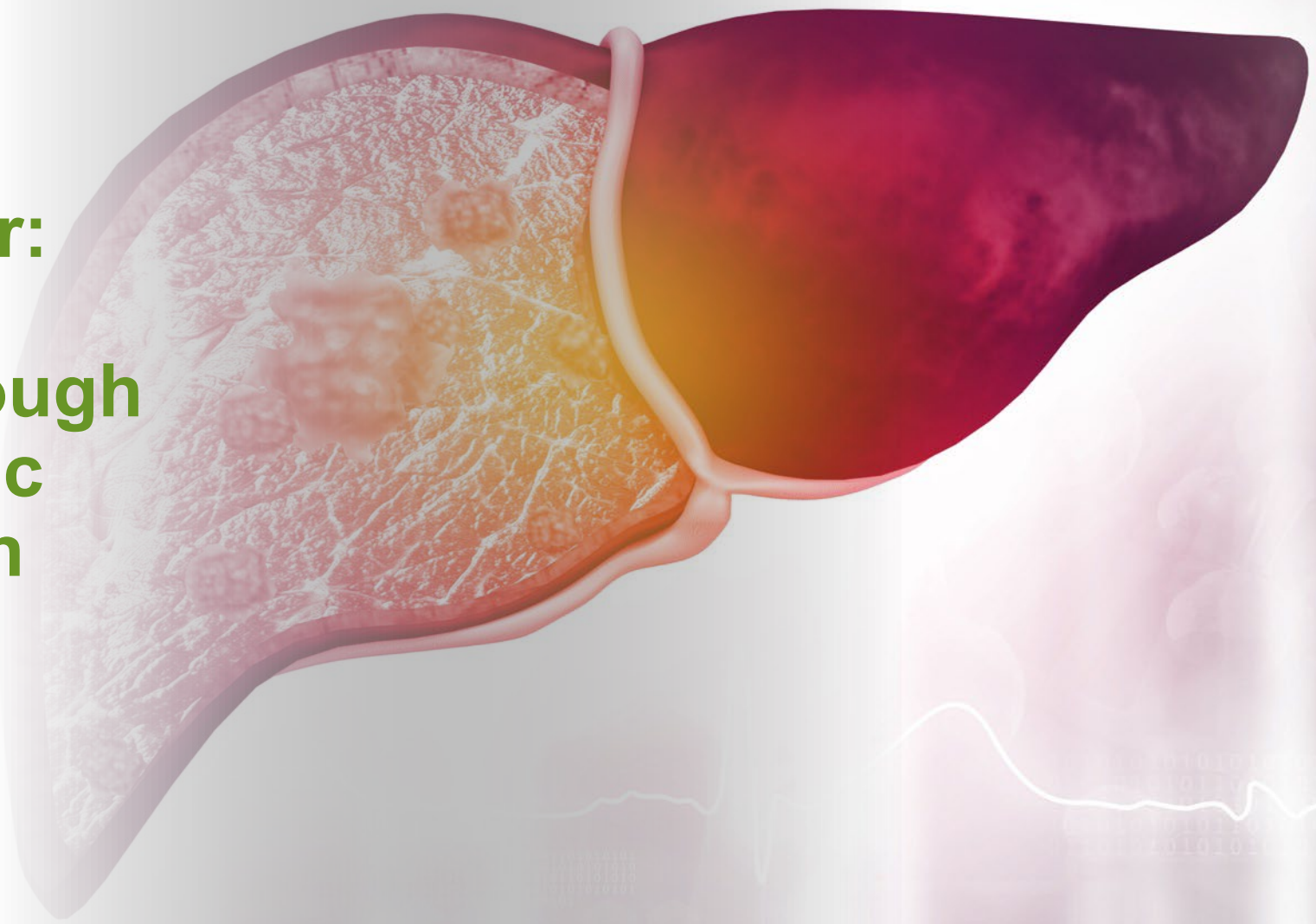
The Comprehensive Impact of Lanifibranor: Addressing the Full MASH Spectrum Through Intra- and Extrahepatic Mechanisms of Action



October 8, 2025

inventiva

Forward Looking Statement

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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

- 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

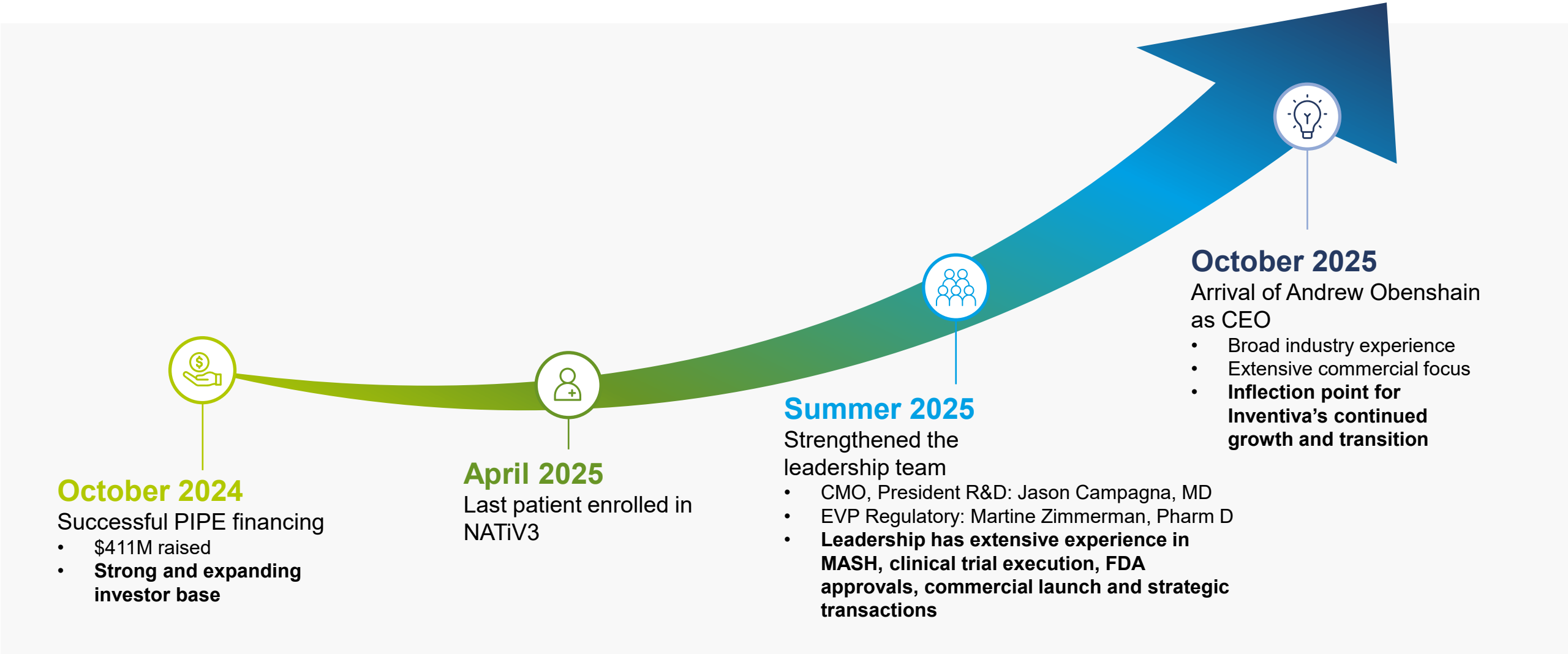
- Q&A
All speakers

A Year in Review

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



October 2024

Successful PIPE financing

- $411M raised
- **Strong and expanding investor base**

April 2025

Last patient enrolled in NATiV3

Summer 2025

Strengthened the leadership team

- CMO, President R&D: Jason Campagna, MD
- EVP Regulatory: Martine Zimmerman, Pharm D
- **Leadership has extensive experience in MASH, clinical trial execution, FDA approvals, commercial launch and strategic transactions**

October 2025

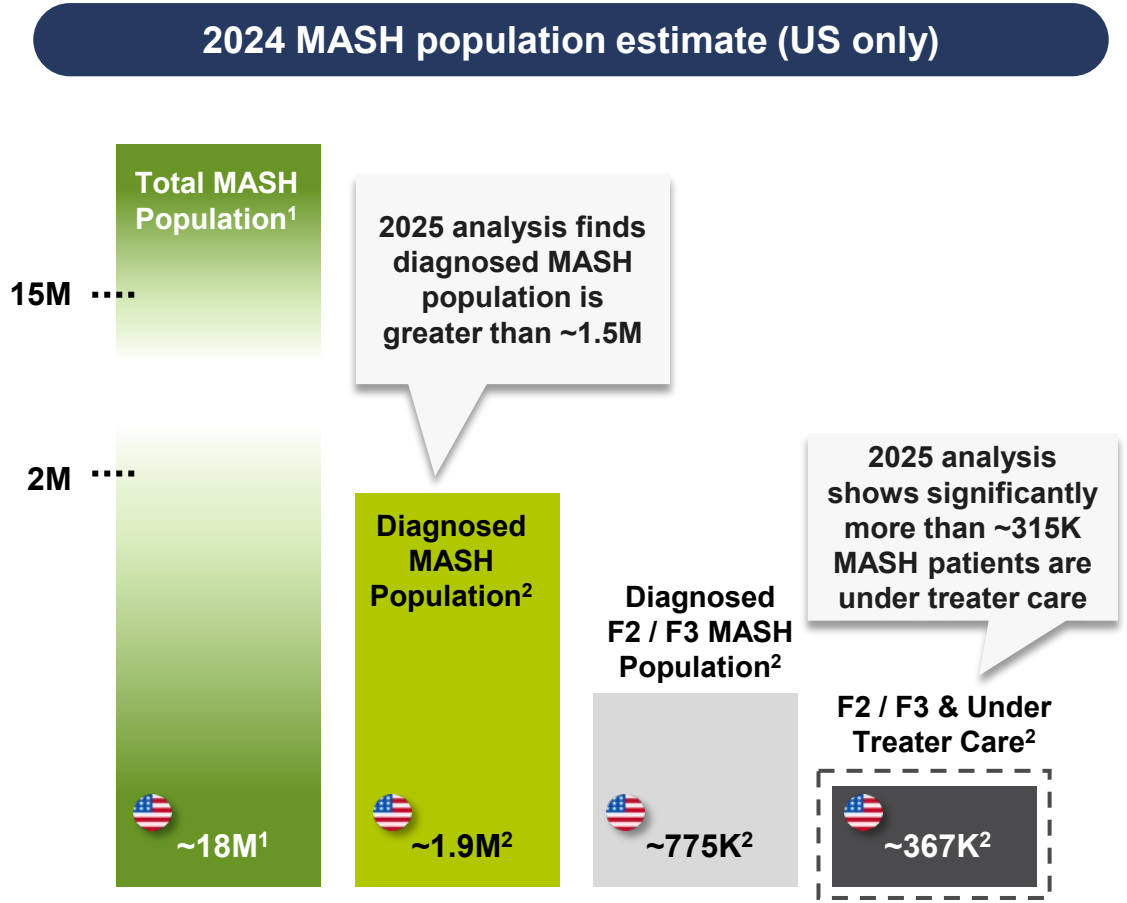
Arrival of Andrew Obenshain as CEO

- Broad industry experience
- Extensive commercial focus
- **Inflection point for Inventiva's continued growth and transition**

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



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™* ;

Despite the emergence of new treatment options, US HCPs feel that unmet need in MASH remains significant[1]

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

Speed to Fibrosis Improvement

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

Cardiometabolic Benefits

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

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

Convenient Route of Administration

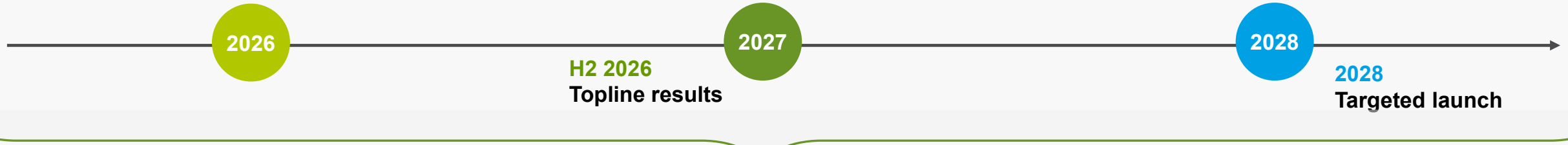
Once-daily, oral administration reduces patient burden, especially for those already on injectables

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



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

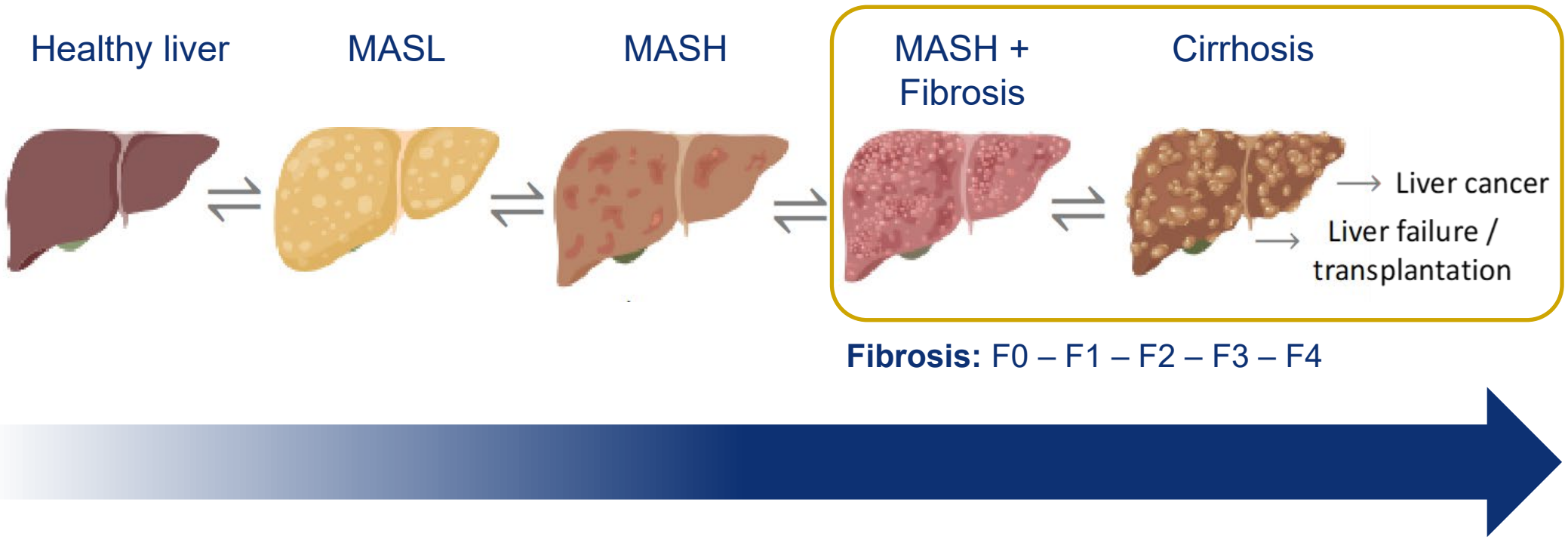
Inventiva is reinforcing the organization to support and drive leadership in MASH

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



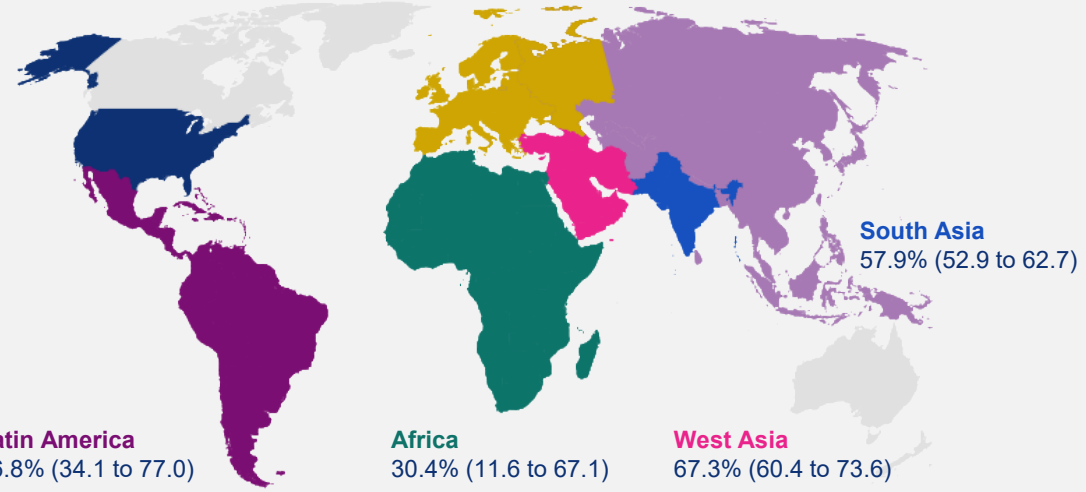
MASLD is highly prevalent in people with type 2 diabetes and obesity

Diabetes

United States
51.8% (31.3 to 71.6)

Europe
68.0% (62.1 to 73.0)

East Asia
52.0% (45.4 to 58.6)



South Asia
57.9% (52.9 to 62.7)

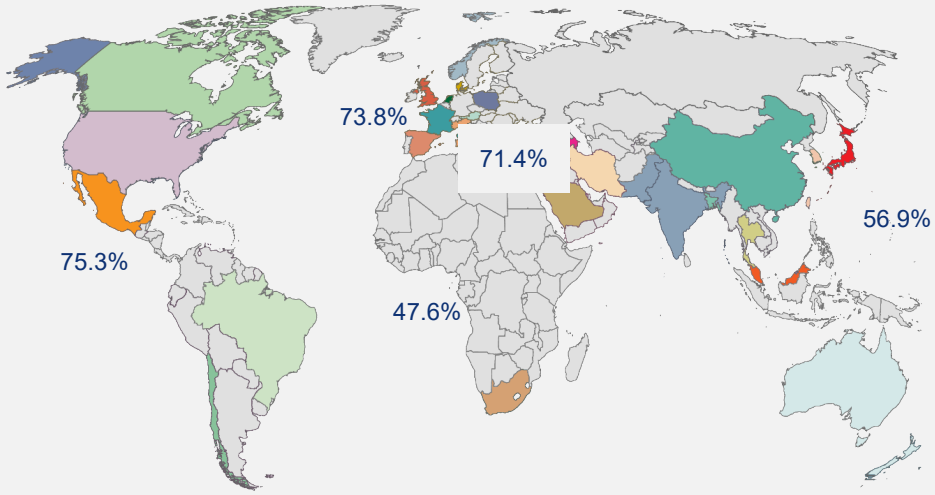
Latin America
56.8% (34.1 to 77.0)

Africa
30.4% (11.6 to 67.1)

West Asia
67.3% (60.4 to 73.6)

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

Obesity

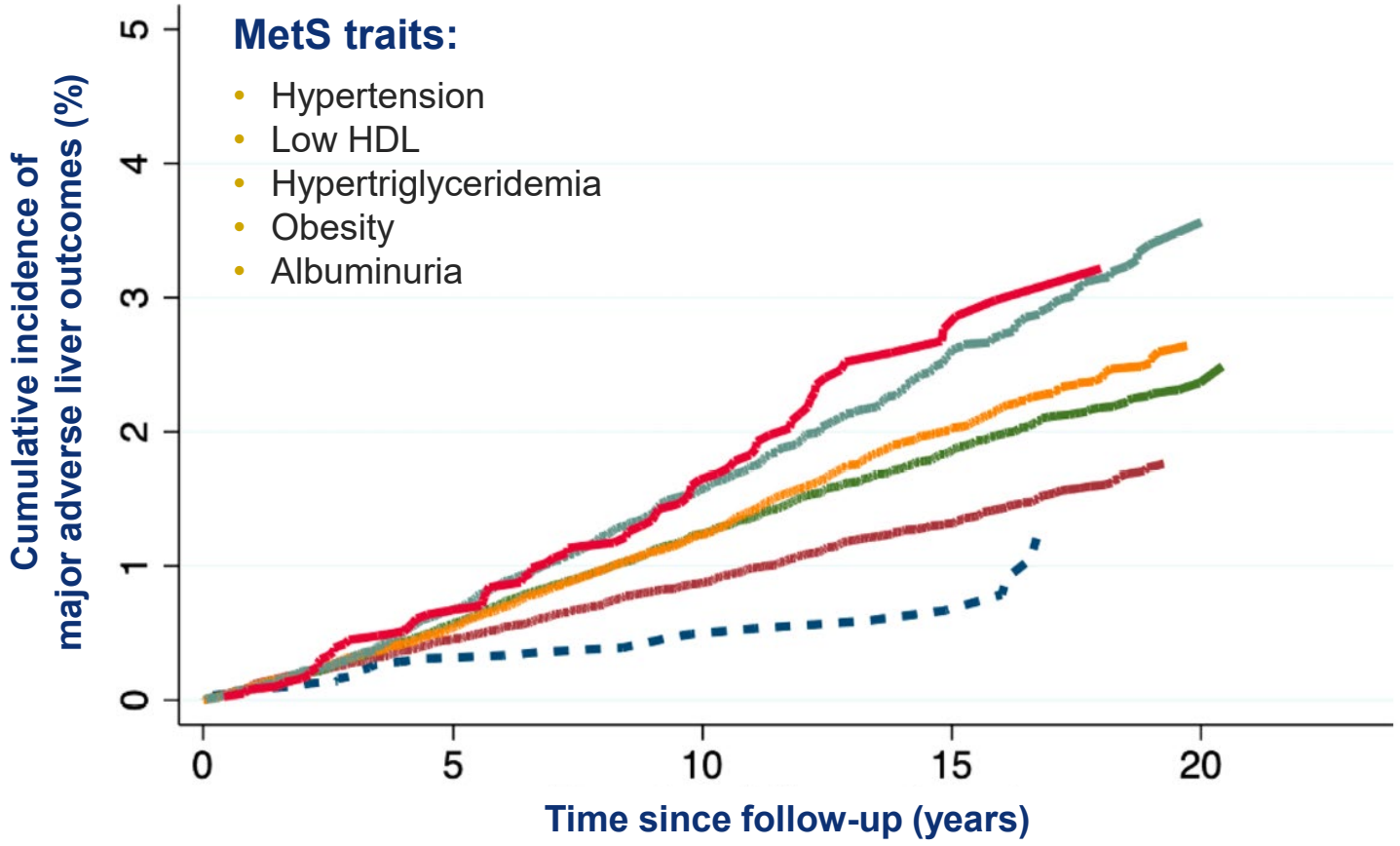


Prevalence of NAFLD in overweight population

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%)

Younossi 2019. Quek et al 2023.

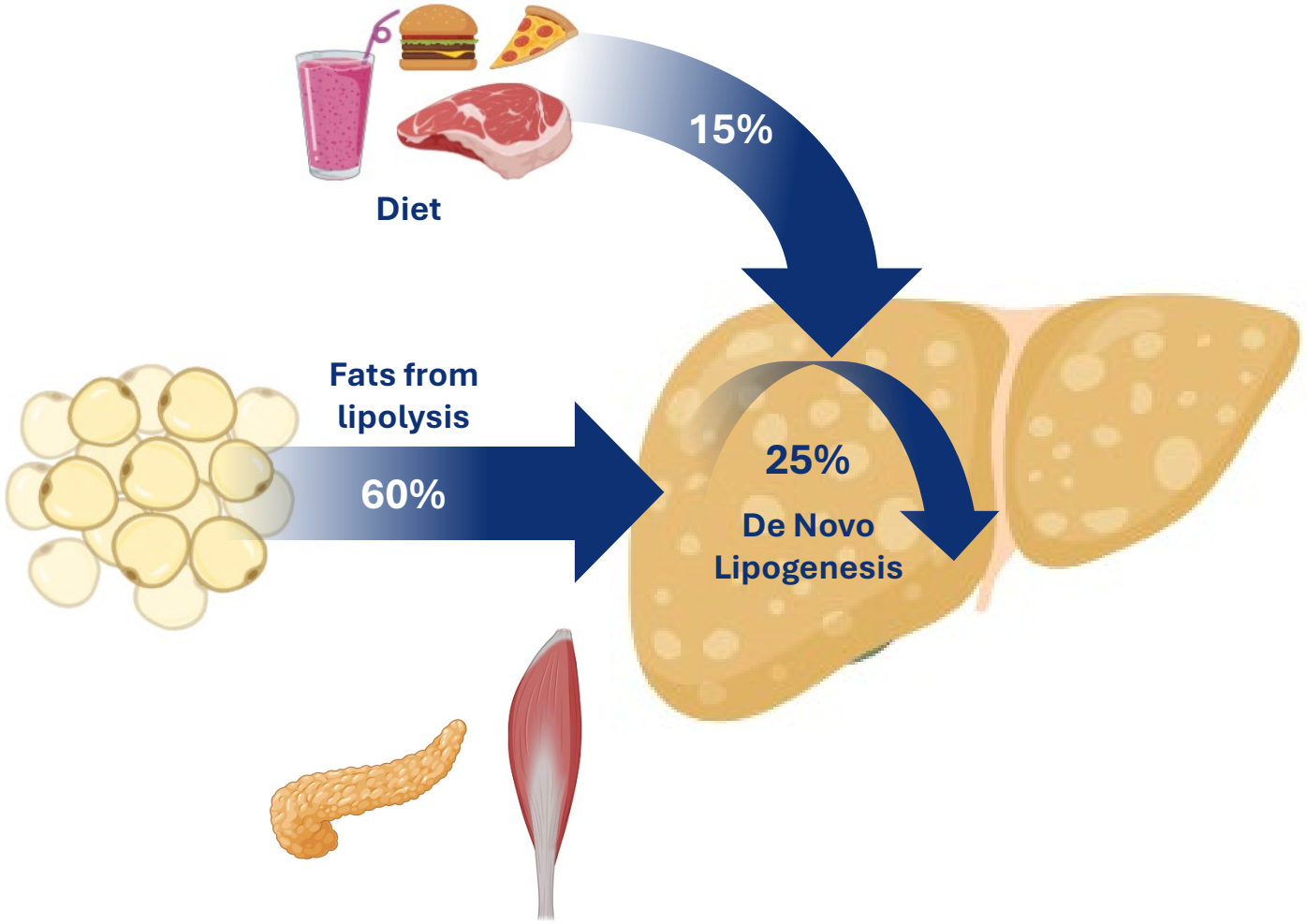
Liver-related outcomes increase with each additional metabolic syndrome (MetS) trait

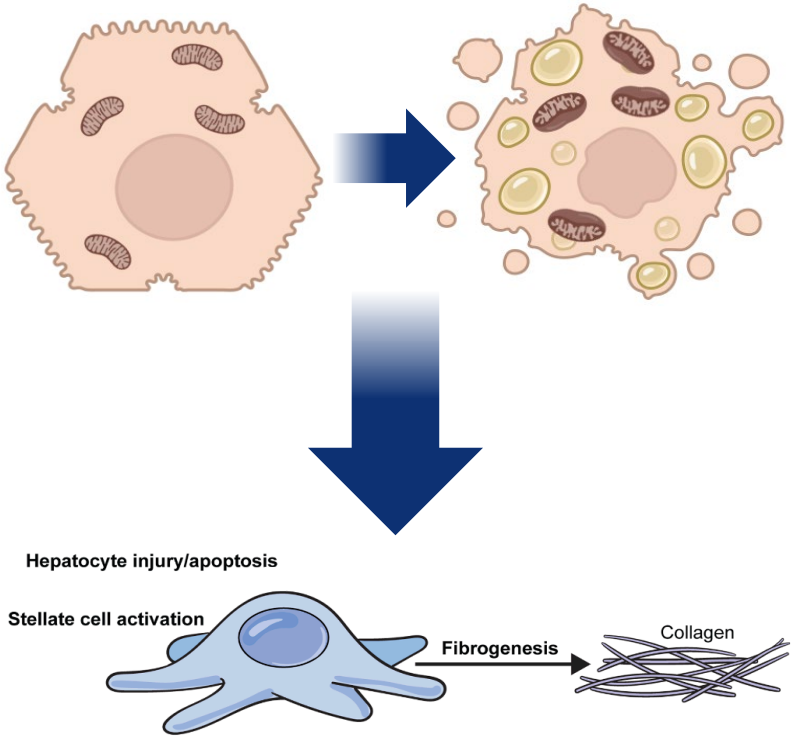


Traits	(Number of events/patients)
T2D + 5 MetS	(71/3,831)
T2D + 4 MetS	(471/25,369)
T2D + 3 MetS	(926/61,632)
T2D + 2 MetS	(1,109/77,706)
T2D + 1 MetS	(609/56,664)
T2D only	(29/5,794)

230,996 individuals from the Swedish National Diabetes Register *Shang et al. Diabetes Care 2024.*

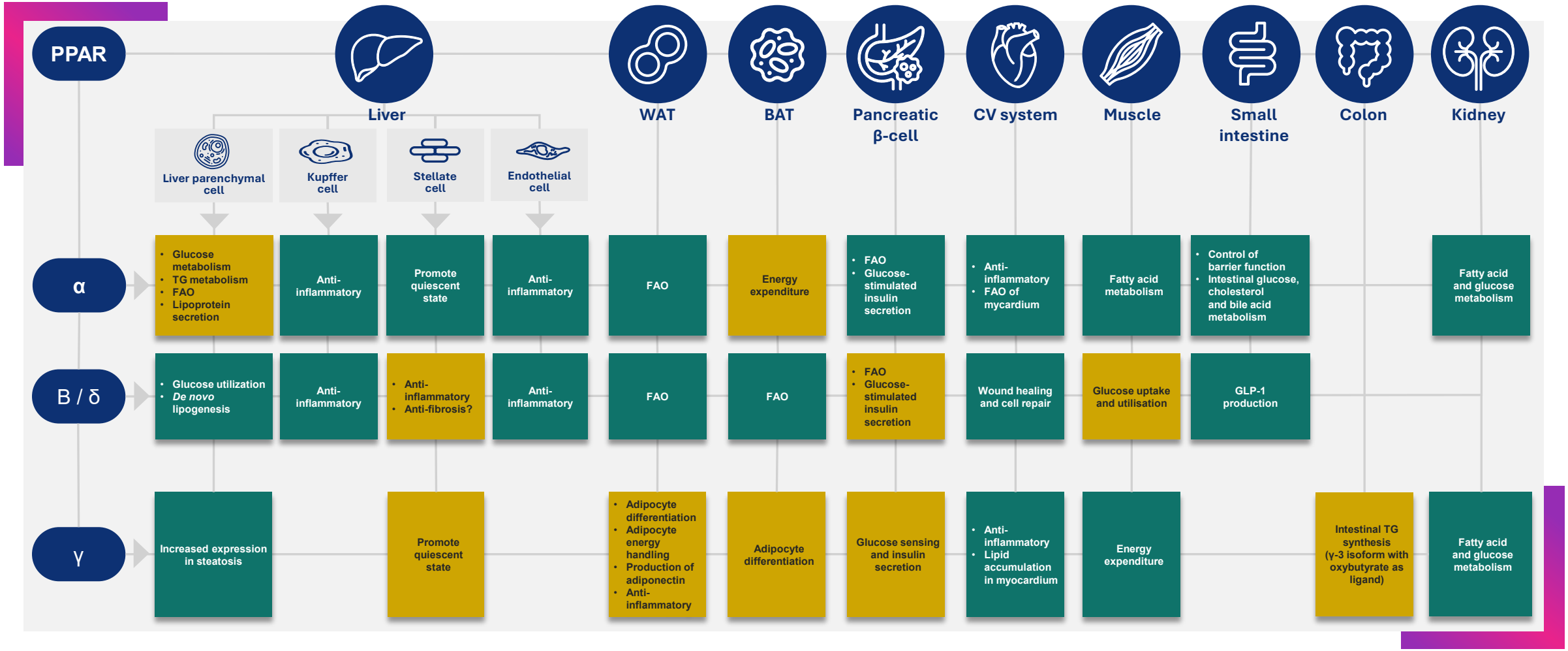
Insulin resistance drives fat accumulation, injury and fibrosis





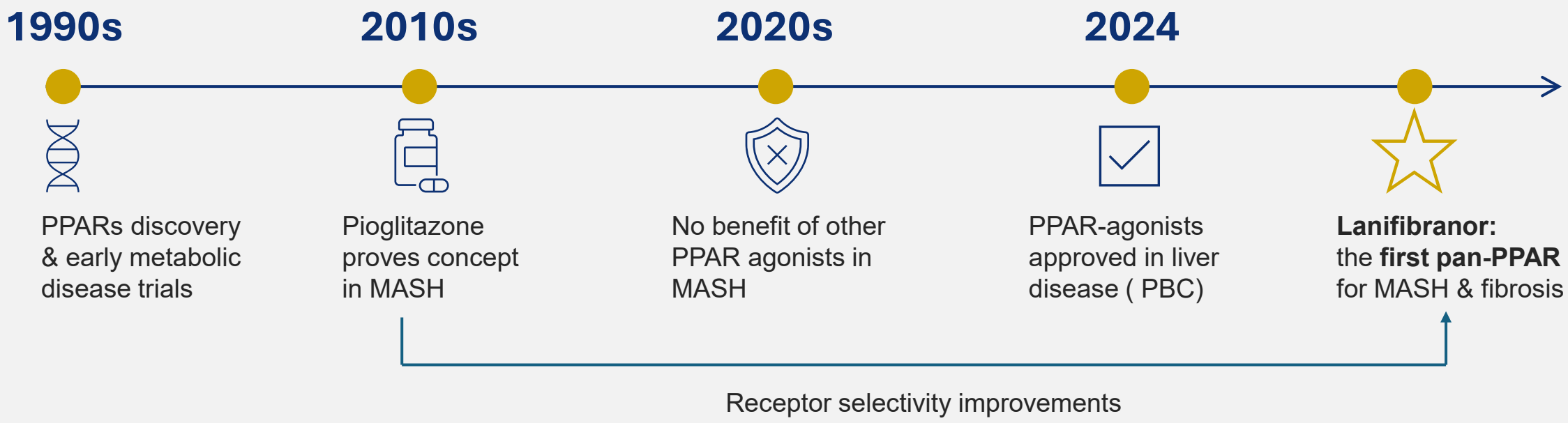
Donnelly et al 2005

PPARs are master regulators of the spectrum of MASH disease biology



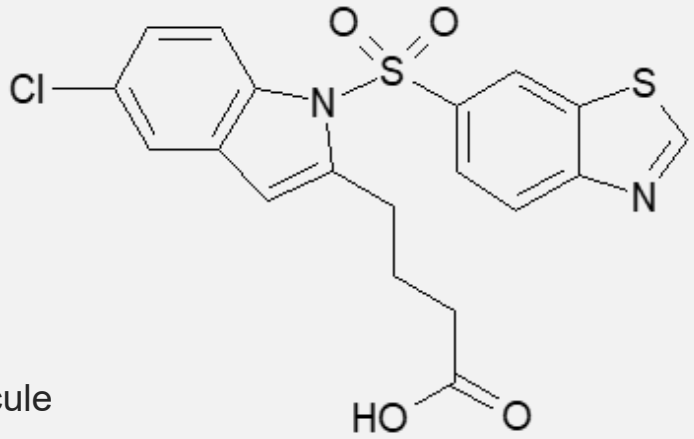
Francque S et al. Nature Rev Gastroenterol Hepatol 2020.

Entering a new era of PPARs and efficacy in MASH



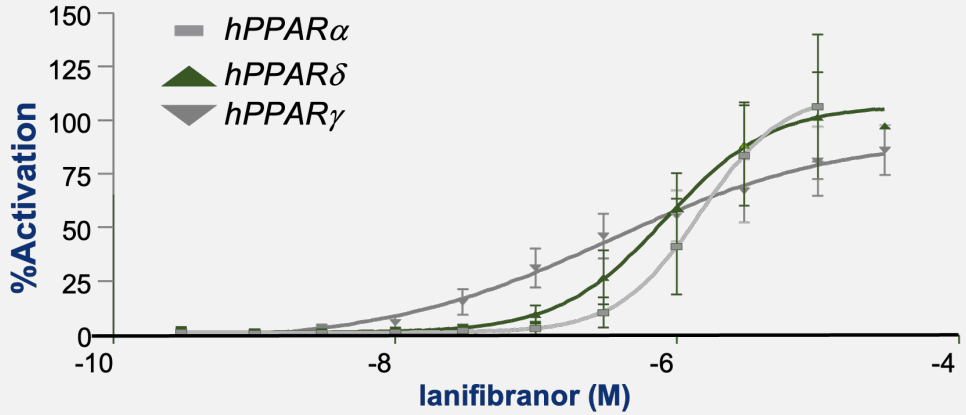
Lanifibranor is a differentiated pan-PPAR agonist with moderate and well-balanced activity on the three PPAR isoforms

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	PPARα EC50 (nM)	PPARδ EC50 (nM)	PPARγ EC50 (nM)
Lanifibranor*	**1630**	**850**	**230**
Fenofibrate	*2400*	-	-
Pioglitazone	-	-	*263*
Rosiglitazone	-	-	*13*
*Elafibranor***	*10*	*100*	-
*Seladelpar^*	-	*2*	-

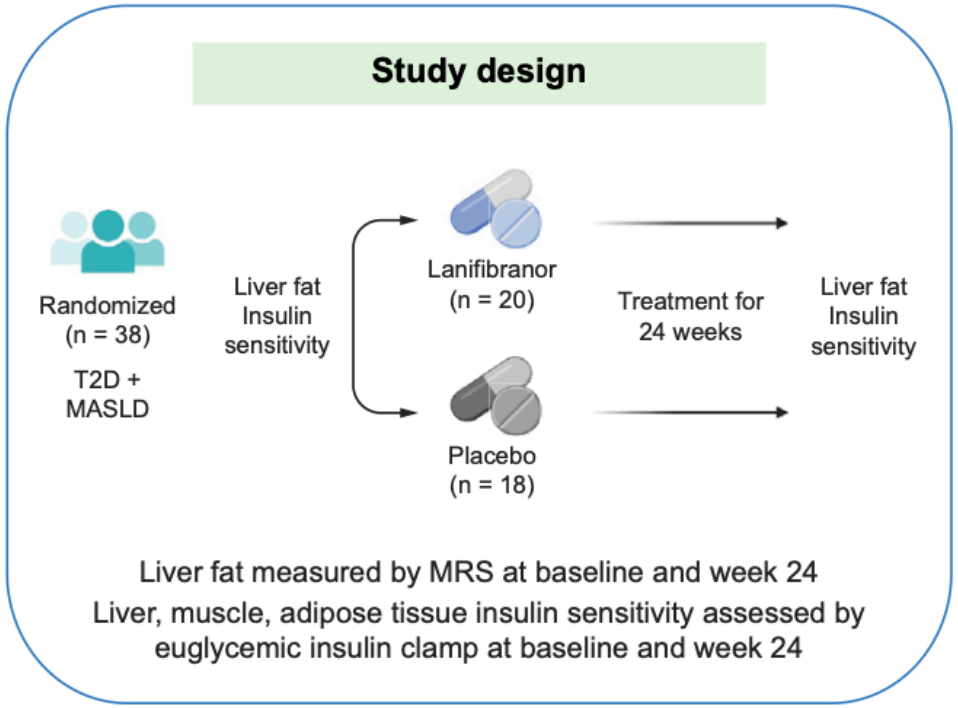
Source: * Company data ** Hanf R et al, Diabetes & Vascular Dis Res 2014 ^ Cymabay company presentation ^^ J Med Chem. 2018 Feb 15. doi: 10.1021/acs.jmedchem.7b01285; *** J Med Chem. 2018 Feb 15. doi: 10.1021/acs.jmedchem.7b01285

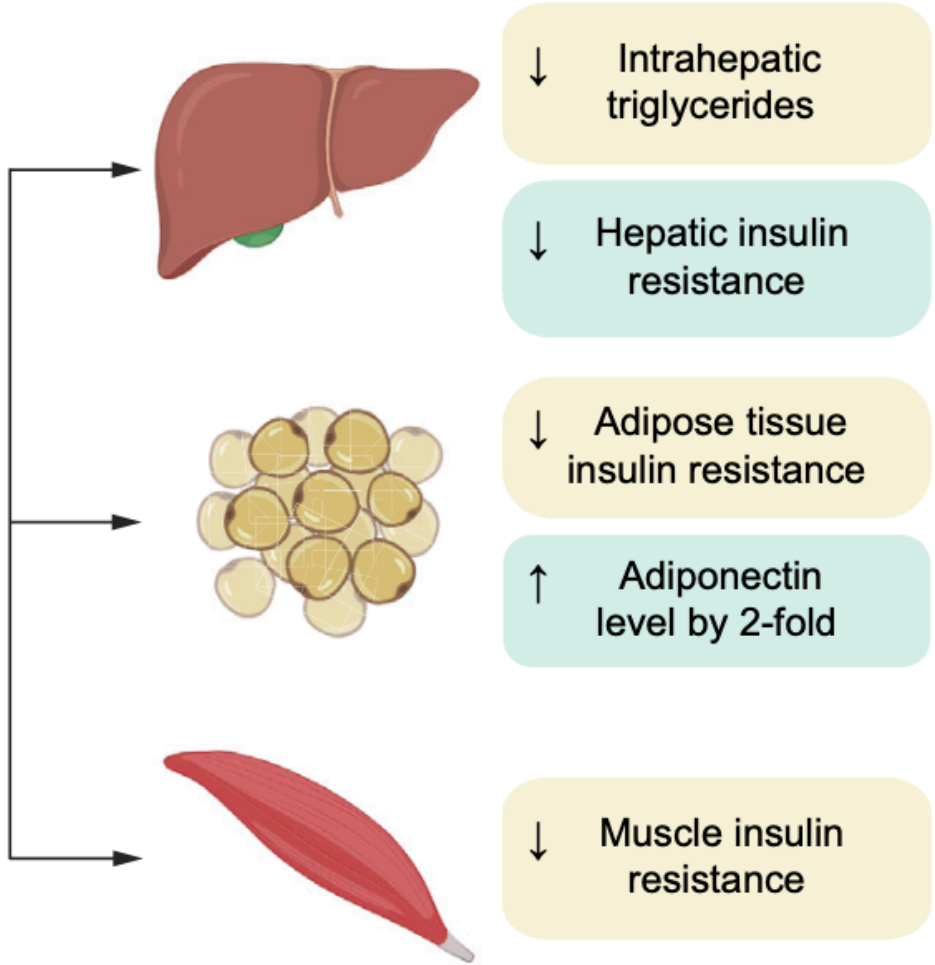
Research Article
MASLD and Alcohol-Related Liver Diseases

JOURNAL
OF HEPATOLOGY

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

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





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

Fasting glucose

Fasting triglycerides

Fasting LDL-C

Fasting HDL-C

- Placebo
- Lanifibranor 800mg
- Lanifibranor 1200mg

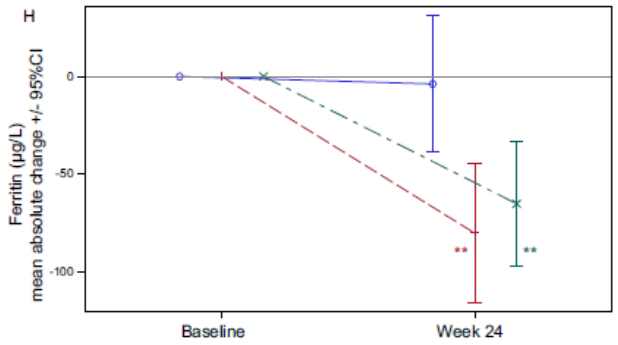
Cooreman MP et al, The PanPPAR agonist lanifibranor improves cardiometabolic health in patients with metabolic dysfunction-associated Steatohepatitis, Nature Comm, 15, 2024

Lanifibranor associated with improved systemic markers of inflammation

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

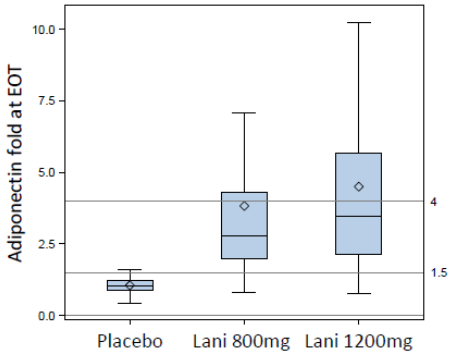
Placebo
Lanifibranor 800mg
Lanifibranor 1200mg

Ferritin



hsCRP

Adiponectin



Cooreman MP et al, The PanPPAR agonist lanifibranor improves cardiometabolic health in patients with metabolic dysfunction-associated Steatohepatitis, Nature Comm, 15, 2024
Cooreman MP et al, Lanifibranor-induced improvement of liver and cardiometabolic markers of NASH is associated with an increase in adipoectin; AASLD 2022

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

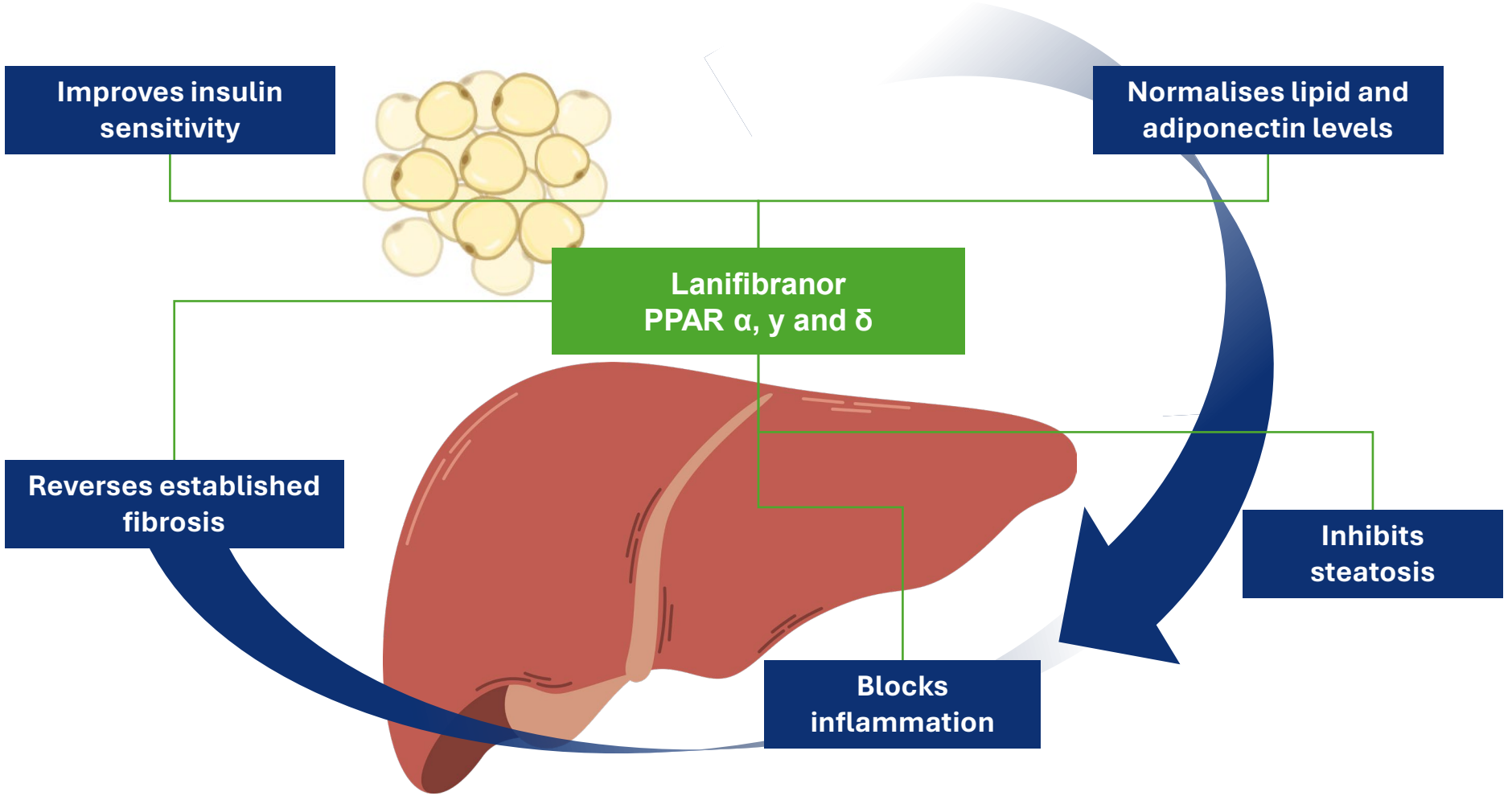
Patients with MASH will be on medication at diagnosis

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

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

Screening
Liver biopsy

24-week treatment + 4-week follow-up
Double blind, randomized, placebo-controlled
ITT: 247 Randomized Patients

End of treatment
Liver biopsy

Placebo

lanifibranor, 800 mg once daily

lanifibranor, 1200 mg once daily

- Randomization 1/1/1
- Stratification on type 2 diabetes

▶ **Main inclusion criteria**: patients with biopsy-proven MASH confirmed by central reader having Steatosis-Activity-Fibrosis (SAF) scores of 1-3 for steatosis, 3-4 for activity, and <4 for fibrosis

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 ≥ least 1 stage

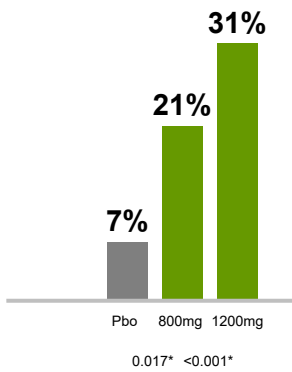
Compares favorably to other oral and injectable compounds

ORAL

PPARs

Lanifibranor (inventiva)

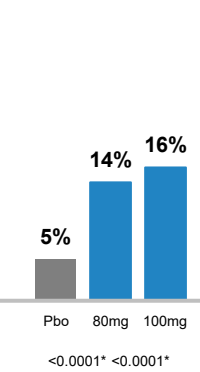
Phase 2 6 months	N=247	ITT	Effect size 24%*



THR-β

Resmetirom** (Madrigal Pharmaceuticals)

Phase 3 12 months	N=955	ITT	Effect size 11%



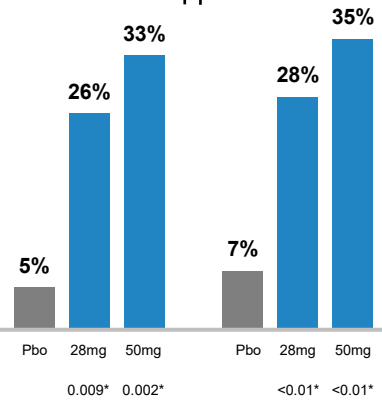
INJECTABLE

FGF-21

Efruxifermin (akero)

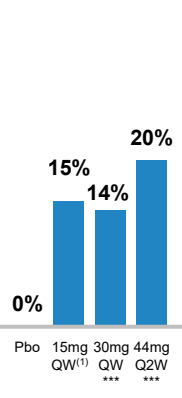
Phase 2b 6 months	N=128	ITT	Effect size 28%

Phase 2b 24 months	N=126	ITT	Effect size 28%



Pegozafermin (89bio)

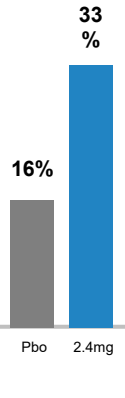
Phase 2 6 months	N=222	PP	Effect size 20%



GLP1-RA and GLP1-RA dual agonists

Semaglutide** (novo nordisk)

Phase 3 18 months	N=800	PP	Effect size 16.6%



Survodutide (Boehringer Ingelheim)

Phase 2 12 months	N=223 (F2/F3)

Tirzepatide (Lilly)

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-alcolohic 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 ≥ 1 stage with no worsening of MASH

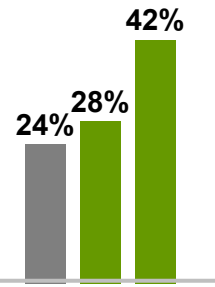
Compares favorably to other oral and injectable compounds

ORAL

PPARs

Lanifibranor (inventiva)

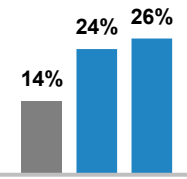
Phase 2, 6 months | N=247 | ITT | Effect size 18%



THR-β

Resmetirom** (Madrigal Pharmaceuticals)

Phase 3, 12 months | N=955 | ITT | Effect size 12%



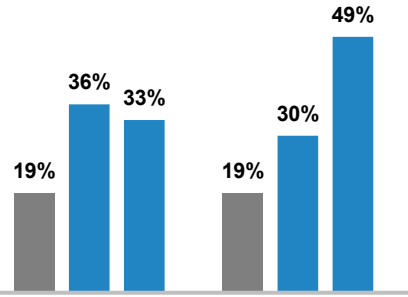
INJECTABLE

FGF-21

Efruxifermin (akero)

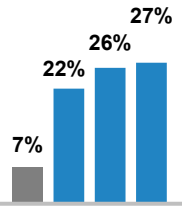
Phase 2b, 6 months | N=128 | ITT | Effect size 14%

Phase 2b, 24 months | N=126 | ITT | Effect size 30%



Pegozafermin (89bio)

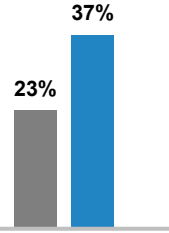
Phase 2, 6 months | N=222 | PP | Effect size 20%



GLP1-RA and GLP1-RA dual agonists

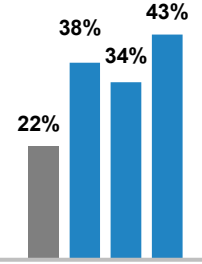
Semaglutide** (novo nordisk)

Phase 3, 18 months | N=800 | PP | Effect size 15%



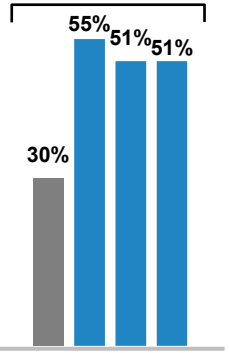
Survodutide (Boehringer Ingelheim)

Phase 2, 12 months | N=293 | ITT | Effect size 21%



Tirzepatide (Lilly)

Phase 2, 12 months | N=190 | ITT | Effect size 21%



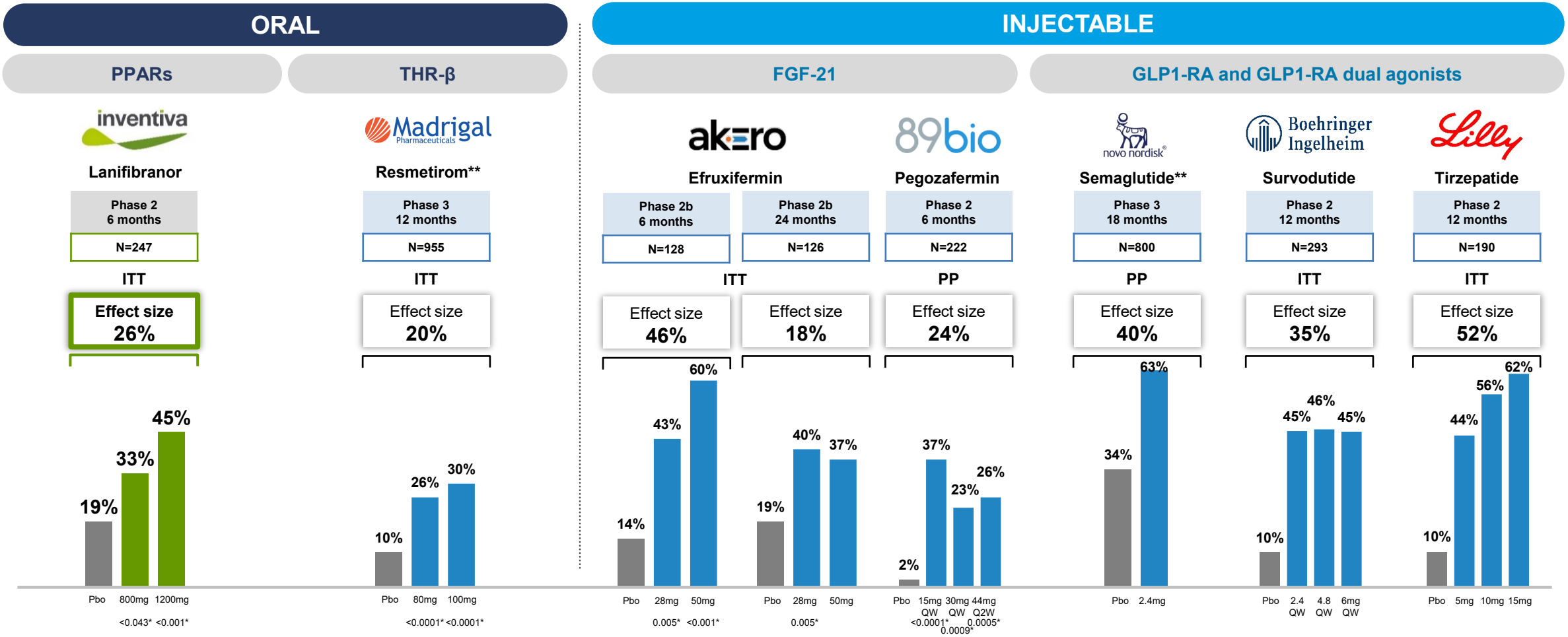
No head-to-head clinical trials have been conducted; results obtained from different trials, with different designs, endpoints and patient populations. Results may not be comparable.

* 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-alcolohic 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



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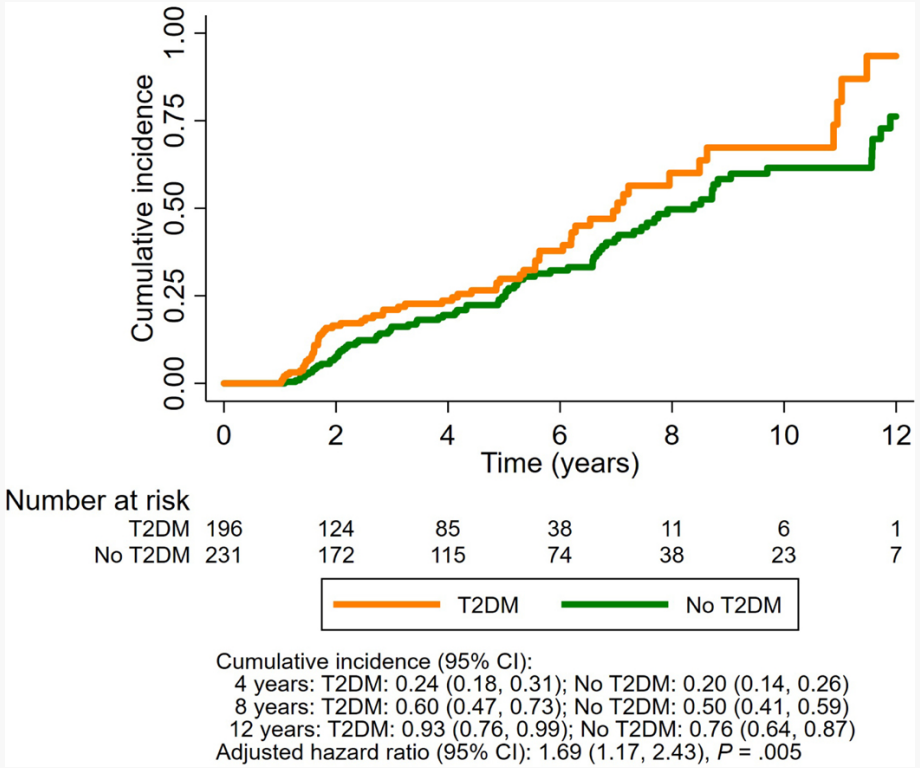
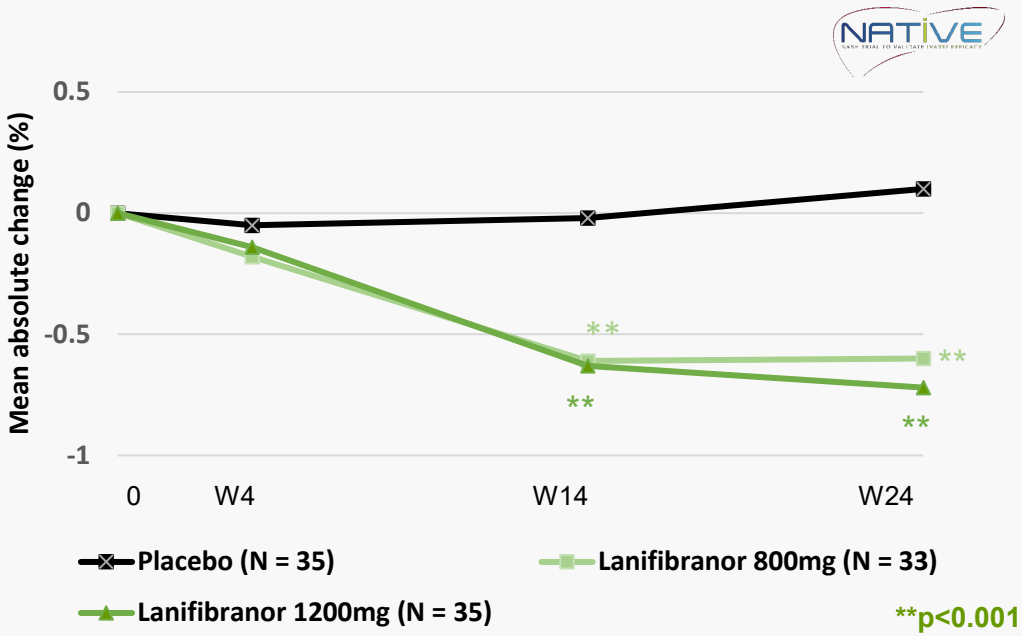
Patients with T2D have a higher cumulative incidence of fibrosis progression making it relevant for a drug to address the metabolic drivers of disease

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

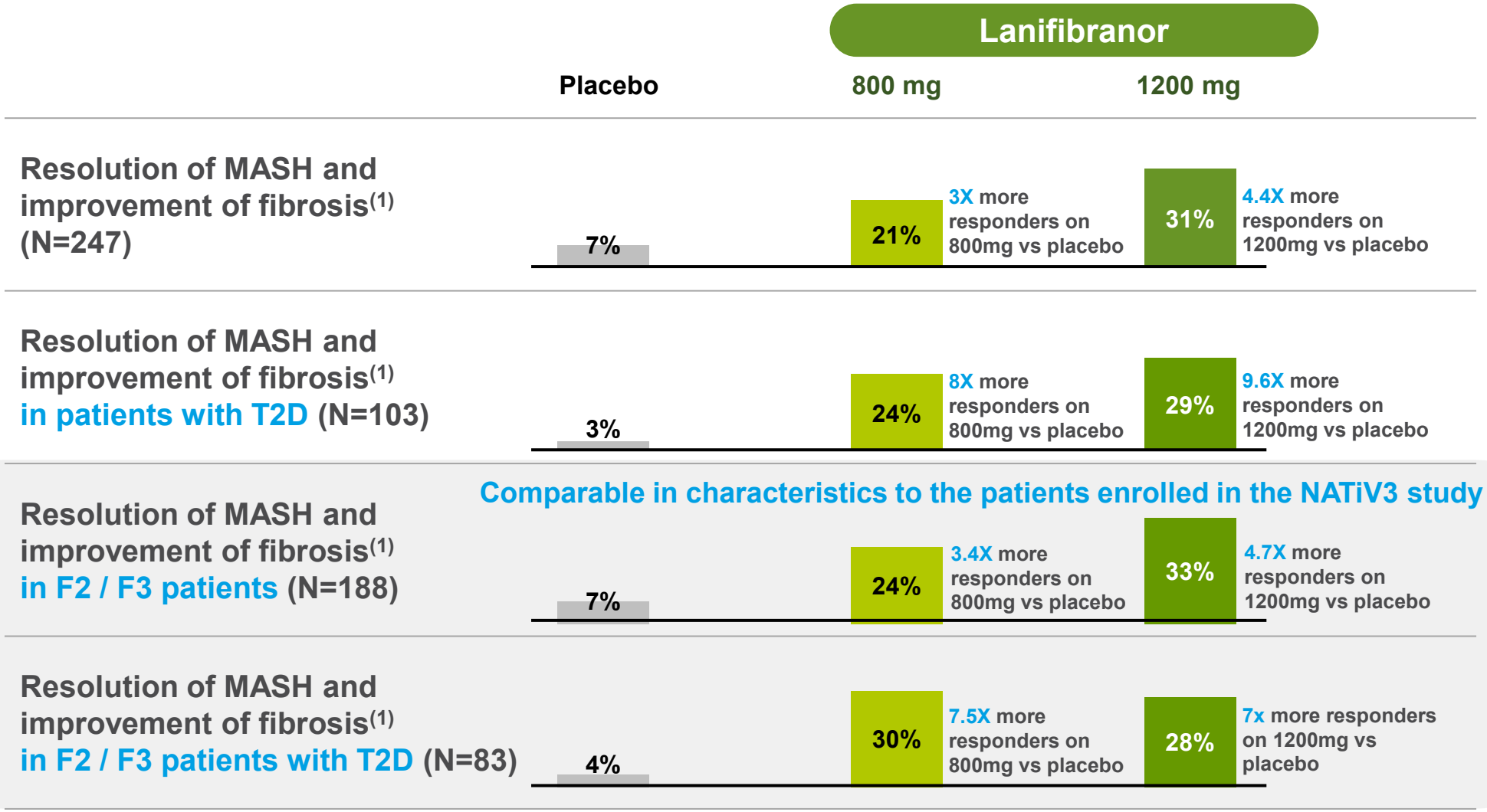


Absolute change from baseline in HbA1c



Huang DQ and all ; NASH Clinical Research Network; Loomba R. Fibrosis Progression Rate in Biopsy-Proven Nonalcoholic Fatty Liver Disease Among People With Diabetes Versus People Without Diabetes: A Multicenter Study. Gastroenterology. 2023 Aug;165(2):463-472.e5.

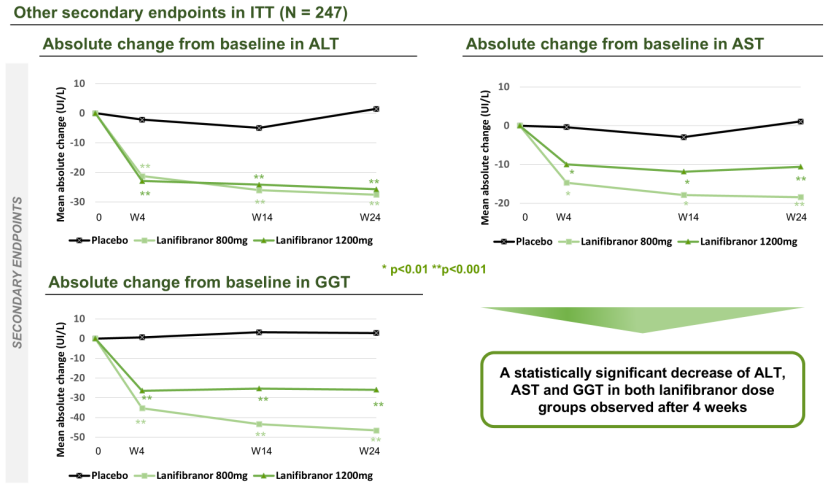
Resolution of MASH and improvement of fibrosis: effect size is increased in F2/F3 patients as well as patients with T2D



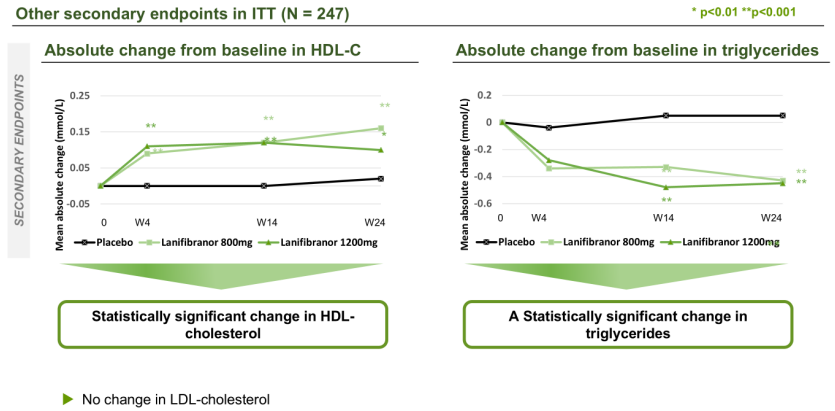
(1)) Resolution of MASH and improvement of fibrosis at week 24: NAS-I = 0 or 1, NAS-B = 0 and an improvement of NAS-F ≥ 1 stage

Improvement seen across key intra and extra hepatic features of MASH

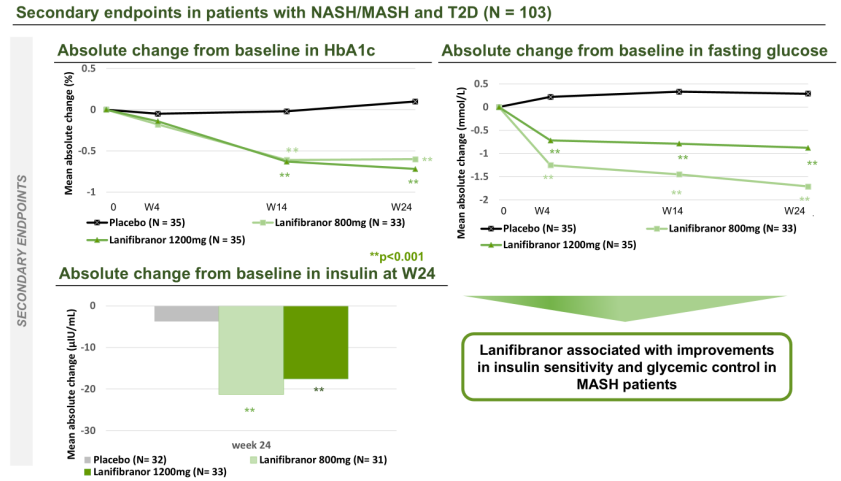
Statistically significant decrease in liver enzymes Liver biomarkers show rapid and sustained improvement



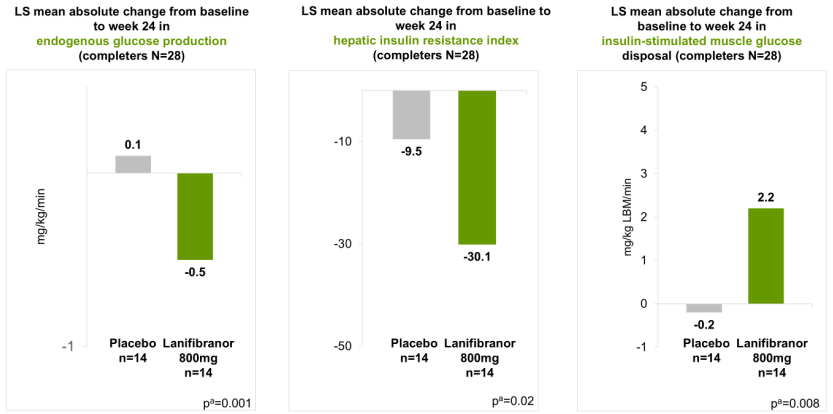
Statistically significant change in lipid profile Improvements in HDL cholesterol and TGs without a change in LDL cholesterol



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[a]	(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)
▶ **Any TEAE**	50 (61.7%)	59 (71.1%)	62 (74.7%)
Drug-related TEAE	19 (23.5%)	25 (30.1%)	23 (27.7%)
▶ **Any TEAE leading to drug withdrawal**	3 (3.7%)	4 (4.8%)	3 (3.6%)
Drug-related TEAE leading to drug withdrawal	2 (2.5%)	1 (1.2%)(1)	2 (2.4%)(2)
▶ **Any Serious TEAE**	3 (3.7%)	3 (3.6%)	7 (8.4%)
Drug-related Serious TEAE	2 (2.5%)(3)	-	-

- 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)
▶ **Peripheral edema**	2 (2.5%)	5 (6.0%)	7* (8.4%)
Drug-related peripheral edema	-	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.

(1) One patient with moderate diarrhea ; (2) One patient with mild cardiac failure; one patient with mild diarrhea, abdominal pain, dizziness ; (3) 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

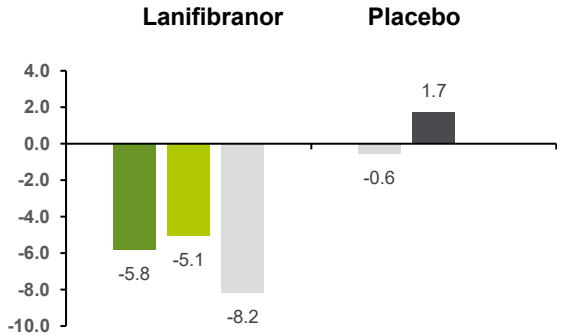
% patients reporting the most frequent AEs (>5% of patients in at least 1 lanifibranor arm)	Placebo (N=81)	800 mg (N=83)	1200 mg (N=83)
Diarrhea	1 (1.2%)	8 (9.6%)	10 (12.0%)
Fatigue[a]	8 (9.9%)	3 (3.6%)	11 (13.3%)
Nausea	3 (3.7%)	8 (9.6%)	7 (8.4%)
Weight increased	-	8 (9.6%)	7 (8.4%)
Edema peripheral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

[a]Fatigue included asthenia. [b]Abdominal pain included upper and lower abdominal pain. [c]Anemia included iron deficiency anemia and decreased hemoglobin level. [d]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.

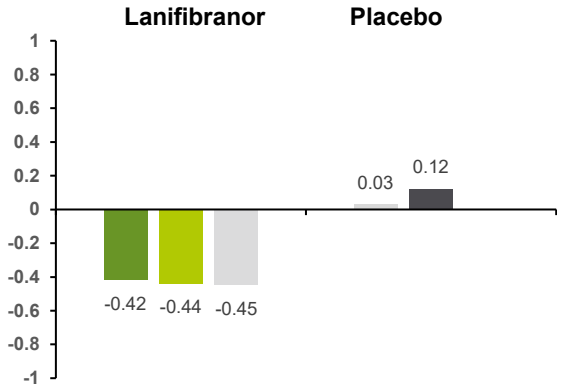
Weight gain comes with improvements in metabolic, cardiometabolic, and liver markers

Insulin Resistance – Metabolic

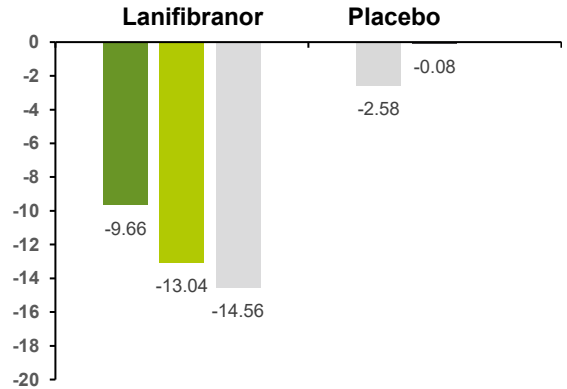
Fasting HOMA-IR
Mean absolute change at Week 24 from baseline



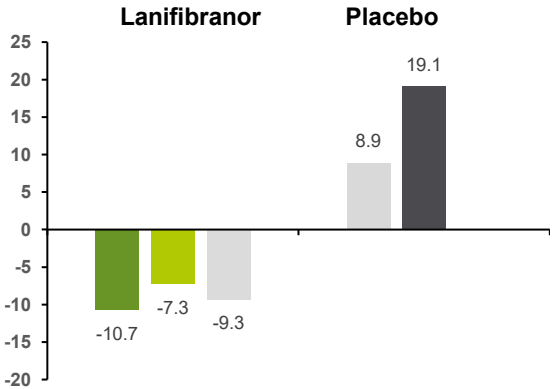
Triglycerides
Mean absolute change at Week 24 from baseline (mmol/L)



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

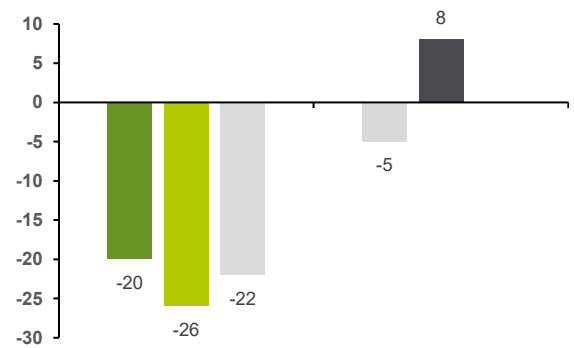


APO-C3
Mean absolute change at week 24 from baseline (µg/ml)



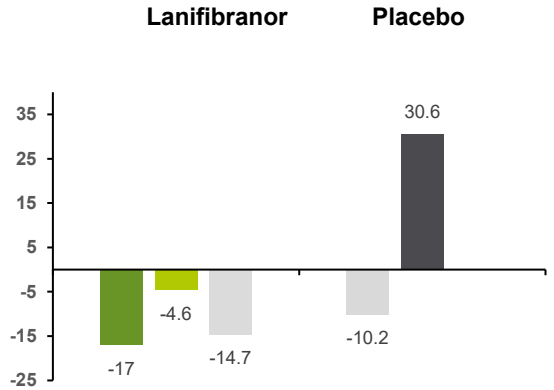
Liver Function

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

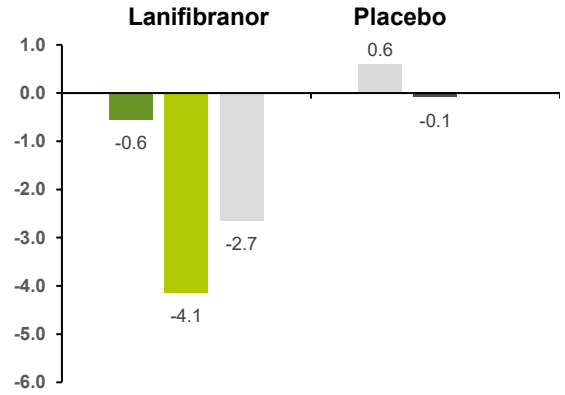


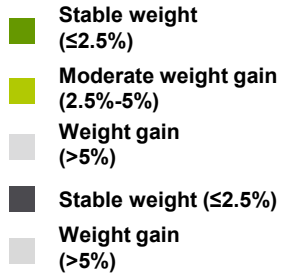
Inflammation

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



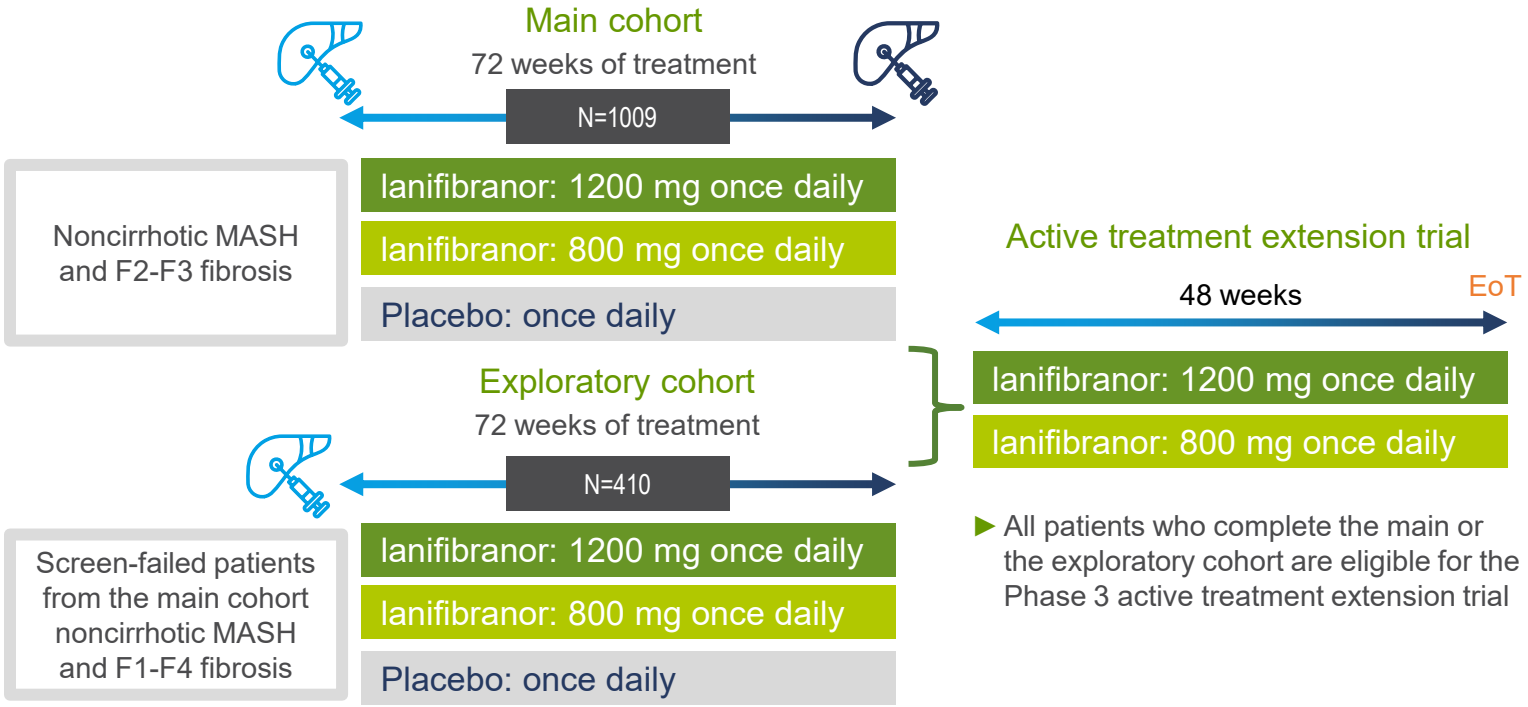
hs-CRP
Mean absolute change at Week 24 from baseline (%)





MP. Cooreman, Lanifibranor improves markers of cardio-metabolic health in NASH patients independent of weight change – EASL 2022

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



- All patients who complete the main or the exploratory cohort are eligible for the Phase 3 active treatment extension trial

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

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

Baseline characteristics of NATiV3 are aligned with those of Phase 2b NATIVE

Demographics & Metabolic Profile

Baseline characteristics of NATiV3 are aligned with those of Phase 2b NATIVE

Liver Disease Profile

Baseline characteristics of NATiV3 are aligned with those of Phase 2b NATIVE

Co-medications

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.

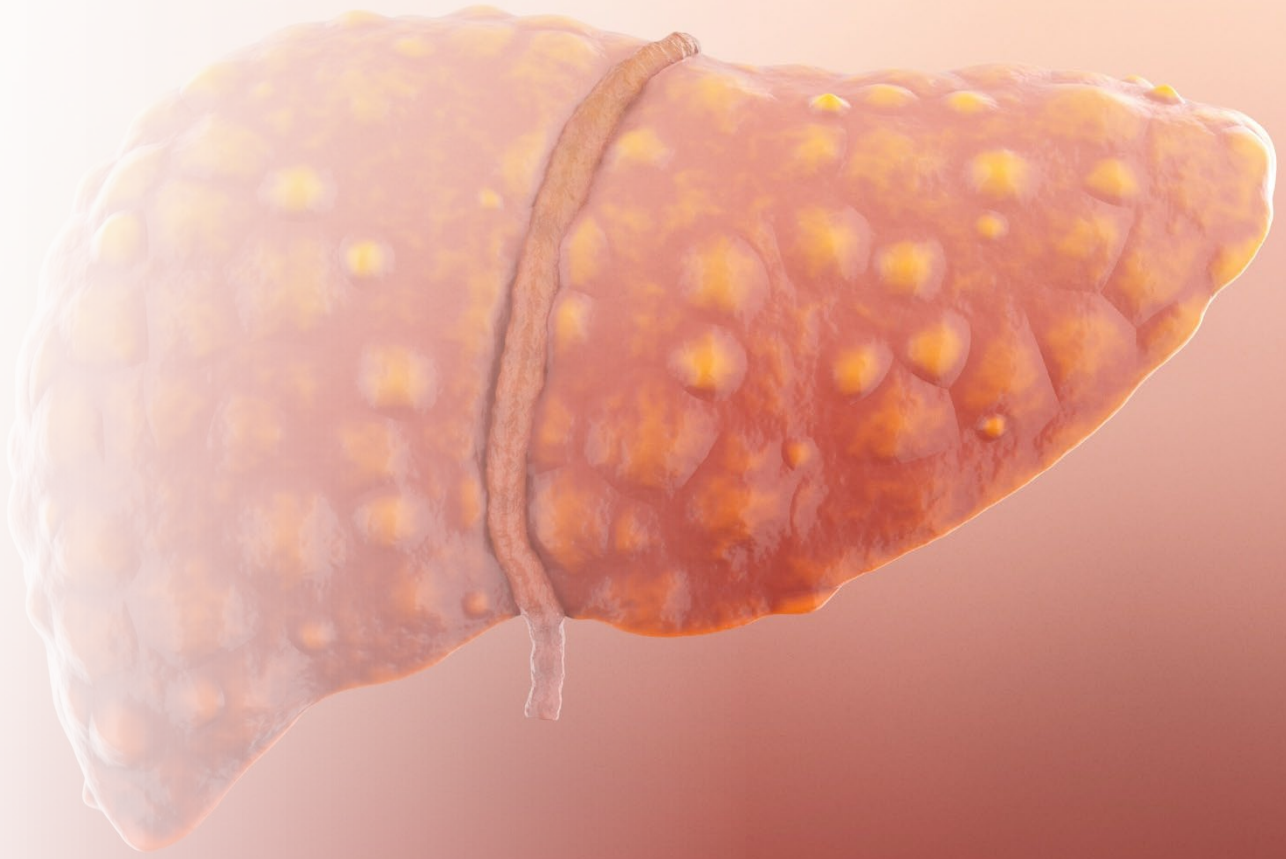
4. **NATiV3 uniquely positioned to assess lanifibranor in combination with GLP-1 and SGLT2 inhibitors: Reflecting the evolving treatment paradigm and supporting its potential as a backbone therapy.**

5. **Lanifibranor's differentiated pan-PPAR mechanism of action:** Purpose-designed to activate PPAR-α, PPAR-δ, and PPAR-γ 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



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Chief of Gastroenterology
Hepatology and Nutrition

Beth Israel Deaconess
Medical Center, Boston

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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

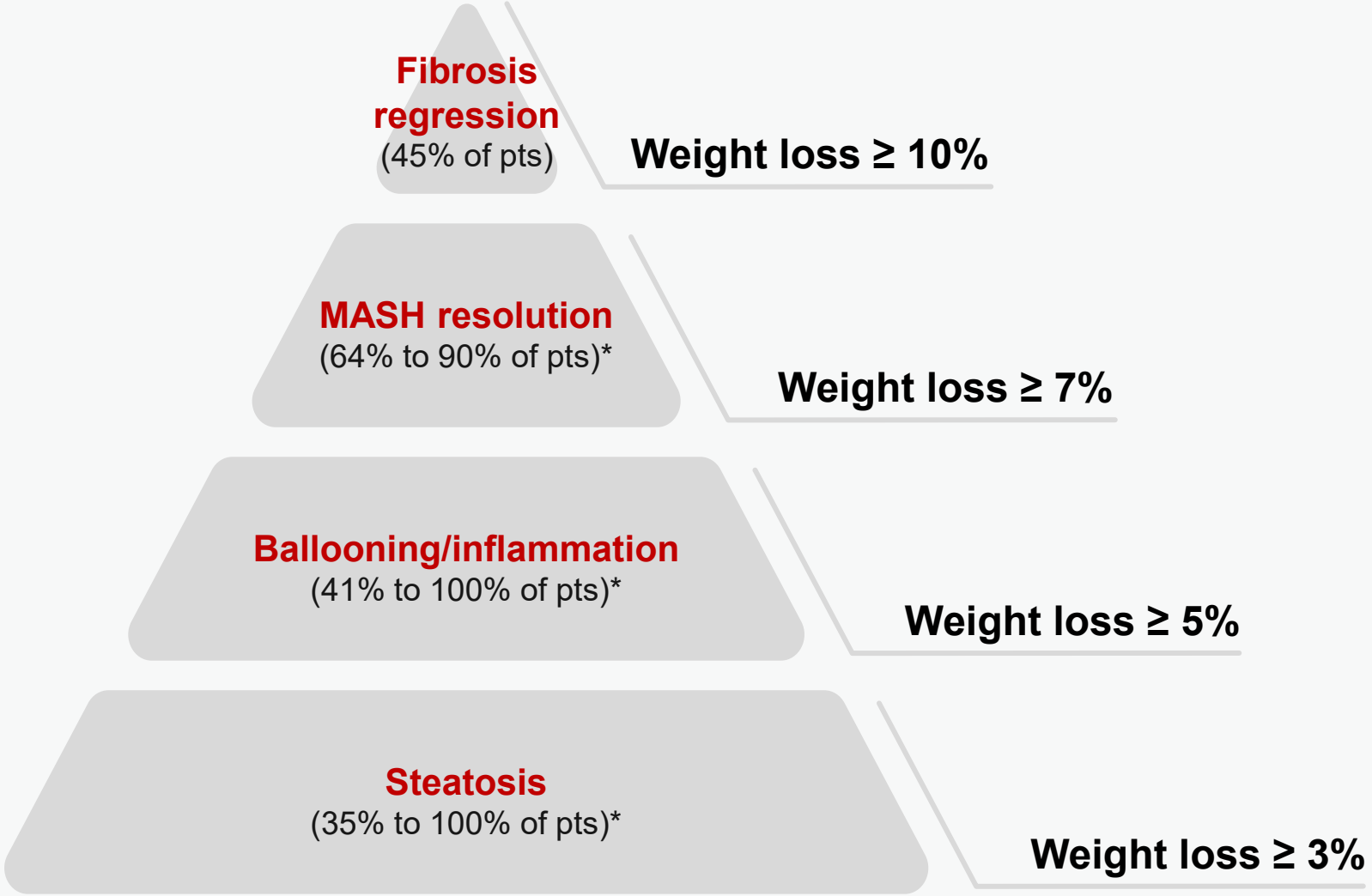
Avoid sugar and sugar containing beverages

Bariatric surgery in those with morbid obesity and co-morbidities

Chalasani N et al. Hepatology. 2018;67(1):328-357; Diehl AM, Day C. New Engl J Med. 2017; 377:2063-72.

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.

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How do GLPs stack up to Resmetirom?

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

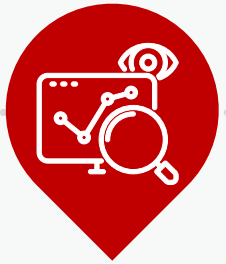
1. Sanyal et al. N Engl J Med 2025;392:2089-2099 DOI: 10.1056/NEJMoa2413258
2. Harrison et al. N Engl J Med 2024;390:497-509 DOI: 10.1056/NEJMoa2309000

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

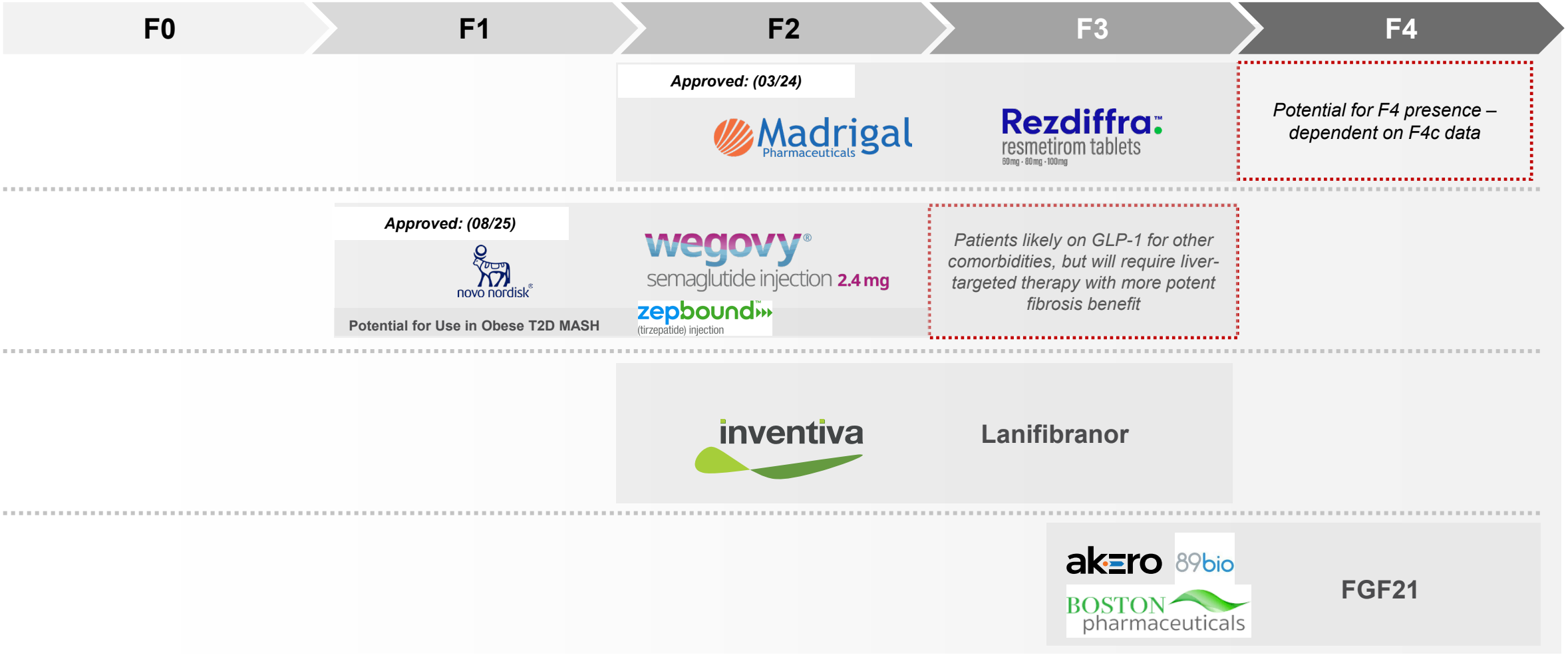
Conclusions

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%*[1] and FGF-21 class ~21%*[2]**

*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

Jason Campagna
President R&D and CMO of Inventiva

Panel Discussion

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

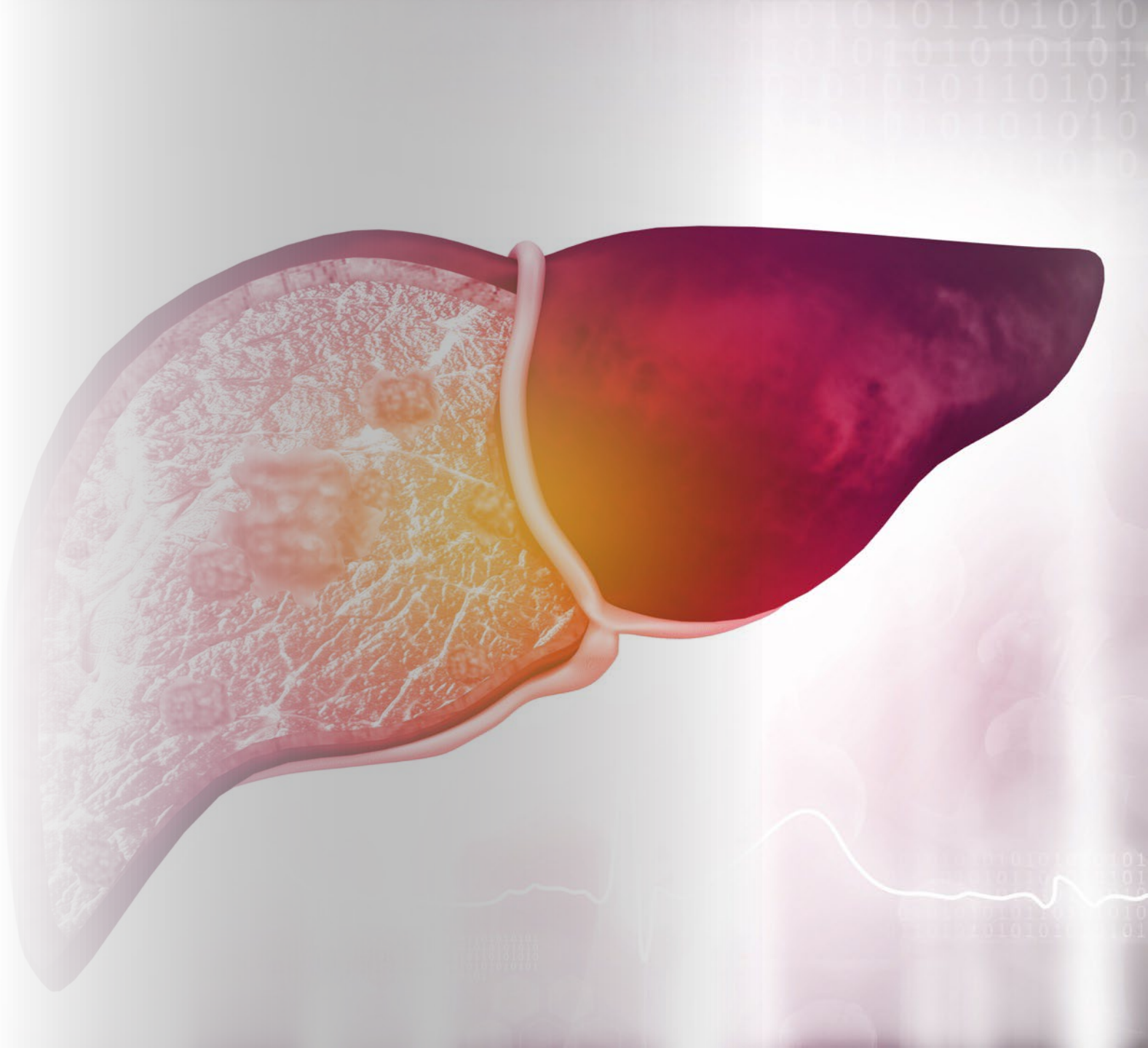
Conclusion

Andrew Obenshain
CEO of Inventiva

Take away messages

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



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