers**

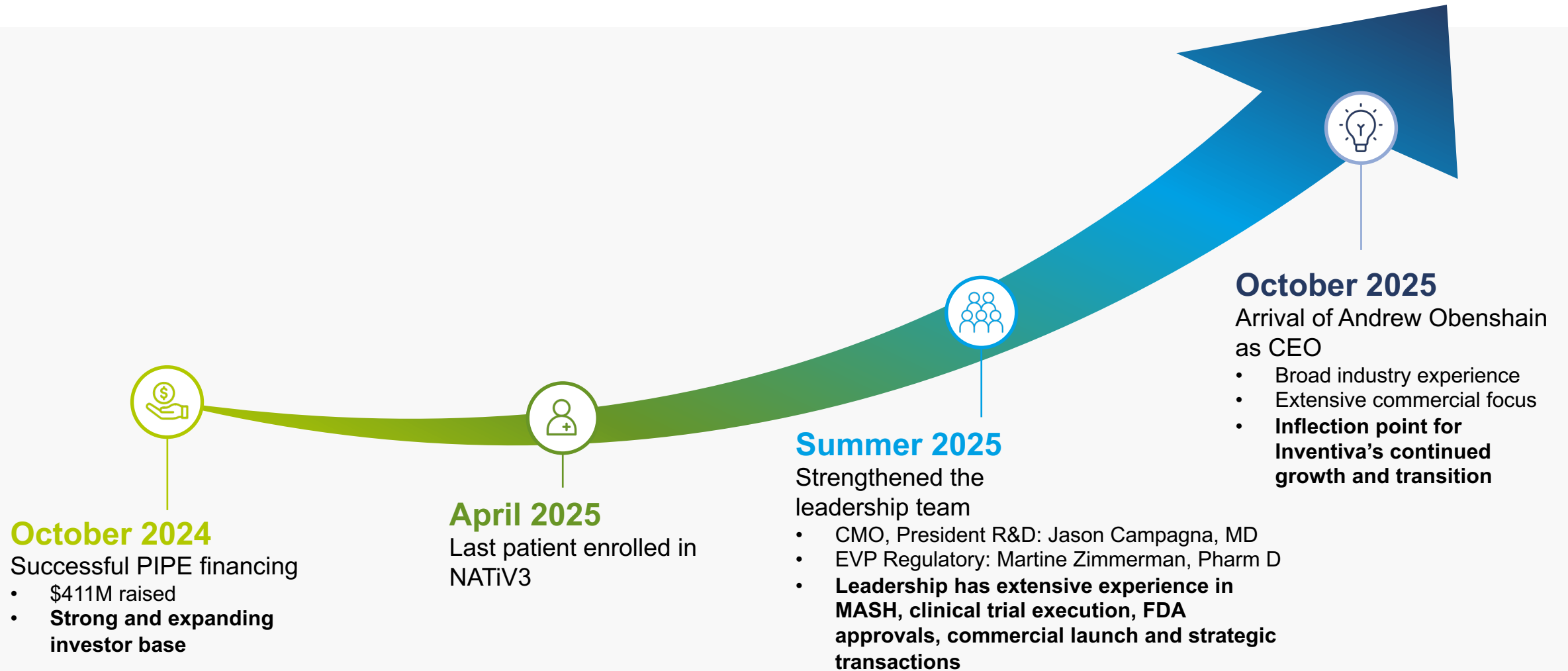
# A Year in Review

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**Mark Pruzanski, MD**  
Chairman of Inventiva

# Inventiva has made significant progress in the past year

We remain on track for NATiV3 topline results in H2 2026



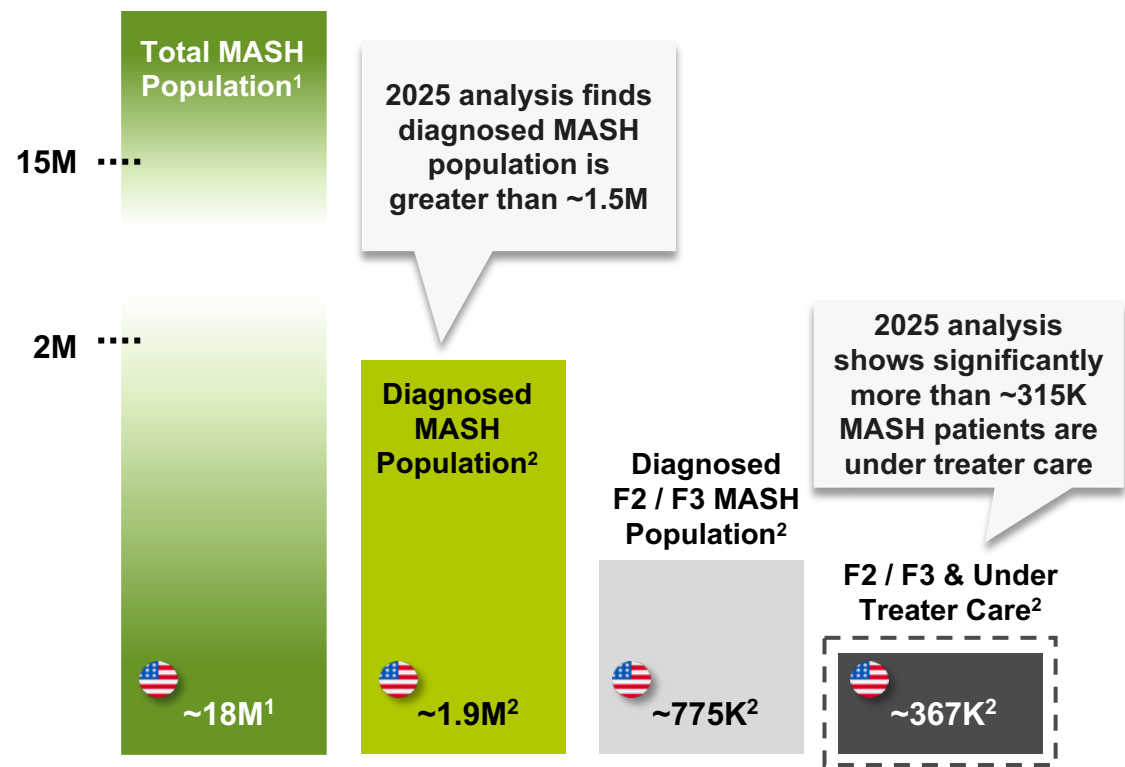
# Leading the Next Chapter of Growth

---

**Andrew Obenshain**  
CEO of Inventiva

# MASH is a chronic, progressive liver disease with ~1.9M diagnosed patients in the US

## 2024 MASH population estimate (US only)



Abbreviations: MAFLD = Metabolic dysfunction-associated steatotic liver disease, MASH = Metabolic dysfunction-associated steatohepatitis  
1) Estes. 2018; Lui et al 2022, Prevalence taken from 2018 and conservative growth adjustments applied; 2) Analysis conducted by Forian using CHRONOS™ ©2025 Forian Inc. and its licensors. All Rights Reserved;





# Despite the emergence of new treatment options, US HCPs feel that unmet need in MASH remains significant<sup>1</sup>



## Current Treatment Options

Rezdiffra™

wegovy®

Manufacturer	 Madrigal Pharmaceuticals	 novo nordisk
Approval Date	Mar. 2024 NDA	Aug. 2025 sNDA
ROA		
MOA	THR-β agonist	GLP-1 agonist
Patient Population	F2 / F3	F2 / F3

## Primary Market Research - 100 US HCPs:



Without a prompt 85% of specialists in the US described the greatest unmet needs as lack of effective, liver directed therapies

*“[The greatest unmet need is] oral therapies that lead to one or more stage improvement in fibrosis without worsening of Steatohepatitis”*

Hepatologist, US

1. Global Primary Quant Patient Journey Market Research Jul. - Sep. '25 (n=100). All HCPs were US MASH treaters

# We believe lanifibranor is uniquely positioned to deliver on physician and patient needs

*A promising novel, once-daily, small molecule, designed to **treat MASH by directly targeting intrahepatic fibrosis progression and extrahepatic manifestations**, delivering **anti-inflammatory & metabolic benefits***

## Differentiated Mechanism of Action

Pan-PPAR agonist rationally designed to address the multiple pathogenic drivers of MASH



## Potential Best-in-Class Oral Efficacy

Phase 2b: 18% improvement in fibrosis with no worsening of MASH vs placebo at 6 months (42% vs 24%,  $p=0.01$ ) & improved cardiovascular, glycemic, and metabolic markers

## Speed to Fibrosis Improvement

Both MASH resolution and direct fibrosis regression at 24 weeks, with no disease worsening observed in Phase 2b NATIVE



## Convenient Route of Administration

Once-daily, oral administration reduces patient burden, especially for those already on injectables

## Cardiometabolic Benefits

Improvement in insulin sensitivity and glycemic control, reduction in triglycerides and increases in HDL and adiponectin observed in Phase 2b NATIVE



## Manageable Safety & Tolerability Profile

Safety data from Phase 2b NATIVE supportive; limited GI side effects

Intellectual property protection through 2041 supports durable market exclusivity

# With a truly differentiated asset and topline data expected in 2026, Inventiva aims to re-define MASH treatment with lanifibranor

2026

H2 2026  
Topline results

2027

2028

2028  
Targeted launch

## GOALS



**Amplify uniqueness of pan PPAR agonism** and lanifibranor clinical data, which are underrecognized, but **highly-valued once understood**



**Capitalize on market momentum and learnings** from recent launches to **reinforce the value of more effective liver targeted therapies**



**Demonstrate lanifibranor's value as monotherapy and in combination** to secure broad and rapid market access

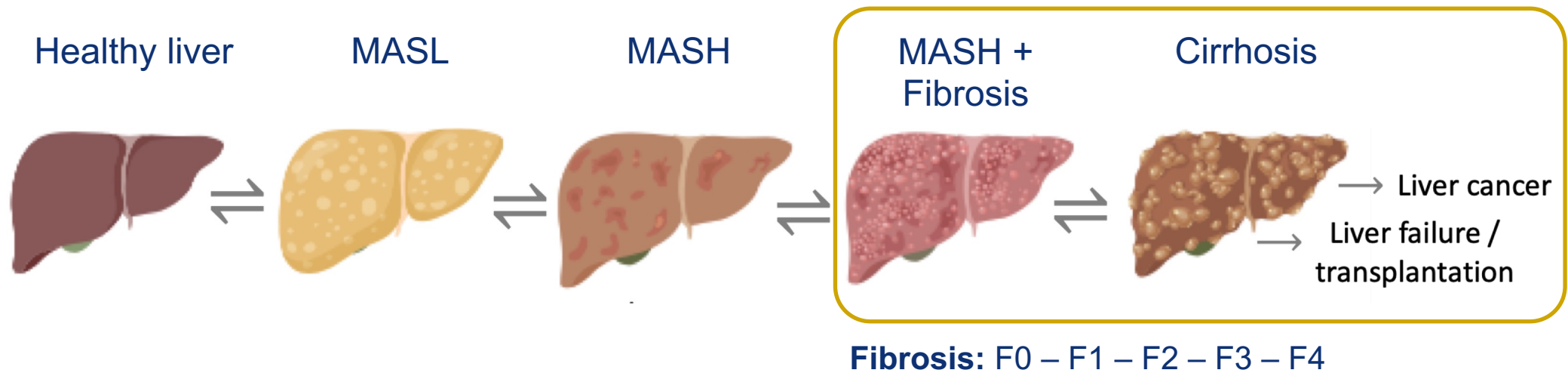
**Inventiva is reinforcing the organization to support and drive leadership in MASH**

# Reimagining PPAR Modulation: The Power of Lanifibranor's pan-PPAR Mechanism of Action

Professor William Alazawi

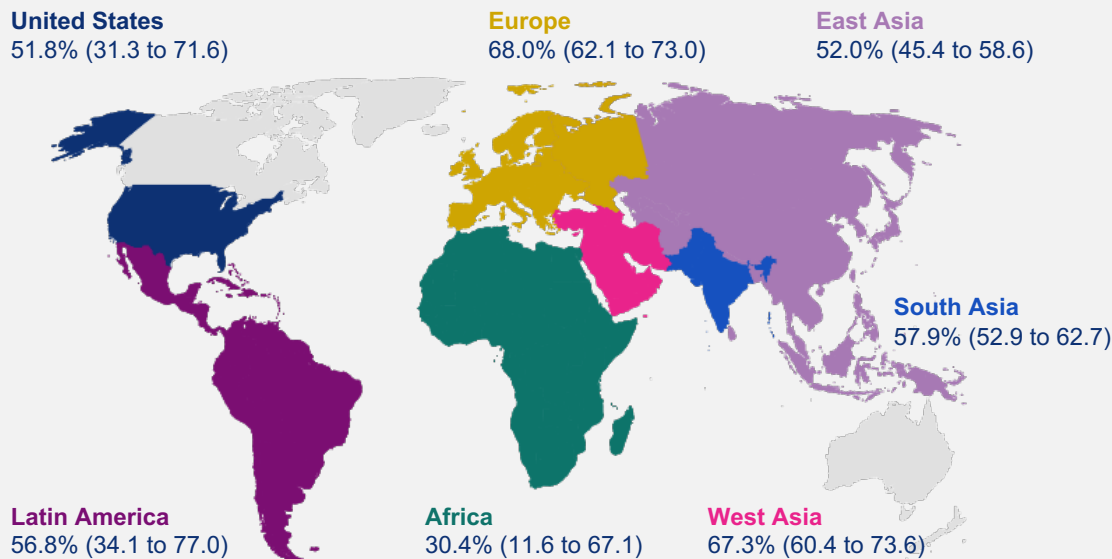
Professor of Hepatology,  
Queen Mary University London

# Patients with MASH and fibrosis are at risk of adverse liver outcomes



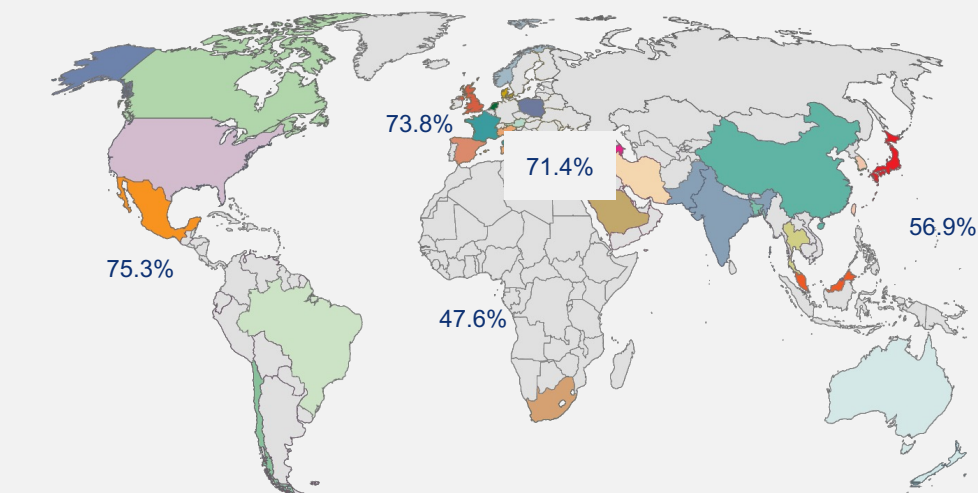
# MASLD is highly prevalent in people with type 2 diabetes and obesity

## Diabetes



Global prevalence of NAFLD among T2DM patients 55.5%  
(90% confidence interval: 47.3-63.7)

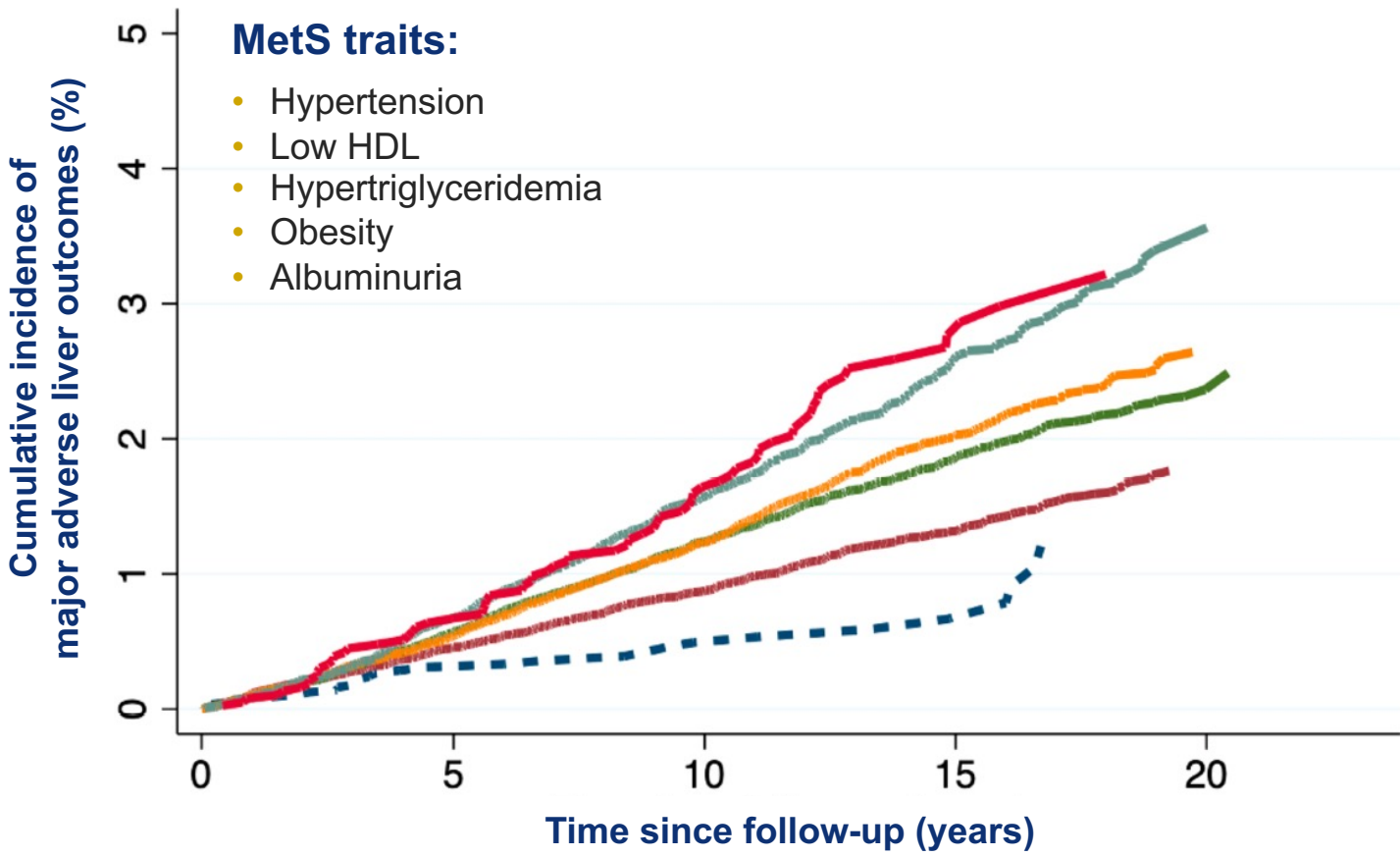
## Obesity



### Prevalence of NAFLD in overweight population

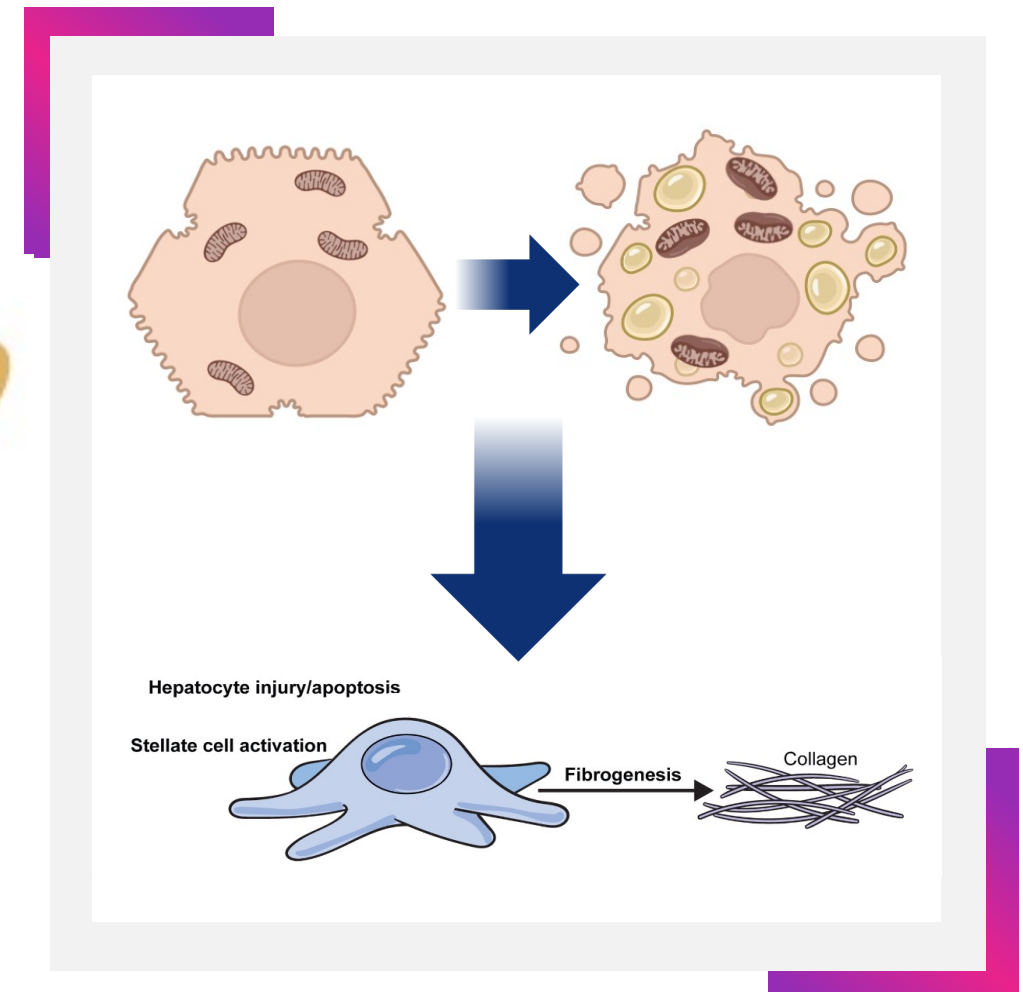
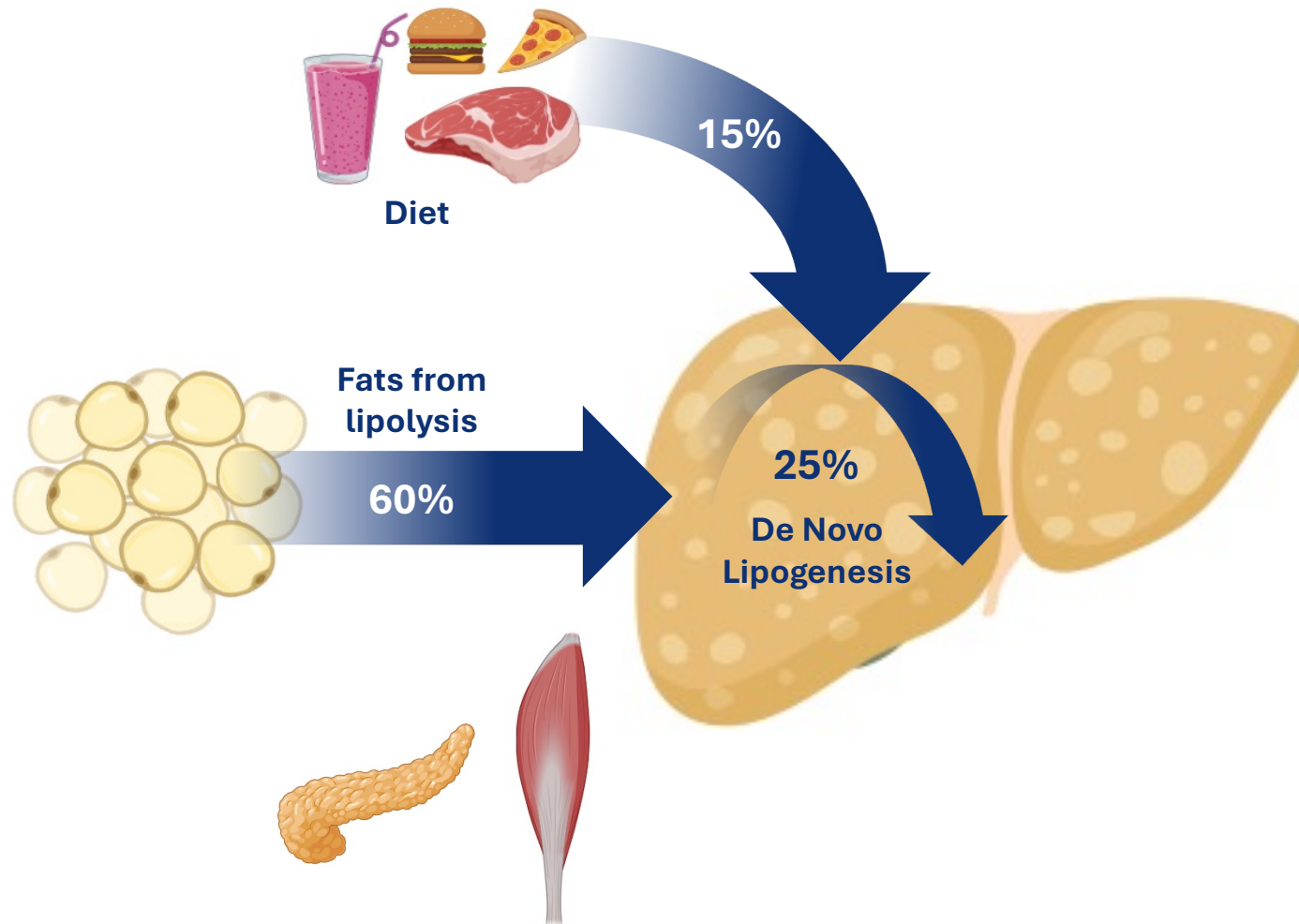
Australia (70.27%)	Croatia (68.06%)	Iraq (68.00%)	New Zealand (88.46%)	South Korea (47.69%)
Austria (84.00%)	Denmark (48.48%)	Italy (82.36%)	Norway (74.91%)	Spain (88.55%)
Bangladesh (30.39%)	France (83.18%)	Japan (63.38%)	Pakistan (71.98%)	Taiwan (53.60%)
Brazil (79.43%)	Germany (69.38%)	Jordan (83.45%)	Poland (57.25%)	Thailand (61.75%)
Canada (76.26%)	Hong Kong (40.69%)	Malaysia (56.60%)	Romania (32.17%)	Türkiye (88.66%)
Chile (62.99%)	India (72.41%)	Mexico (63.48%)	Saudi Arabia (75.66%)	USA (73.24%)
China (60.33%)	Iran (57.85%)	Netherlands (31.04%)	South Africa (47.64%)	UK (30.64%)

# Liver-related outcomes increase with each additional metabolic syndrome (MetS) trait

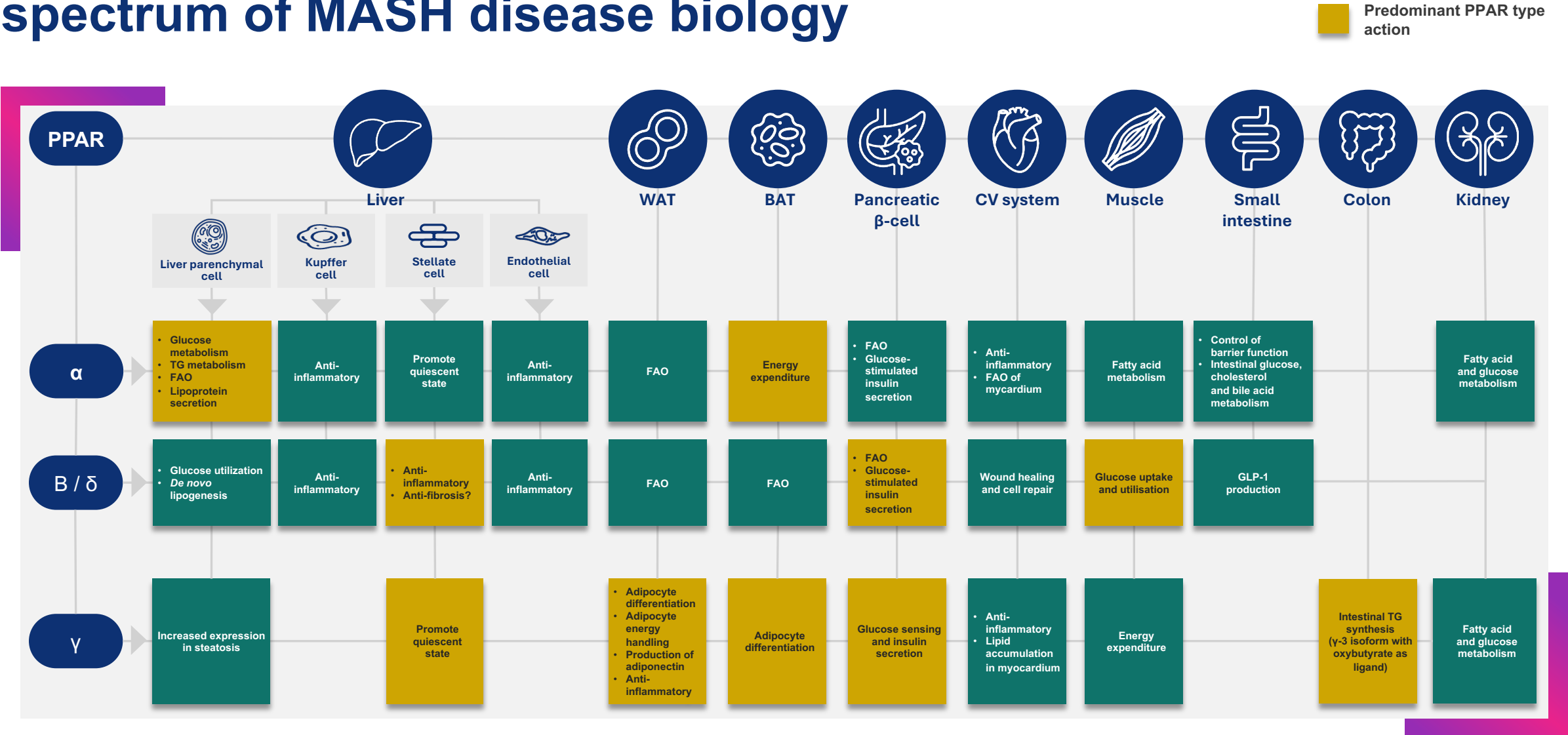


Traits	(Number of events/patients)
T2D + 5 MetS	(71/3,831)
T2D + 4 MetS	(471/25,369)
T2D + 3 MetS	(926/61,632)
T2D + 2 MetS	(1,109/77,706)
T2D + 1 MetS	(609/56,664)
T2D only	(29/5,794)

# Insulin resistance drives fat accumulation, injury and fibrosis



# PPARs are master regulators of the spectrum of MASH disease biology



# Entering a new era of PPARs and efficacy in MASH

1990s



PPARs discovery  
& early metabolic  
disease trials

2010s



Pioglitazone  
proves concept  
in MASH

2020s



No benefit of other  
PPAR agonists in  
MASH

2024



PPAR-agonists  
approved in liver  
disease ( PBC)

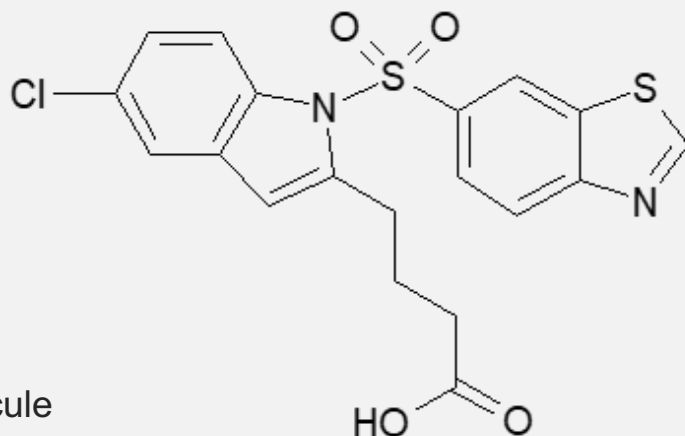


**Lanifibranor:**  
the **first pan-PPAR**  
for MASH & fibrosis

Receptor selectivity improvements

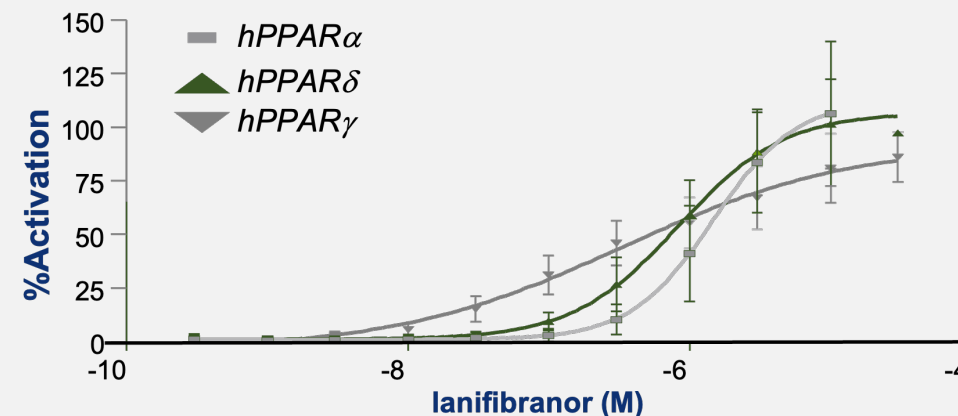
# Lanifibranor is a differentiated pan-PPAR agonist with moderate and well-balanced activity on the three PPAR isoforms

## Differentiated oral small molecule...



- Small molecule
- Differentiated structure – not a glitazone
- Induces different coactivators\*\*\*
- Once daily
- Two doses: 800mg and 1200mg

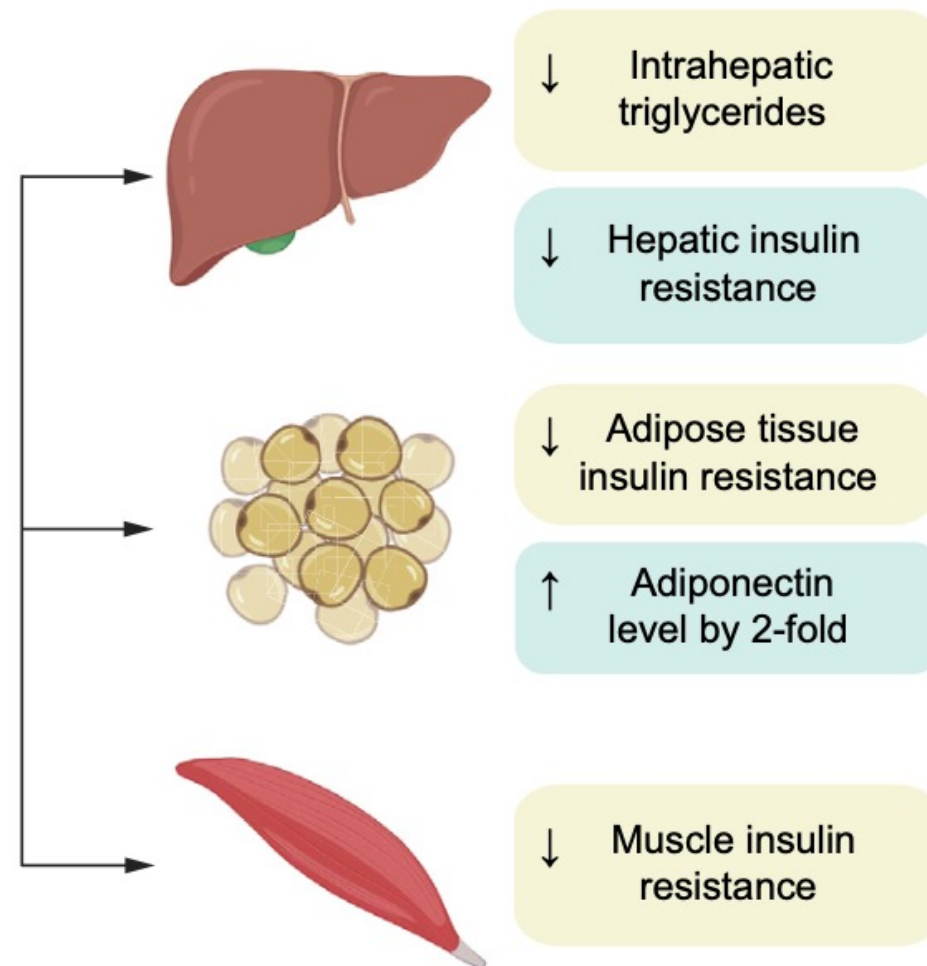
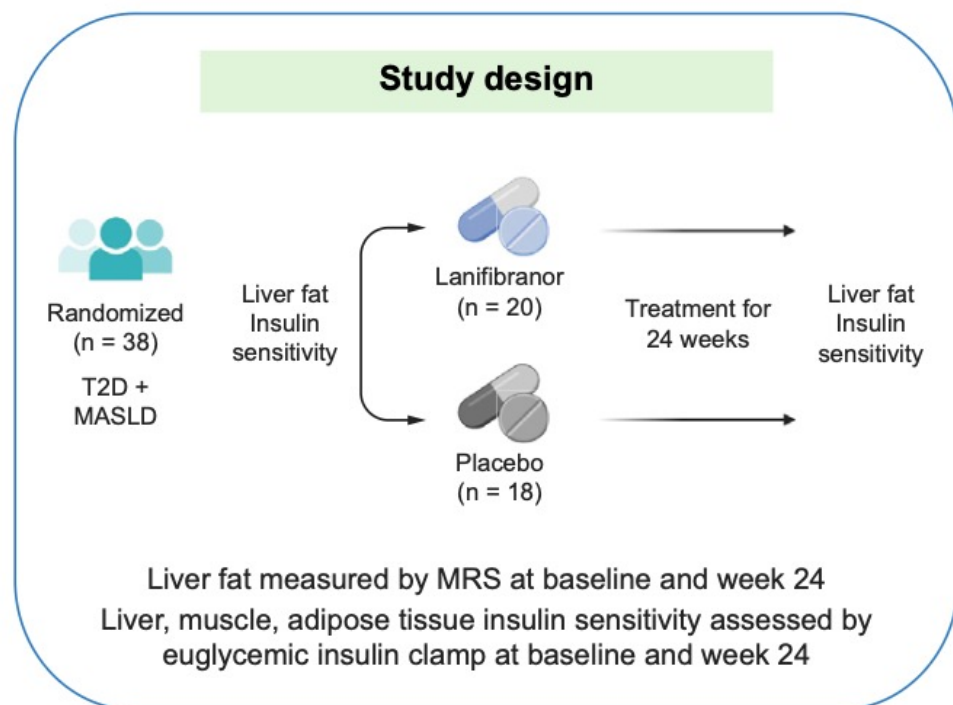
## Moderate and balanced pan-PPAR agonist activity



Compound	PPAR $\alpha$ EC50 (nM)	PPAR $\delta$ EC50 (nM)	PPAR $\gamma$ EC50 (nM)
<b>Lanifibranor*</b>	<b>1630</b>	<b>850</b>	<b>230</b>
Fenofibrate	2400	-	-
Pioglitazone	-	-	263
Rosiglitazone	-	-	13
Elafibranor**	10	100	-
Seladelpar^	-	2	-

## Pan-PPAR agonist lanifibranor improves insulin resistance and hepatic steatosis in patients with T2D and MASLD

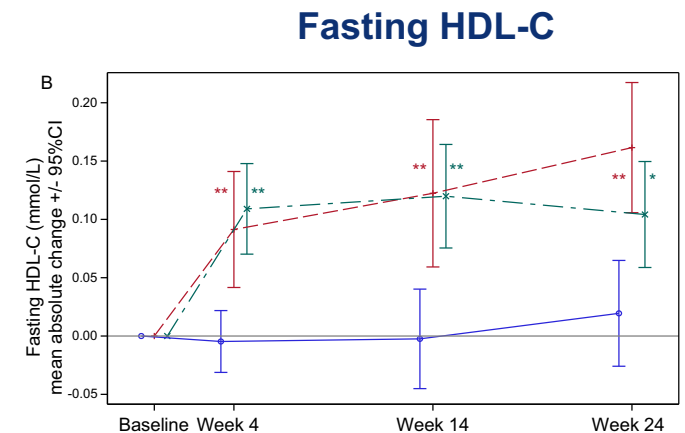
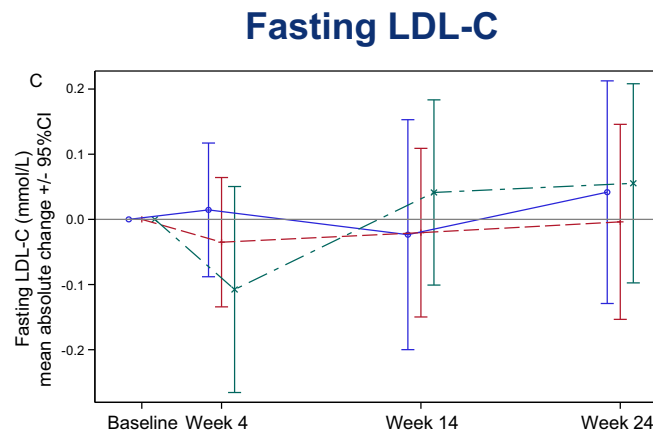
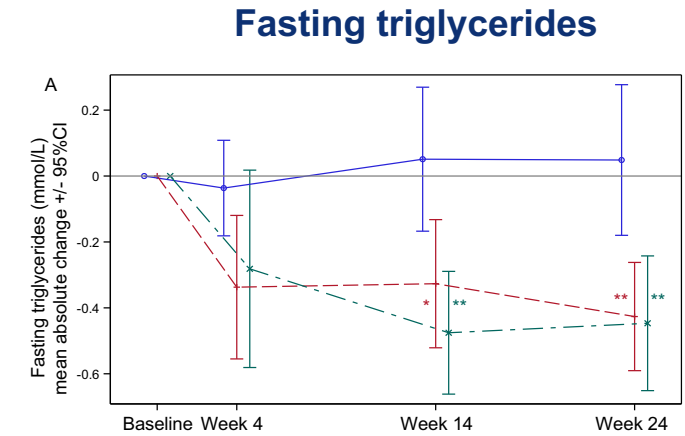
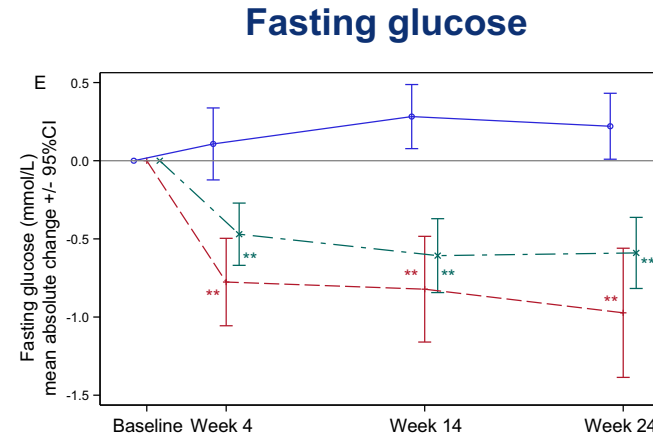
Diana Barb<sup>1</sup>, Srilaxmi Kalavalapalli<sup>1</sup>, Eddison Godinez Leiva<sup>1</sup>, Fernando Bril<sup>2</sup>, Philippe Huot-Marchand<sup>3</sup>, Lucile Dzen<sup>3</sup>, Jens T. Rosenberg<sup>4</sup>, Jean-Louis Junien<sup>3</sup>, Pierre Broqua<sup>3</sup>, Andrea Ortiz Rocha<sup>1</sup>, Romina Lomonaco<sup>1</sup>, Jean-Louis Abitbol<sup>3</sup>, Michael P. Cooreman<sup>3</sup>, Kenneth Cusi<sup>1,\*</sup>



# The pan-PPAR agonist lanifibranor improves cardiometabolic health in patients with metabolic dysfunction-associated steatohepatitis

NATIVE Phase 2b trial  
N=247 MASH / F2-3

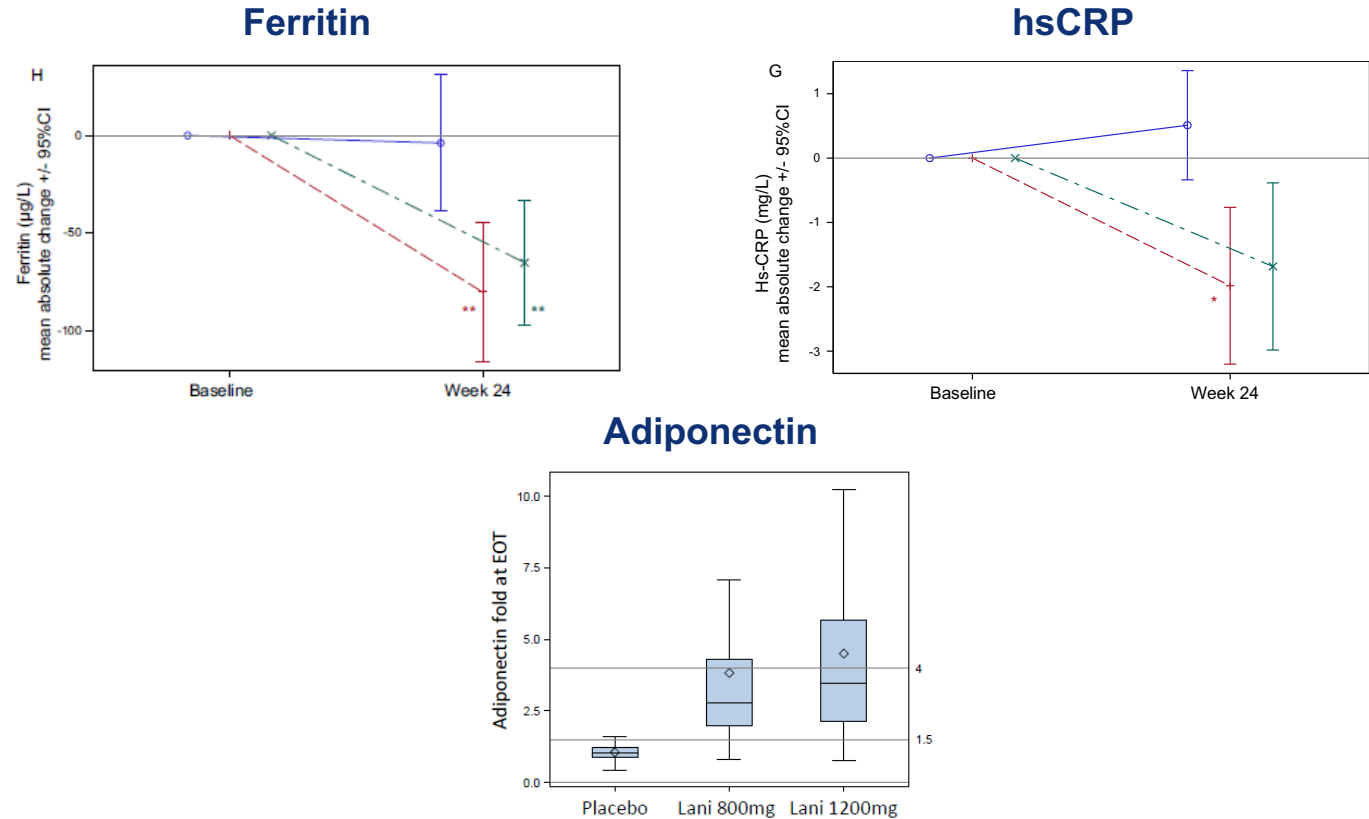
— Placebo  
— Lanifibranor 800mg  
— Lanifibranor 1200mg



# Lanifibranor associated with improved systemic markers of inflammation

NATIVE Phase 2b trial  
N=247 MASH / F2-3

- Placebo
- Lanifibranor 800mg
- Lanifibranor 1200mg



# The metabolic disease treatment landscape is changing

## **GLP1/incretin and SGLT2-i use more widespread**

Evidence base is across  
metabolic spectrum

?dose / adherence /  
reimbursement

## **Updated guidance recommend earlier use in T2D**

## **Patients with MASH will be on medication at diagnosis**

## **MASH drug selection will be on this background**

# Potential synergy between pan-PPAR and GLP-1 reduces metabolic burden and fibrogenic drive



Improvement in HbA1c, insulin sensitization and lipid profile



Weight loss-independent PPAR benefit with weight-dependent mechanism of GLP-1s

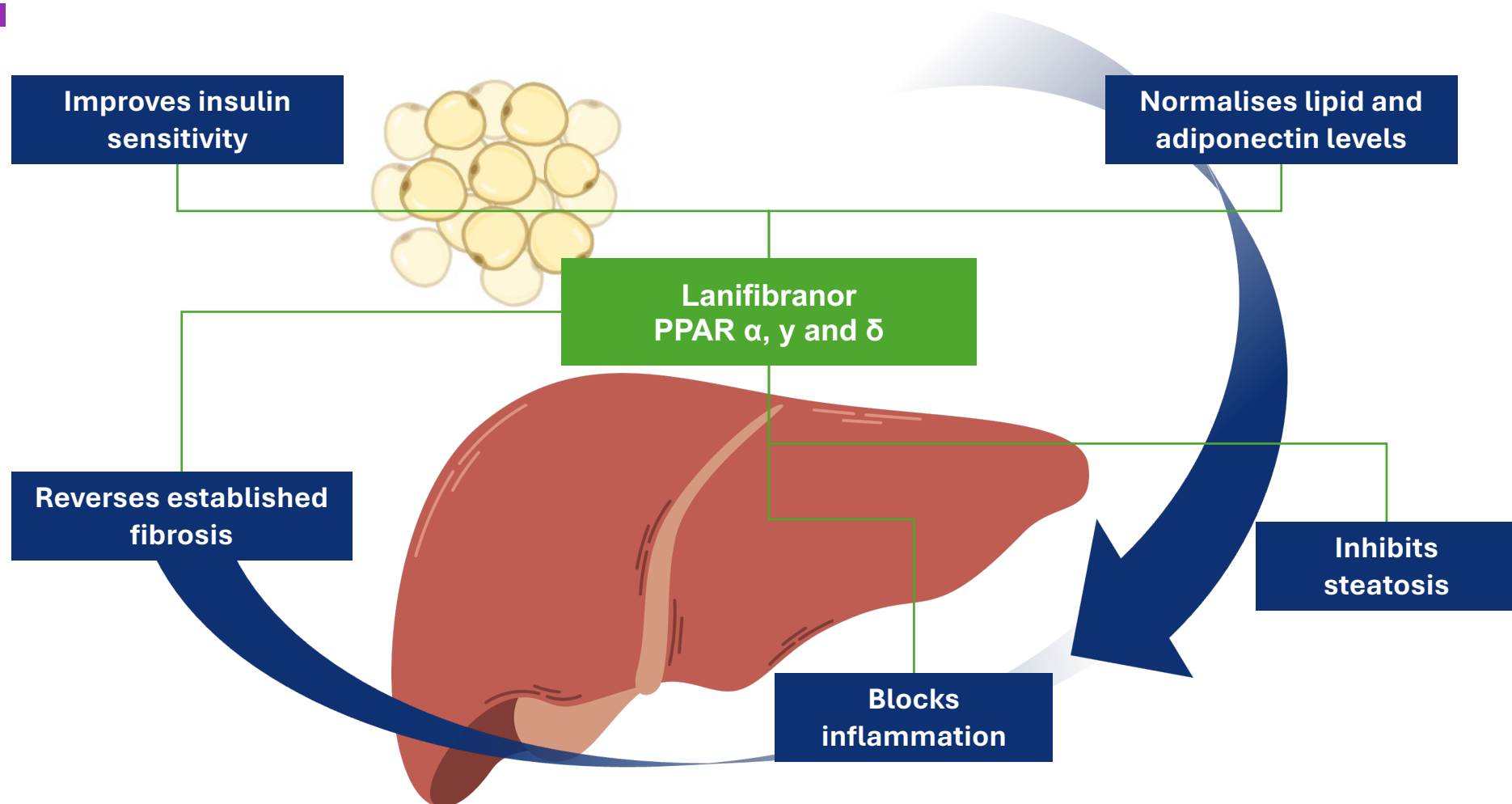


Improved dyslipidaemia (PPAR) and lower triglyceridaemia: CVD benefit?



Adiponectin benefits of PPAR with enhanced insulin secretion and beta-cell function (GLP-1)

# Lanifibranor is a liver-directed drug candidate with multiple targets highly relevant to MASH



# A Foundational Asset for MASH- The Case for Lanifibranor

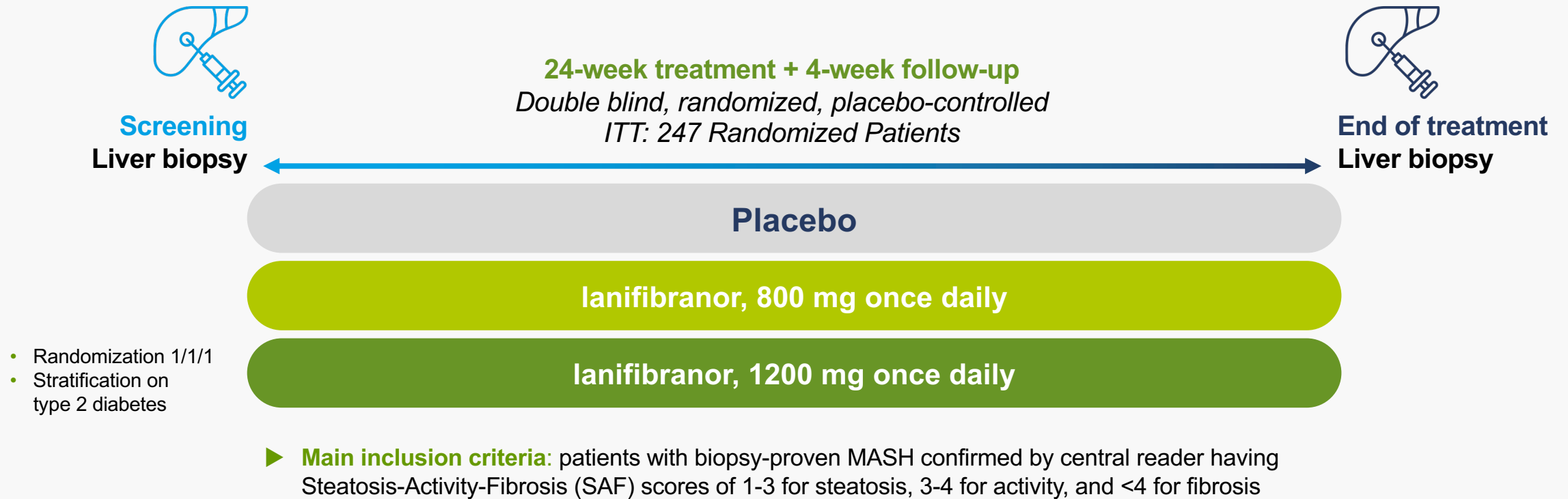
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## **Professor Arun Sanyal**

Director at the Stravitz-Sanyal Institute for Liver Disease and Metabolic Health  
School of Medicine Internal Medicine Virginia Commonwealth University  
Co-Principal Investigator NATiV3 Study

# The Phase 2b NATIVE trial – fibrosis improvement observed at 6 months

Evaluated 800 and 1200mg, oral, once-daily, 247 patients



A Randomized, Controlled Trial of the Pan-PPAR Agonist Lanifibranor in NASH, N Engl J Med 2021;385:1547-1558 (2) The pan-PPAR agonist lanifibranor improves cardiometabolic health in patients with metabolic dysfunction-associated steatohepatitis | Nature Communications

# Resolution of MASH and fibrosis improvement $\geq$ least 1 stage

Compares favorably to other oral and injectable compounds



## ORAL

### PPARs



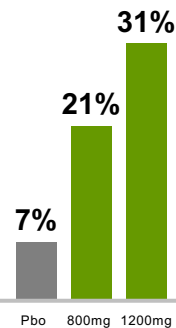
#### Lanifibranor

Phase 2  
6 months

N=247

ITT

Effect size  
**24%\***



0.017\* <0.001\*

### THR- $\beta$



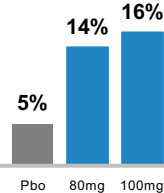
#### Resmetirom\*\*

Phase 3  
12 months

N=955

ITT

Effect size  
**11%**



<0.0001\* <0.0001\*

## INJECTABLE

### FGF-21



#### Efruxifermin

Phase 2b  
6 months

N=128

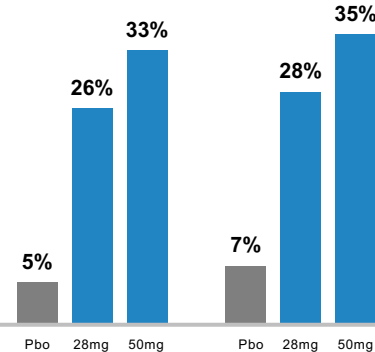
ITT

Effect size  
**28%**

Phase 2b  
24 months

N=126

Effect size  
**28%**



0.009\* 0.002\* <0.01\* <0.01\*



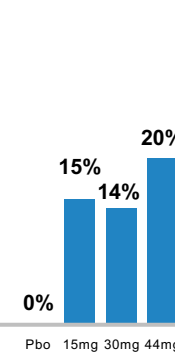
#### Pegozafermin

Phase 2  
6 months

N=222

PP

Effect size  
**20%**



\*\*\*

### GLP1-RA and GLP1-RA dual agonists



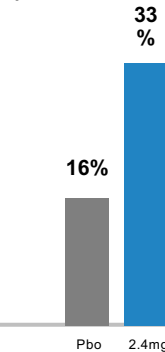
#### Semaglutide\*\*

Phase 3  
18 months

N=800

PP

Effect size  
**16.6%**



#### Survodutide

Phase 2  
12 months

N=223 (F2/F3)



#### Tirzepatide

Phase 2  
12 months

N=190

Endpoint not  
disclosed

**No head-to-head clinical trials have been conducted; results obtained from different trials, with different designs, endpoints and patient populations. Results may not be comparable.**

\*Effect size was 26% in the 1200 mg arm in patients with T2D \*\*Resmetirom and semaglutide have been approved under accelerated approval by the FDA.

Source: lanifibranor native results; Efruxifermin Safety and efficacy of once-weekly efruxifermin versus placebo in non-alcoholic steatohepatitis (HARMONY): a multicentre, randomised, double-blind, placebo-controlled, Phase 2b trial. Lancet Gastroenterology October 2023 ; Semaglutide Phase 3 ESSENCE trial of semaglutide 2.4mg in participants with non-cirrhotic non-alcoholic steatohepatitis; Newsome et al.; Resmetirom MAESTRO MASH top-line results webcast Dec. 19 2022, pg 10 and EASL 2023 presentation pg. 8; Efruxifermin EASL 2023 presentation pg. 8, corporate presentation of March 2024 pg 22; Survodutide A Phase 2 randomized trial for Survodutide in MASH and fibrosis, The NEJM DOI: 10.1056/NEJMoa2401755; Tirzepatide Tirzepatide for Metabolic Dysfunction-Associated Steatohepatitis with Liver Fibrosis, The NEJM DOI: 10.1056/NEJMoa2401943



# Fibrosis improvement $\geq 1$ stage with no worsening of MASH

Compares favorably to other oral and injectable compounds



## ORAL

### PPARs



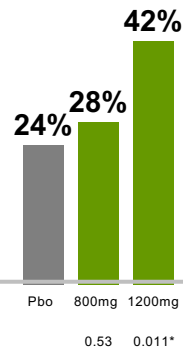
#### Lanifibranor

Phase 2  
6 months

N=247

ITT

Effect size  
18%



### THR- $\beta$



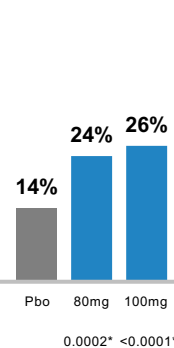
#### Resmetirom\*\*

Phase 3  
12 months

N=955

ITT

Effect size  
12%



## INJECTABLE

### FGF-21



#### Efruxifermin

Phase 2b  
6 months

N=128

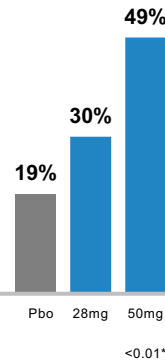
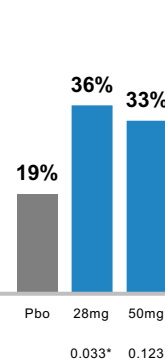
Phase 2b  
24 months

N=126

ITT

Effect size  
14%

Effect size  
30%



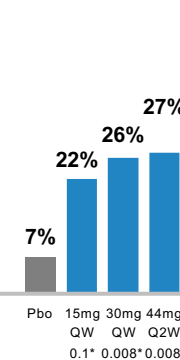
#### Pegozafermin

Phase 2  
6 months

N=222

PP

Effect size  
20%



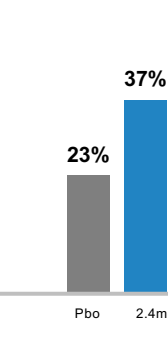
#### Semaglutide\*\*

Phase 3  
18 months

N=800

PP

Effect size  
15%



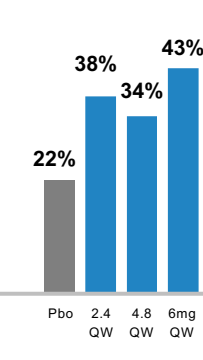
#### Survodutide

Phase 2  
12 months

N=293

ITT

Effect size  
21%



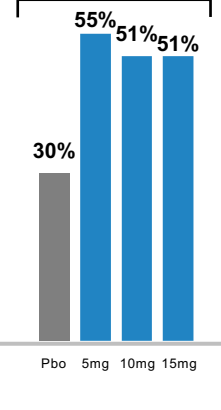
#### Tirzepatide

Phase 2  
12 months

N=190

ITT

Effect size  
21%



**No head-to-head clinical trials have been conducted; results obtained from different trials, with different designs, endpoints and patient populations. Results may not be comparable.**

\* Resmetirom and semaglutide have been approved under accelerated approval by the FDA.

Source: lanifibranor native results; resmetirom MAESTRO MASH top-line results webcast Dec. 19 2022, pg 10; resmetirom : Harrison et al, Lancet 2019 ; S0140-6736(19) 32517-6 Efruxifermin Safety and efficacy of once-weekly efruxifermin versus placebo in non-alcoholic steatohepatitis (HARMONY): a multicentre, randomised, double-blind, placebo-controlled, Phase 2b trial. Lancet Gastroenterology October 2023; corporate presentation of March 2024 pg15; Semaglutide Phase 3 ESSENCE trial of semaglutide 2.4mg in participants with non-cirrhotic non-alcoholic steatohepatitis; Newsome et al.; Pegozafermin, 89Bio Phase 2b ENLIVEN Topline Results presentation; Survodutide A Phase 2 randomized trial for Survodutide in MASH and fibrosis, The NEJM DOI: 10.1056/NEJMoa2401755 ; Tirzepatide Tirzepatide for Metabolic Dysfunction-Associated Steatohepatitis with Liver Fibrosis, The NEJM DOI: 10.1056/NEJMoa2401943



# MASH resolution with no worsening of fibrosis

Compares favorably to other oral and injectable compounds



## ORAL

### PPARs



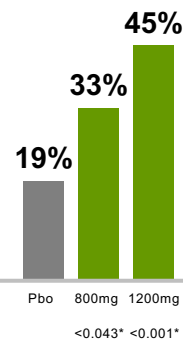
#### Lanifibranor

Phase 2  
6 months

N=247

ITT

Effect size  
26%



### THR-β



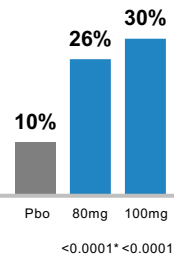
#### Resmetirom\*\*

Phase 3  
12 months

N=955

ITT

Effect size  
20%



## INJECTABLE

### FGF-21



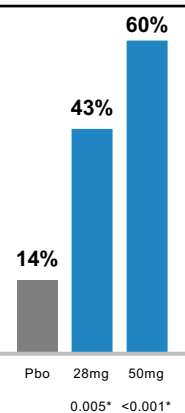
#### Efruxifermin

Phase 2b  
6 months

N=128

ITT

Effect size  
46%



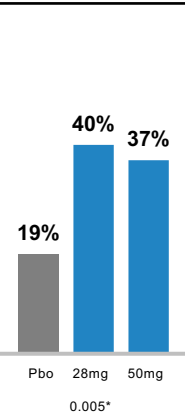
#### Pegozafermin

Phase 2b  
24 months

N=126

PP

Effect size  
18%



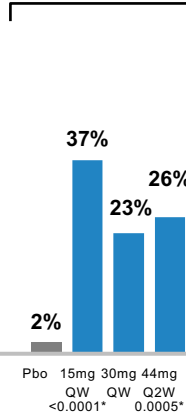
#### Pegozafermin

Phase 2  
6 months

N=222

PP

Effect size  
24%



### GLP1-RA and GLP1-RA dual agonists



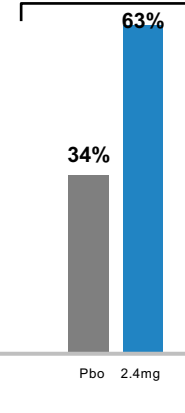
#### Semaglutide\*\*

Phase 3  
18 months

N=800

PP

Effect size  
40%



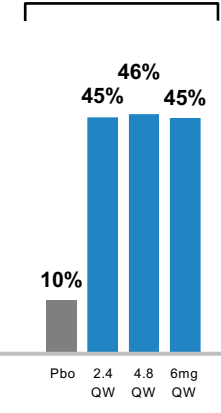
#### Survodutide

Phase 2  
12 months

N=293

ITT

Effect size  
35%



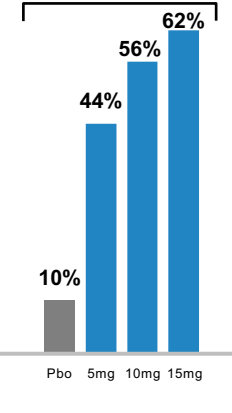
#### Tirzepatide

Phase 2  
12 months

N=190

ITT

Effect size  
52%



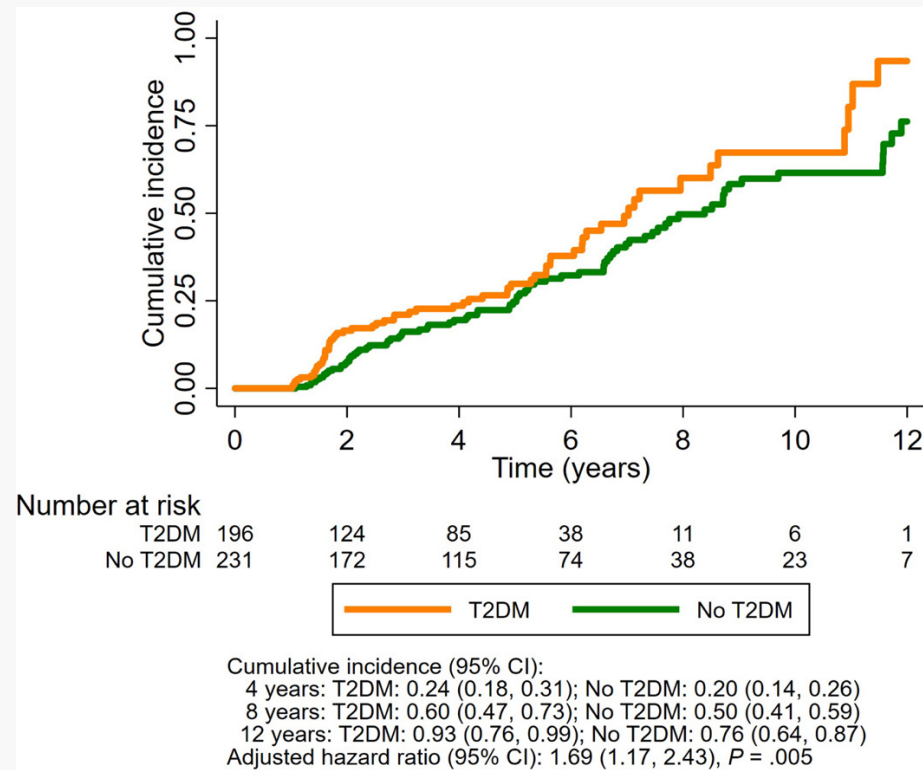
**No head-to-head clinical trials have been conducted; results obtained from different trials, with different designs, endpoints and patient populations. Results may not be comparable.**

\* Resmetirom and semaglutide have been approved under accelerated approval by the FDA.

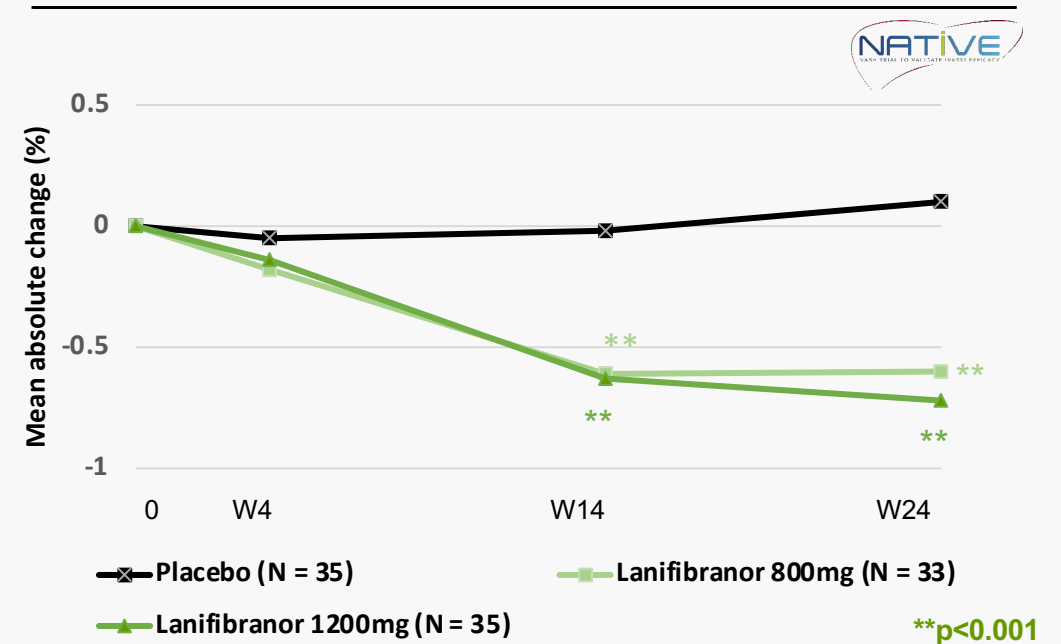
Source: lanifibranor native results; resmetirom MAESTRO NASH top-line results webcast Dec. 19 2022, pg 10; resmetirom : Harrison et al, Lancet 2019 ; S0140-6736(19) 32517-6 Efruxifermin Safety and efficacy of once-weekly efruxifermin versus placebo in non-alcoholic steatohepatitis (HARMONY): a multicentre, randomised, double-blind, placebo-controlled, Phase 2b trial. Lancet Gastroenterology October 2023; corporate presentation of March 2024 pg15; Semaglutide Phase 3 ESSENCE trial of semaglutide 2.4mg in participants with non-cirrhotic non-alcoholic steatohepatitis; Newsome et al.; Pegozafermin, 89Bio Phase 2b ENLIVEN Topline Results presentation; Survodutide A Phase 2 randomized trial for Survodutide in MASH and fibrosis, The NEJM DOI: 10.1056/NEJMoa2401755 ; Tirzepatide Tirzepatide for Metabolic Dysfunction-Associated Steatohepatitis with Liver Fibrosis, The NEJM DOI: 10.1056/NEJMoa2401943

# Patients with T2D have a higher cumulative incidence of fibrosis progression making it relevant for a drug to address the metabolic drivers of disease

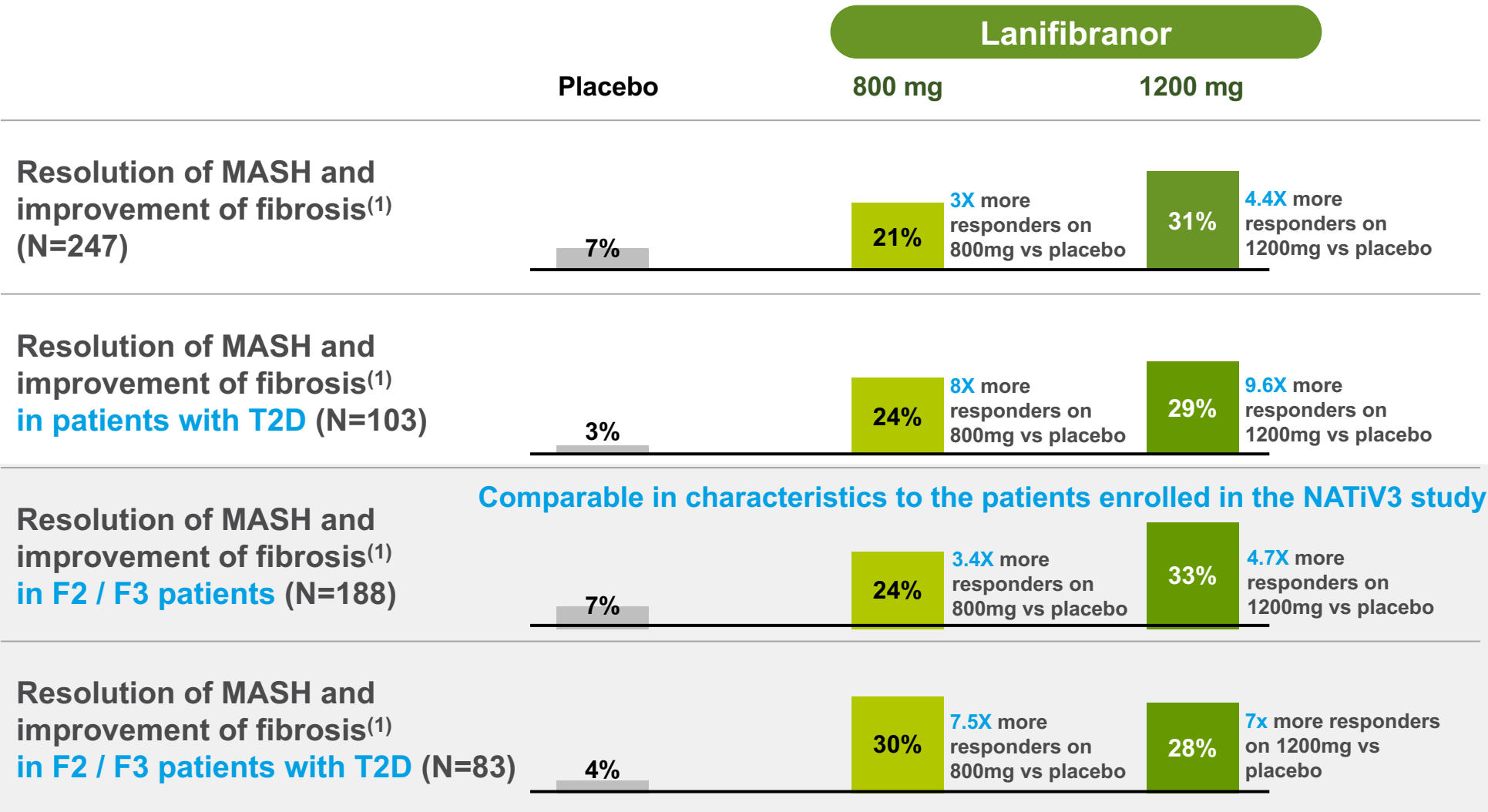
- Cumulative incidence of fibrosis progression in nonalcoholic fatty liver disease, among participants with T2D versus participants without T2D



## Absolute change from baseline in HbA1c



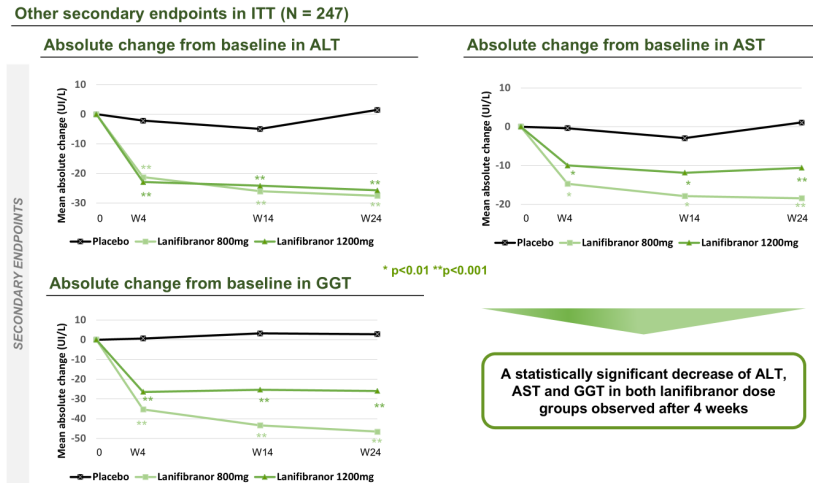
# Resolution of MASH and improvement of fibrosis: effect size is increased in F2/F3 patients as well as patients with T2D



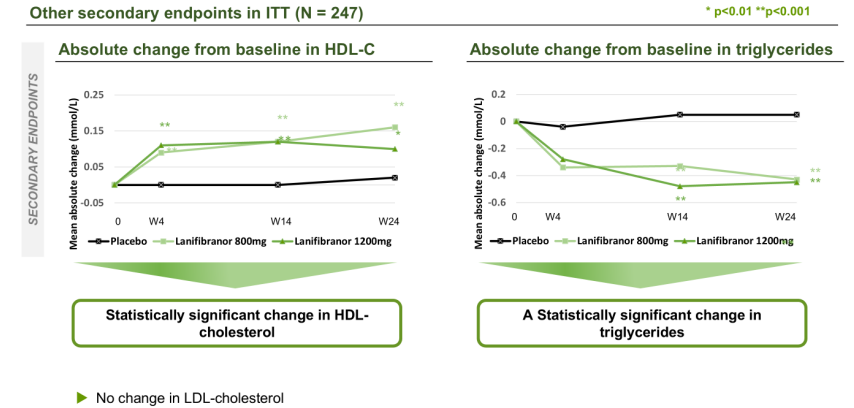
(1) ) Resolution of MASH and improvement of fibrosis at week 24: NAS-I = 0 or 1, NAS-B = 0 and an improvement of NAS-F ≥ 1 stage

# Improvement seen across key intra and extra hepatic features of MASH

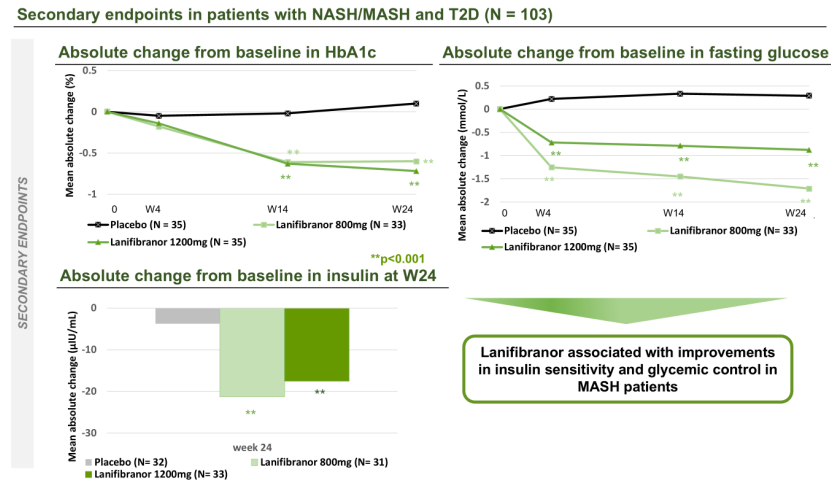
Statistically significant decrease in liver enzymes  
Liver biomarkers show rapid and sustained improvement



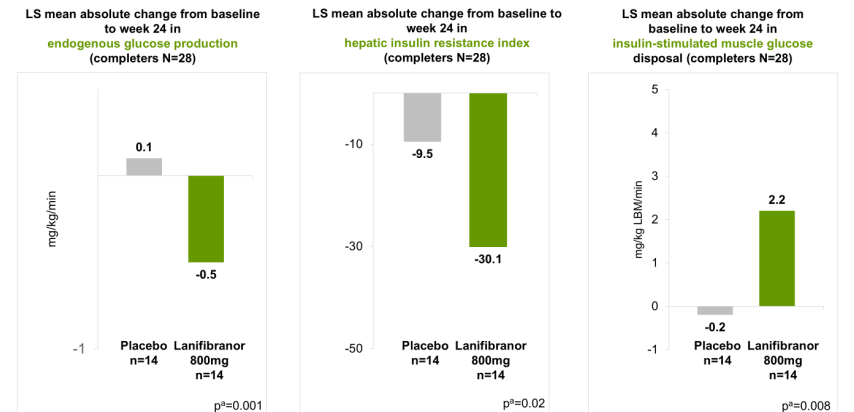
Statistically significant change in lipid profile  
Improvements in HDL cholesterol and TGs without a change in LDL cholesterol



Significant reductions in HbA1c  
Clear benefit in patients with MASH with T2D, across multiple studies



Significant improvements in hepatic and muscular insulin sensitivity  
Strong benefit observed across multiple studies



(1) Data from the clinical study conducted by Dr. Kenneth Cusi from the University of Florida, evaluating lanifibranor (800mg/day) in patients with NAFLD and type 2 diabetes mellitus (T2D) for 24 weeks

ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; HbA1c, glycated hemoglobin (a measure of long-term blood glucose); HDL, high-density lipoprotein; ITT, insulin tolerance test; LDL, low-density lipoprotein; T2D, type 2 diabetes; TGs, triglycerides.

# Lanifibranor observed to induce a decrease in key serum biomarkers consistent with histologic endpoints



- Data from Phase 2b NATIVE clinical trial evaluating lanifibranor (800 mg/day and 1200 mg/day) in patients with MASH for 24 weeks

Median relative change (%)		Placebo	Lanifibranor (2 doses pooled)	p-value
Fibrosis	Pro-C3	(4.1%)	(13.9%)	$p=0.005^b$
	Pro-C3 >14 at baseline <sup>a</sup>	(12.8%)	(20.5%)	$p=0.017^b$
	Ratio TIMP-1/MMP-2	(4.6%)	(22.5%)	$p<0.001^b$
Apoptosis	CK18-M30	0.5%	(41.1%)	$p<0.001^b$
Inflammation	Ferritin	(9.1%)	(29.4%)	$p<0.001^b$
	hs-CRP	13.0%	(35.5%)	$p<0.001^b$

# Phase 2b NATIVE study: lanifibranor has a favorable safety profile



N (%) patients reporting Adverse Event (AE)	Placebo (N = 81)	800 mg (N = 83)	1200 mg (N = 83)
► <b>Any TEAE</b>	50 (61.7%)	59 (71.1%)	62 (74.7%)
<i>Drug-related TEAE</i>	19 (23.5%)	25 (30.1%)	23 (27.7%)
► <b>Any TEAE leading to drug withdrawal</b>	3 (3.7%)	4 (4.8%)	3 (3.6%)
<i>Drug-related TEAE leading to drug withdrawal</i>	2 (2.5%)	1 (1.2%) <sup>(1)</sup>	2 (2.4%) <sup>(2)</sup>
► <b>Any Serious TEAE</b>	3 (3.7%)	3 (3.6%)	7 (8.4%)
<i>Drug-related Serious TEAE</i>	2 (2.5%) <sup>(3)</sup>	-	-

- Consistent with known insulin sensitizing pharmacology, a mean weight increase from baseline of 2.4 kg (2.6%) at the 800 mg/day dose and 2.7 kg (3.1%) at the 1200 mg/day dose was observed.

	Placebo (N = 81)	800 mg (N = 83)	1200 mg (N = 81)
► <b>Peripheral edema</b>	2 (2.5%)	5 (6.0%)	7* (8.4%)
<i>Drug-related peripheral edema</i>	-	2 (2.4%)	2 (2.4%)

- Peripheral edema (bilateral ankle edema): usually mild, in most cases no treatment was required, a few patients received diuretics. 4 cases were considered study drug related by the investigator (2 at 800 and 1200 mg each). One case of severe intensity, which resolved by stopping treatment (lanifibranor 1200mg) for 12 days, without reoccurrence when the study treatment was resumed. All were female patients.

<sup>(1)</sup> One patient with moderate diarrhea ; <sup>(2)</sup> One patient with mild cardiac failure; one patient with mild diarrhea, abdominal pain, dizziness ; <sup>(3)</sup> 2 SUSARs in the placebo arm: one patient with mild cardiac failure; one patient with moderate urticaria  
\* One AE of severe intensity

# Phase 2b NATIVE study: most frequently reported AEs



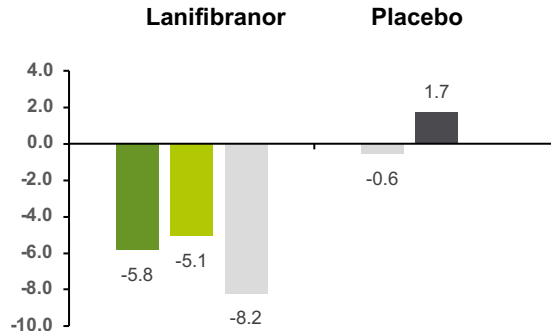
% patients reporting the most frequent AEs (>5% of patients in at least 1 lanifibranor arm)	Placebo (N=81)	800 mg (N=83)	1200 mg (N=83)
Diarrhea	1 (1.2%)	8 (9.6%)	10 (12.0%)
Fatigue <sup>a</sup>	8 (9.9%)	3 (3.6%)	11 (13.3%)
Nausea	3 (3.7%)	8 (9.6%)	7 (8.4%)
Weight increased	-	8 (9.6%)	7 (8.4%)
Edema peripheral	2 (2.5%)	5 (6.0%)	7 (8.4%)
Headache	4 (4.9%)	4 (4.8%)	7 (8.4%)
Abdominal pain <sup>b</sup>	4 (4.9%)	4 (4.8%)	5 (6.0%)
Dizziness	3 (3.7%)	2 (2.4%)	6 (7.2%)
Anemia <sup>c</sup>	-	1 (1.2%)	6 (7.2%)
Constipation	6 (7.4%)	3 (3.6%)	5 (6.0%)
Transaminases increased <sup>d</sup>	1 (1.2%)	5 (6.0%)	3 (3.6%)

<sup>a</sup>Fatigue included asthenia. <sup>b</sup>Abdominal pain included upper and lower abdominal pain. <sup>c</sup>Anemia included iron deficiency anemia and decreased hemoglobin level. <sup>d</sup>Increase in aminotransferase level included increased alanine aminotransferase level, increased aspartate aminotransferase level, or abnormal liver function test result.  
AE, adverse event. Francque SM, et al. *N Engl J Med*. 2021;385(17):1547-1558.

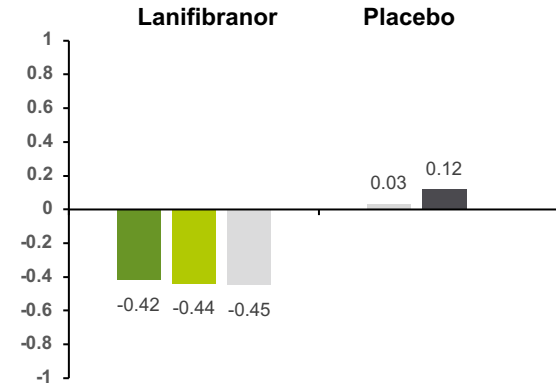
# Weight gain comes with improvements in metabolic, cardiometabolic, and liver markers

## Insulin Resistance – Metabolic

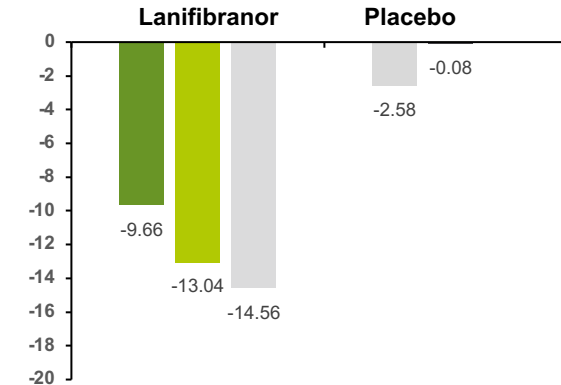
**Fasting HOMA-IR**  
Mean absolute change at Week 24 from baseline



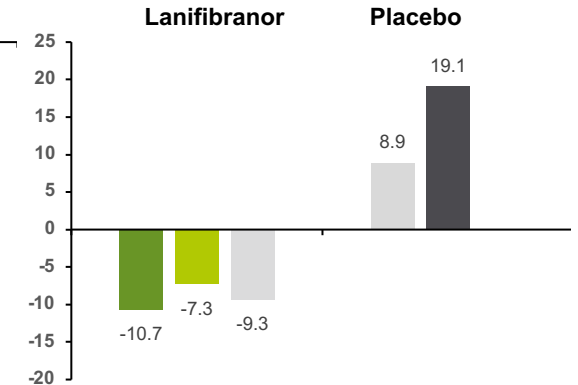
**Triglycerides**  
Mean absolute change at Week 24 from baseline (mmol/L)



**APO-B**  
Mean absolute change at week 24 from baseline (mg/dl)

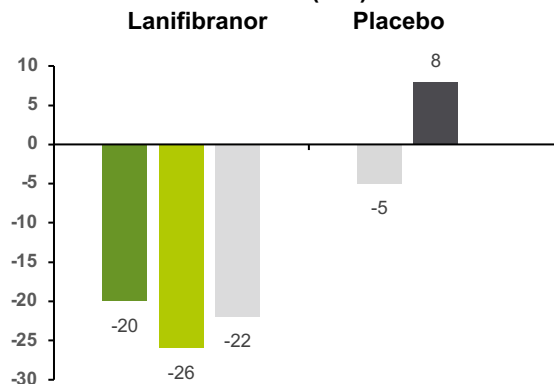


**APO-C3**  
Mean absolute change at week 24 from baseline (µg/ml)



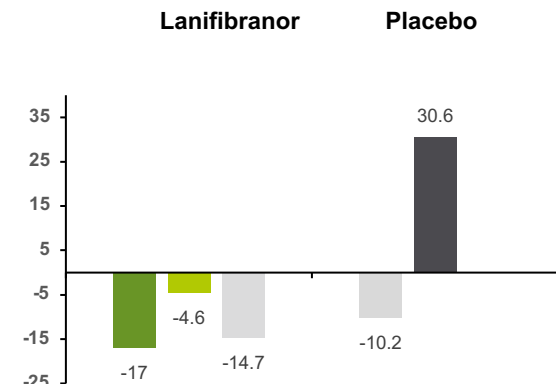
## Liver Function

**ALT**  
Mean absolute change at Week 24 from baseline (U/L)

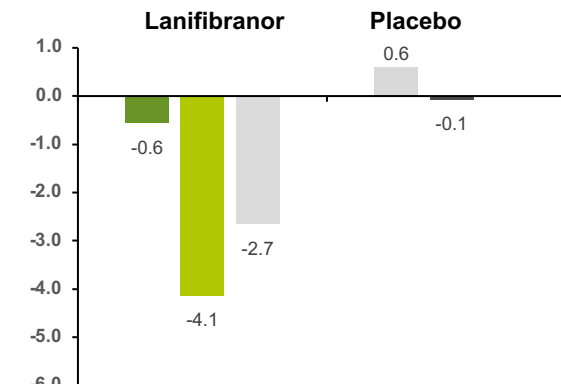


## Inflammation

**CAP**  
Mean absolute change at Week 24 from baseline (dB.m-1)

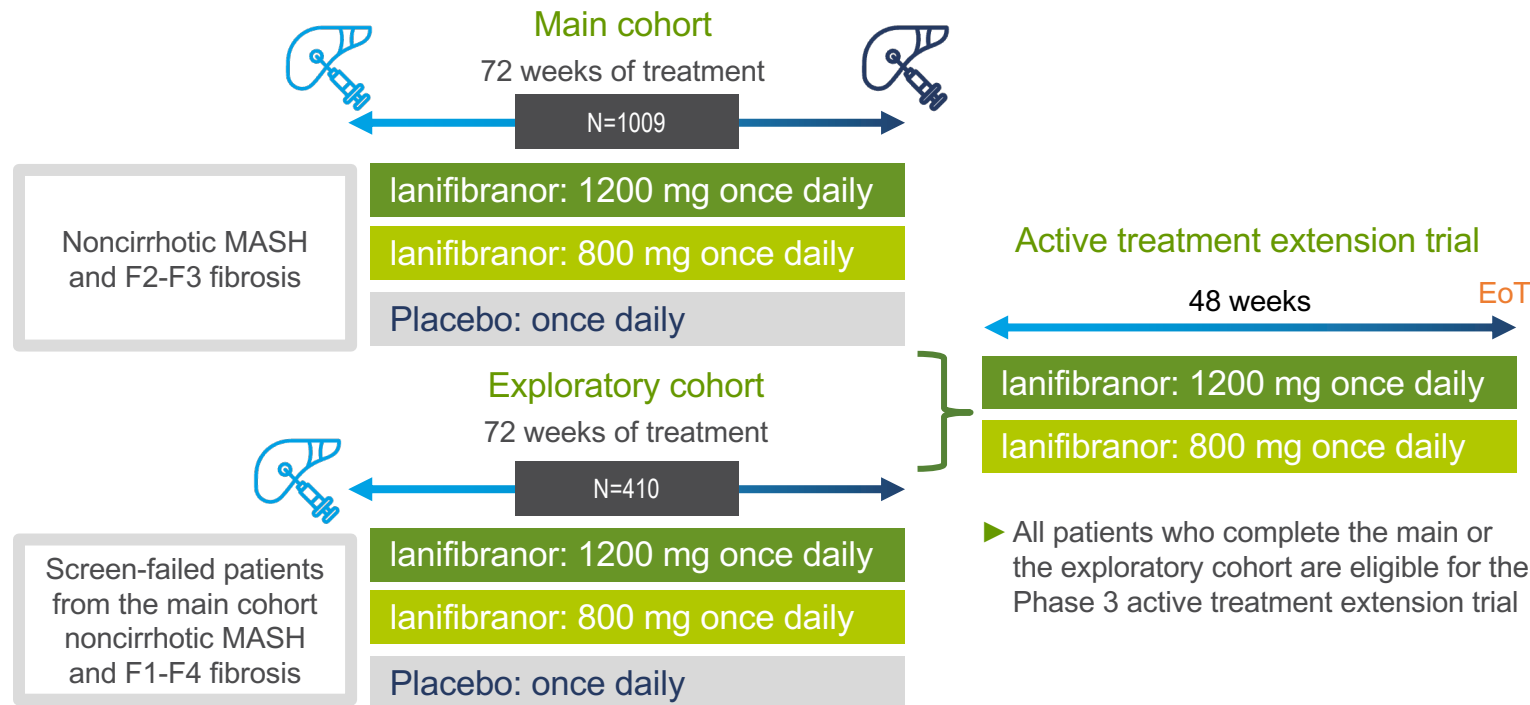


**hs-CRP**  
Mean absolute change at Week 24 from baseline (%)



- Stable weight ( $\leq 2.5\%$ )
- Moderate weight gain (2.5%-5%)
- Weight gain ( $> 5\%$ )
- Stable weight ( $\leq 2.5\%$ )
- Weight gain ( $> 5\%$ )

# NATiV3 fully recruited: trial design mirrors the successful Phase 2b study



## Primary end point:

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

## Key secondary end points:

MASH resolution and no worsening of fibrosis, fibrosis improvement, and no worsening of MASH

## GLP-1:

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 1009 patients in the main cohort and 410 in the exploratory cohort

Only a few hundred patients remaining to complete their 72-week biopsy

# Baseline characteristics of NATiV3 are aligned with those of Phase 2b NATiVE

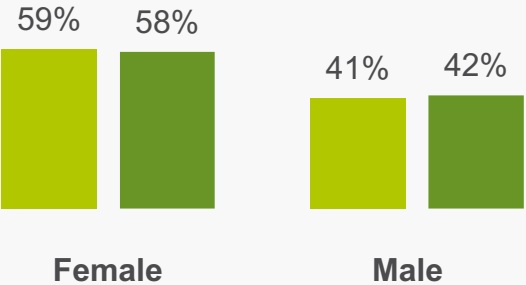
## Demographics & Metabolic Profile



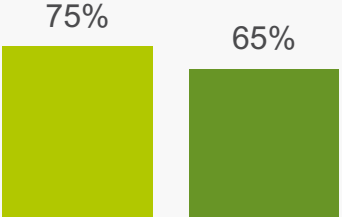
NATiV3  
N=1009



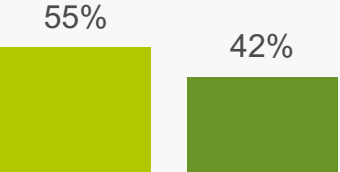
NATiVE  
N=247



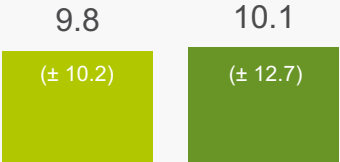
Weight (kg) mean ± SD  
median: NATiV3 = 95kg | NATiVE = 92kg



BMI class: obese (≥30)



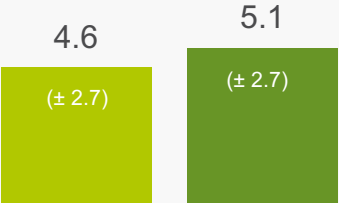
T2D



HOMA-IR mean ± SD  
median: NATiV3 = 7.3 | NATiVE = 6.7




HbA1c mean ± SD  
median: NATiV3 = 6.2% | NATiVE = 5.9%




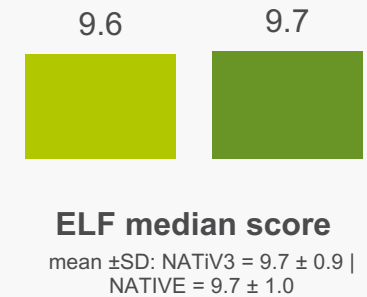
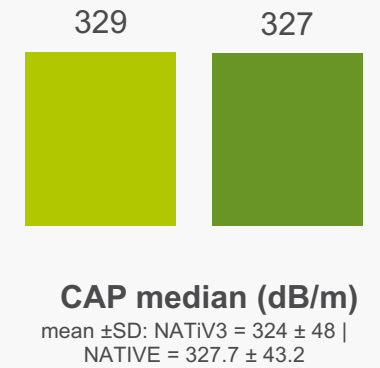
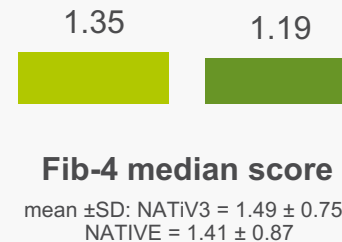
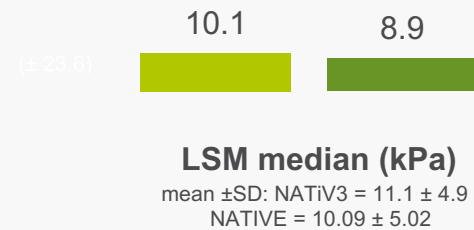
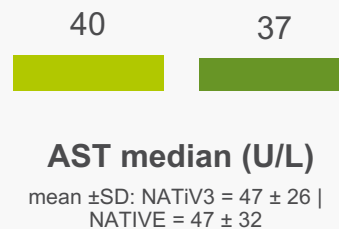
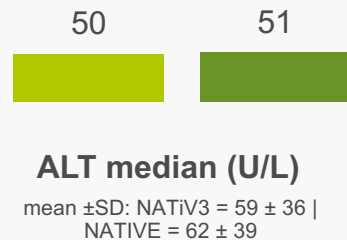
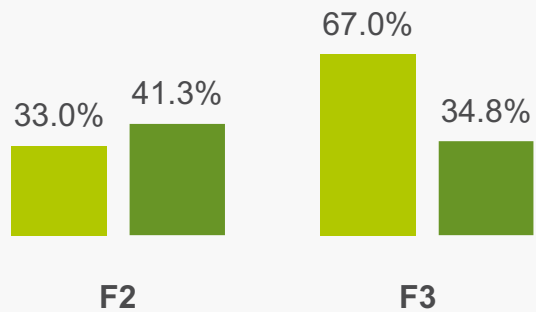
Adiponectin (µg/mL) mean ± SD  
median: NATiV3 = 4.0 | NATiVE = 4.5

# Baseline characteristics of NATiV3 are aligned with those of Phase 2b NATiVE

## Liver Disease Profile

 **NATiV3**  
N=1009

 **NATiVE**  
N=247

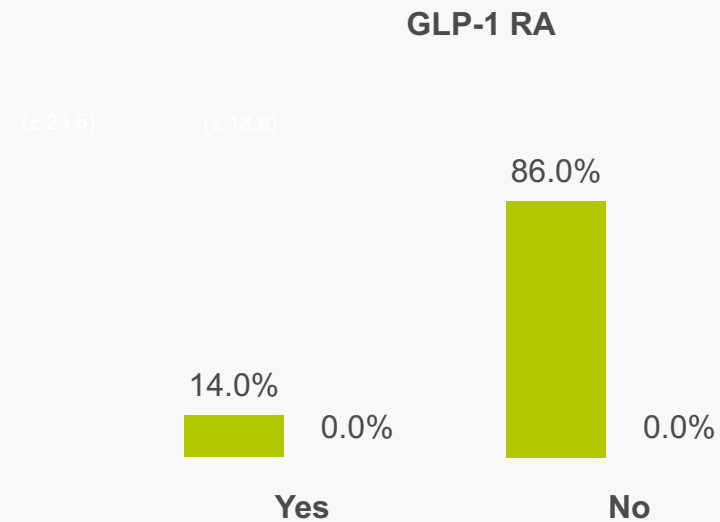
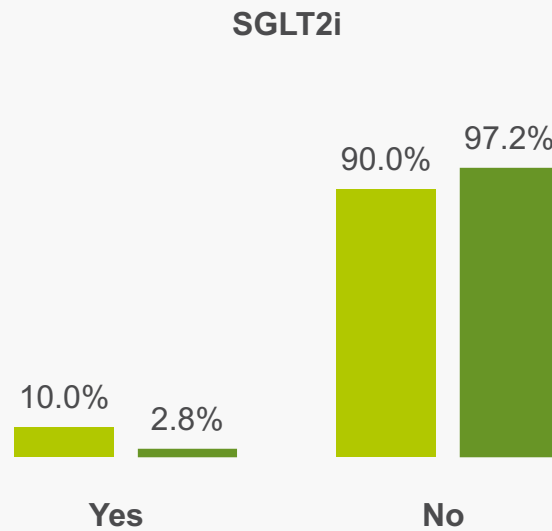


# Baseline characteristics of NATiV3 are aligned with those of Phase 2b NATiVE

## Co-medication

  
NATiV3  
N=1009

  
NATiVE  
N=247



# Conclusion

1

**Baseline characteristics consistent with Phase 2b (NATIVE):** NATiV3 population is broadly comparable, reinforcing confidence in the robustness of study design.

2

**Greater representation of patients with T2D (55% vs 42% in Phase 2b):** Enhances the relevance of NATiV3 for real-world MASH populations.

3

**Stronger efficacy signal in T2D patients in Phase 2b:**

- Fibrosis improvement and MASH resolution rates were higher in patients with T2D.
- With lanifibranor: **21% (800 mg) and 26% (1200 mg)** in T2D vs **7% and 22%** in non-T2D.

4

**NATiV3 uniquely positioned to assess lanifibranor in combination with GLP-1 and SGLT2 inhibitors:** Reflecting the evolving treatment paradigm and supporting its potential as a backbone therapy.

5

**Lanifibranor's differentiated pan-PPAR mechanism of action:** Purpose-designed to activate PPAR- $\alpha$ , PPAR- $\delta$ , and PPAR- $\gamma$  in a balanced way, addressing both intra-hepatic (liver) and extra-hepatic (metabolic/cardiovascular) components of MASH.

**Published Phase 2b data demonstrated that lanifibranor, oral drug in development, achieved clinically meaningful improvements on liver histology endpoints, including the composite of fibrosis improvement and MASH resolution, within 6 months.**



HARVARD  
UNIVERSITY

# Real World Management of MASLD

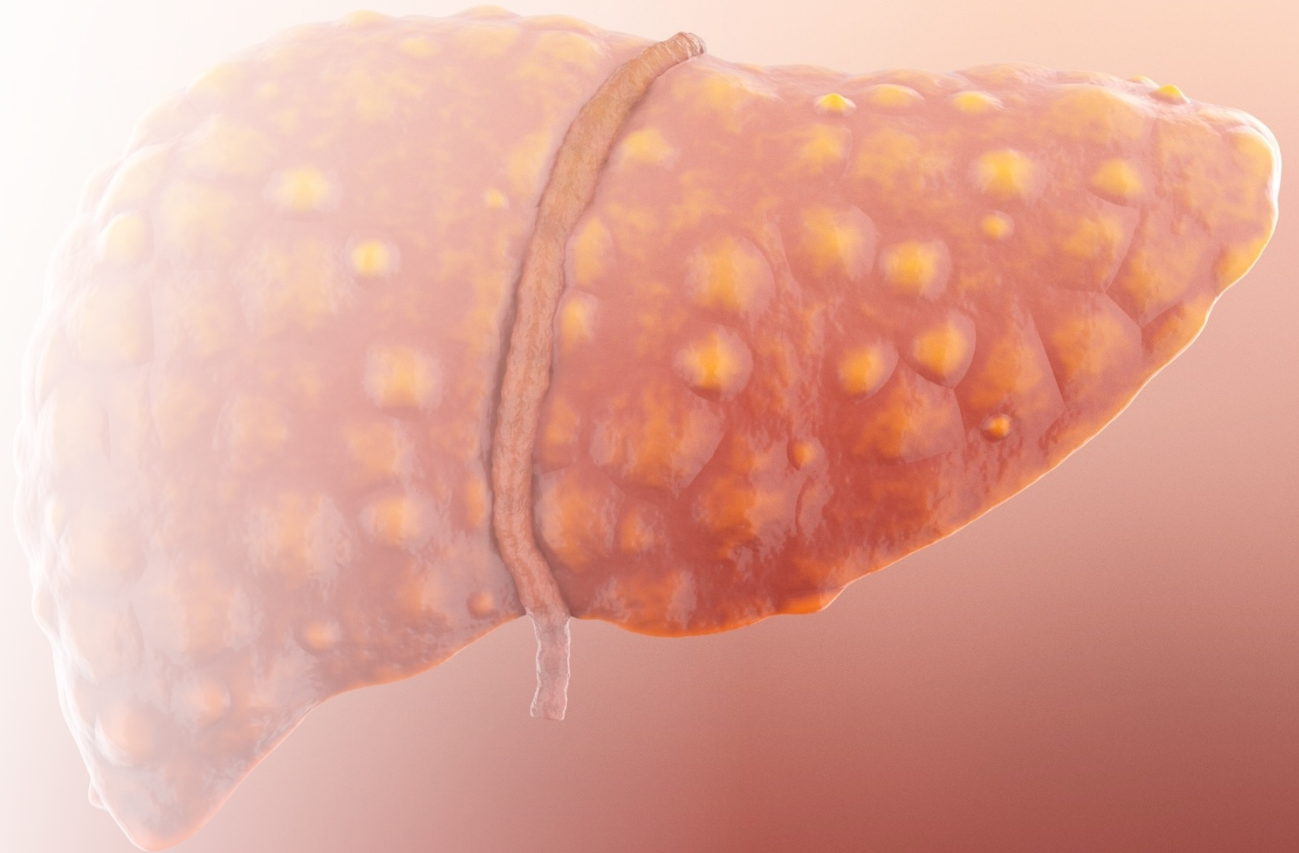
**Nezam H. Afdhal M.D, DSc**

**Charlotte and Irving Rabb Professor of Medicine**

Harvard Medical School,  
Chief of Gastroenterology  
Hepatology and Nutrition

**Beth Israel Deaconess**

Medical Center, Boston



# Lifestyle Recommendations for Treating MASLD/MASH



## Caloric intake reduction

≥30% or ~750-1,000 kcal/day improved insulin resistance and hepatic steatosis

\*Limit consumption of fructose-enriched beverages



## Weight loss

of 3% to 5% can improve steatosis, but 6% to 10% is needed to improve MASH/fibrosis



## Exercise

alone may reduce steatosis, but effect on other histologic features unknown



## No heavy alcohol consumption

Insufficient data to guide recommendations regarding nonheavy alcohol consumption

\*\*Drink ≥2 cups of caffeinated coffee daily



Statin use in patients with dyslipidemia



Aspirin use in diabetics



Mediterranean diet



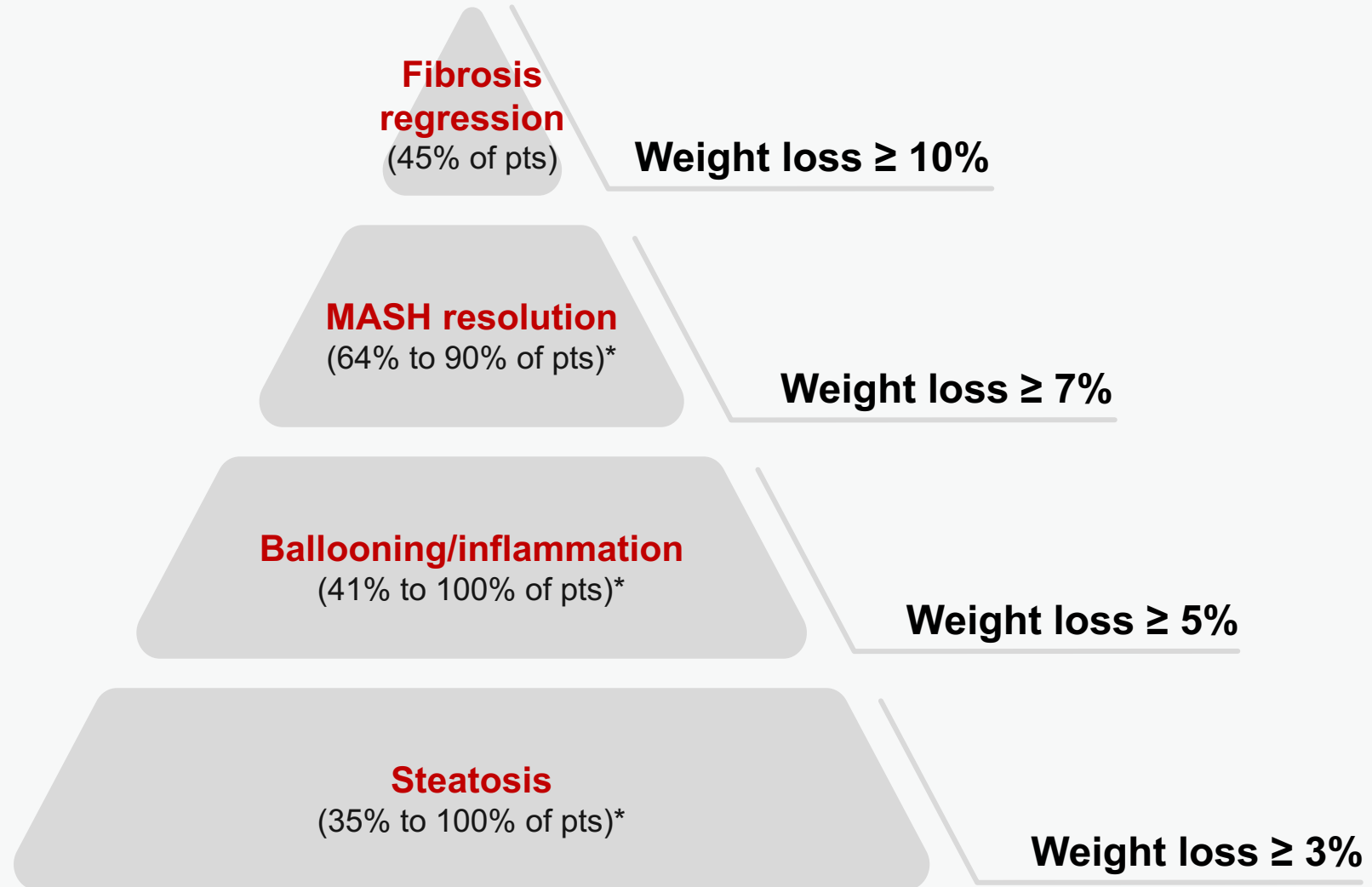
Avoid sugar and sugar containing beverages



Bariatric surgery in those with morbid obesity and co-morbidities

# Weight Loss for MASLD & Fibrosis Progression

Analysis of data from 4 randomized studies








\*Depending on degree of weight loss.  
Hannah WN, et al. Clin Liver Dis. 2016;20:339-350.

# If lifestyle changes don't cut it... what about Bariatric surgery?

Subgroup Name	Resolution of steatosis, % (95% CI)	Resolution of lobular inflammation, % (95% CI)	Resolution of ballooning degeneration, % (95% CI)	Resolution of fibrosis, % (95% CI)	Worsening of NAFLD, % (95% CI)	NAS score, mean difference (95% CI)	P
Original analysis	66% (56%–75%)	50% (35%–64%)	76% (64%–86%)	40% (29%–51%)	12% (5%–20%)	2.39 (1.58–3.20)	<.0001
Prospective studies only	67% (53%–80%)	57% (39%–73%)	76% (61%–88%)	42% (27%–58%)	7% (2%–15%)	2.25 (1.43–3.07)	<.0001
Retrospective studies only	64% (48%–79%)	40% (17%–64%)	75% (51%–93%)	37% (22%–54%)	15% (5%–28%)	2.54 (0.94–4.13)	<.0001
Short-term follow-up evaluation (<1 y)	67% (54%–78%)	50% (30%–70%)	66% (41%–87%)	31% (18%–46%)	9% (0%–34%)	2.01 (1.76–2.25)	<.0001
Long-term follow-up evaluation (>1 y)	65% (50%–79%)	54% (32%–75%)	81% (69%–91%)	46% (30%–63%)	14% (7%–22%)	2.48 (1.49–3.46)	<.0001
RYGB only	80% (66%–91%)	57% (29%–83%)	80% (65%–91%)	51% (39%–63%)	8% (2%–15%)	2.42 (1.43–3.41)	<.0001
Needle biopsy only	67% (56%–78%)	51% (36%–66%)	76% (63%–87%)	41% (30%–52%)	12% (4%–22%)	2.67 (1.92–3.43)	<.0001
Wedge biopsy only	62% (46%–77%)	60% (30%–86%)	68% (53%–81%)	37% (17%–59%)	9% (2%–20%)	N/A	<.0001
Brunt grading system only	51% (41%–62%)	44% (28%–61%)	66% (40%–88%)	27% (18%–36%)	12% (2%–28%)	2.21 (0.81–3.61)	<.0001
Dixon grading system only	89% (53%–100%)	41% (6%–94%)	87% (76%–96%)	40% (27%–53%)	16% (7%–27%)	N/A	<.0001
NASH CRN grading system only	82% (74%–89%)	62% (39%–83%)	78% (62%–91%)	50% (21%–79%)	5% (0%–21%)	2.45 (1.04–3.86)	<.0001
Low baseline NAS (score, 0–4)	79% (69%–88%)	70% (57%–83%)	77% (60%–91%)	44% (23%–67%)	11% (4%–21%)	1.73 (1.25–2.21)	<.0001
High baseline NAS (score, >4)	84% (45%–100%)	41% (0%–100%)	93% (72%–100%)	38% (0%–94%)	11% (4%–22%)	3.17 (2.13–4.21)	<.0001

CRN, Clinical Research Network; N/A, <2 studies according to this criterion performed a meta-analysis; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis.

# How do GLPs stack up to Resmetirom?

		Incretins	Resmetirom
	<b>MASH Resolution</b> Placebo Adjusted	29% <sup>1</sup>	16-20% <sup>2</sup>
	<b>Fibrosis Improvement</b> Placebo Adjusted	14% <sup>1</sup>	10-12% <sup>2</sup>
	<b>T2D / Weight loss Benefits</b>	+++	-
	<b>Cardiometabolic benefits</b>	+++	+
	<b>Ease of Use</b>	Titration, tolerability concerns, high discontinuation rate	+++

1. Sanyal et al. N Engl J Med 2025;392:2089-2099 DOI: 10.1056/NEJMoa2413258

2. Harrison et al. N Engl J Med 2024;390:497-509 DOI: 10.1056/NEJMoa2309000

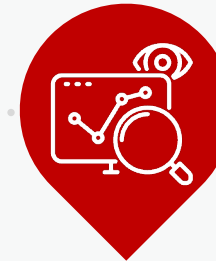
# MASH Diagnosis, Retention and Monitoring in the Real World is Resource-Intensive for Incretins

**Access to Medication Pre-authorization:**  
by dedicated Pharm D, 340B resource allocation  
(resource intensive)

**Follow up:** Dedicated Nurse Practitioner Team for Incretin titration, side effect management, telehealth = 85% retention (resource intensive)



**NIT diagnostics:**  
100% elastography,  
no serological tests,  
rare biopsy



**Monitoring:**  
**Month 6:** Repeat elastography for CAP evaluation, > 20% reduction  
**Month 12:** Repeat elastography for LS and CAP  
**Access** - No issues with renewal of treatment at 12 months to date

# Conclusions

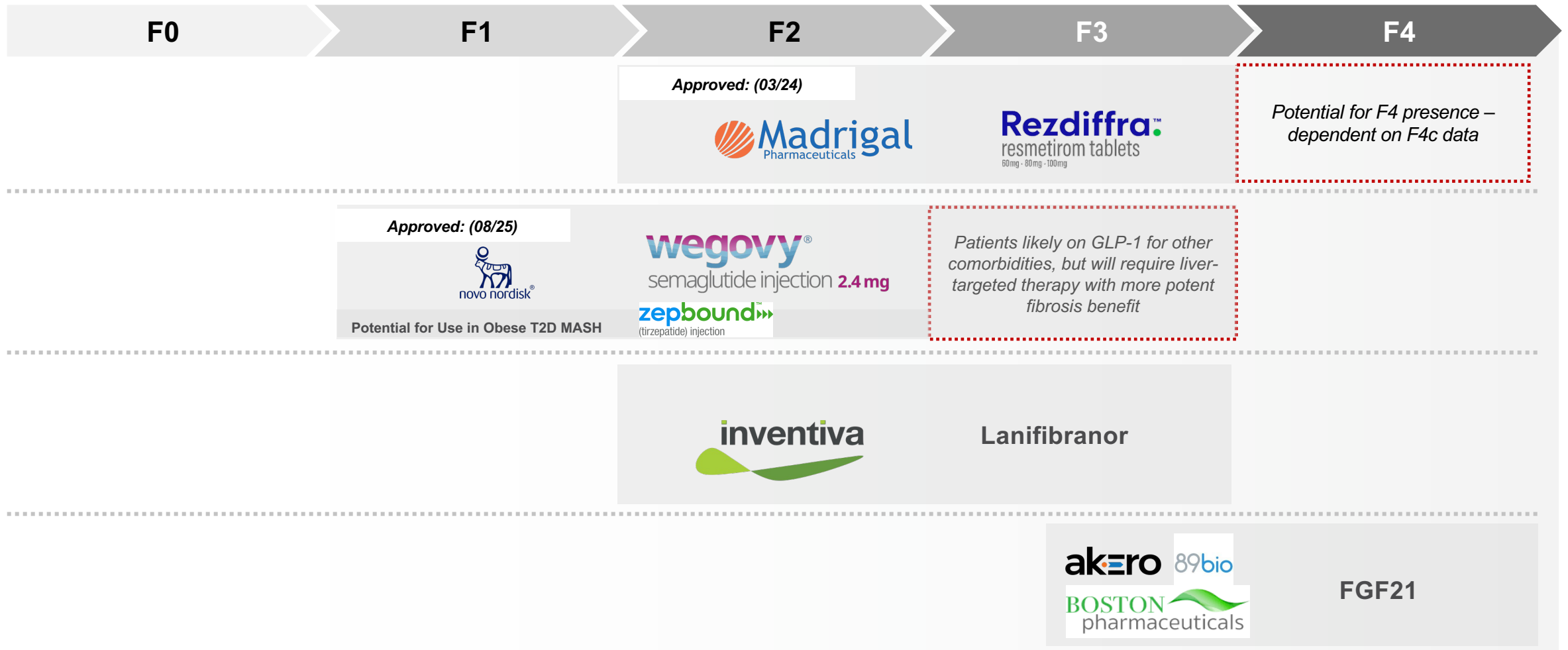
- 1 MASH treatment does not follow guidelines for Incretins since T2D and Obesity expand utilization outside of MASH alone**
- 2 In a real-world chart review, diagnostics for staging not rigid – only 30% have a fibroscan, serological tests or biopsy**
- 3 Resources needed for incretins administration are significant**
- 4 Resmetirom use is simple but mostly prescribed in F2 / F3**
- 5 Overall efficacy for both agents is underwhelming but secondary benefits of incretins clearly drive current utilization**
- 6 Significant need for better antifibrotic agents – Phase 2 lanifibranor Improvement in Fibrosis with no worsening of MASH 18%\*<sup>1</sup> and FGF-21 class ~21%\*<sup>2</sup>**

\*Placebo adjusted

1. Francque S. M., et al. New England Journal of Medicine 2021; 385:1547-1558. DOI: 10.1056/NEJMoa2036205

2. Harrison SA, et al. Lancet Gastroenterology & Hepatology. 2023. DOI: 10.1016/S2468-1253(23)00272-8;Loomba et al. NEJM. 2023;389:999–1008 (article). DOI: 10.1056/NEJMoa2304286

# Opportunities in MASLD for Approved and Upcoming Therapies



**If NATiV3 results are positive and fibrosis data are strong, lanifibranor has the potential to be the therapy of choice in F2 / F3 alone or in combination with a GLP-1, if approved**

# Panel Discussion

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**Jason Campagna**

President R&D and CMO of Inventiva

# Panel Discussion

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**HENRY E. CHANG**

Executive Director of the Fatty Liver Foundation



**ARUN SANYAL, MD**

Director at the Stravitz-Sanyal Institute for Liver Disease and Metabolic Health School of Medicine Internal Medicine Virginia Commonwealth University  
Co-principal investigator of the Phase 3 NATiv3 study



**NEZAM AFDHAL, MD**

Chief of the division of Gastroenterology, Hepatology and Nutrition at Beth Israel Deaconess Medical Center and Professor of Medicine at Harvard Medical School



**WILLIAM ALAZAWI, MD**

Professor of Hepatology and Director of Research at the Queen Mary University of London

# Conclusion

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**Andrew Obenshain**  
CEO of Inventiva

# Take away messages

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- 1** Treatments have been approved but unmet medical need persists for liver-directed therapies.
- 2** Lanifibranor: Oral liver-targeted drug candidate addressing both intra-hepatic (liver) and extra-hepatic (metabolic/cardiovascular) components of MASH within 6 months.
- 3** Phase 3 NATiV3 fully recruited: Trial design and patient population mirror the successful Phase 2b study.
- 4** Inventiva is focused and structured to execute on the delivery of topline data expected in H2 2026.

**Thank You**

