Corporate Presentation

January 2025

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Disclaimer

This presentation contains “forward-looking statements” within the meaning of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. All statements, other than statements of historical facts, included in this presentation are forward-looking statements. These statements include, but are not limited to, forecasts and estimates with respect to Inventiva’s pre- clinical programs and clinical trials, including design, duration, timing, recruitment costs, last patient first visit, screening, randomization, enrollment, and last patient last visit for those trials, including the ongoing NATiV3 Phase clinical trial with lanifibranor in MASH, and the results and timing thereof and regulatory matters with respect thereto, clinical trial data releases and publications, the information, insights and impacts that may be gathered from clinical trials, the potential therapeutic benefits of Inventiva’s product candidates, including lanifibranor alone and in combination with empagliflozin in patients with MASH and T2D, the potential of lanifibranor to address patient needs, market forecasts including with respect to products developed by other companies, estimates of addressable markets, and targeted development and commercial timelines, including with respect to relative market position, potential regulatory submissions, approvals and commercialization, Inventiva’s pipeline and preclinical and clinical development plans, the expected benefit of having received Breakthrough Therapy Designation from the FDA, including its impact on the development and review timeline of Inventiva’s product candidates, the opportunity for lanifibranor based on the current clinical program, future activities, expectations, plans, growth and prospects of Inventiva and its partners, the expected benefit of Inventiva’s partnerships, conclusions drawn from expectations in survey results and analyses of blinded interim results, the anticipated proceeds from Inventiva’s multi-tranche equity financing and Inventiva’s expected use of such proceeds. 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 not historical facts but rather are statements of future expectations and other forward-looking statements that 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. Actual events are difficult to predict and may depend upon factors that are beyond Inventiva's control. There can be no guarantees with respect to pipeline product candidates that the clinical trial results will be available on their anticipated timeline, that future clinical trials will be initiated as anticipated, that product candidates will receive the necessary regulatory approvals, or that any of the anticipated milestones by Inventiva or its partners will be reached on their expected timeline, or at all. Future results may turn out to be materially different from the anticipated future results, performance or achievements expressed or implied by such statements, forecasts and estimates due to a number of factors, including that Inventiva cannot provide assurance on the impacts of the SUSAR, including the ultimate impact on the results or timing of the NATiV3 trial or regulatory matters with respect thereto, that Inventiva is a clinical-stage company with no approved products and no historical product revenues, Inventiva has incurred significant losses since inception, Inventiva has a limited operating history and has never generated any revenue from product sales, Inventiva will require additional capital to finance its operations, in the absence of which, Inventiva may be required to significantly curtail, delay or discontinue one or more of its research or development programs or be unable to expand its operations or otherwise capitalize on its business opportunities and may be unable to continue as a going concern, Inventiva’s ability to obtain financing and to enter into potential transactions or further arrangements with its creditors and the impacts therefrom, Inventiva's future success is dependent on the successful clinical development, regulatory approval and subsequent commercialization of current and any future product candidates, preclinical studies or earlier clinical trials are not necessarily predictive of future results and the results of Inventiva's and its partners’ clinical trials may not support Inventiva's and its partners’ product candidate claims, Inventiva's expectations with respect to its clinical trials may prove to be wrong and regulatory authorities may require holds and/or amendments to Inventiva’s clinical trials, Inventiva’s expectations with respect to the clinical development plan for lanifibranor for the treatment of MASH may not be realized and may not support the approval of a New Drug Application, Inventiva and its partners may encounter substantial delays beyond expectations in their clinical trials or fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities, the ability of Inventiva and its partners to recruit and retain patients in clinical studies, enrollment and retention of patients in clinical trials is an expensive and time-consuming process and could be made more difficult or rendered impossible by multiple factors outside Inventiva's and its partners’ control, Inventiva's product candidates may cause adverse drug reactions or have other properties that could delay or prevent their regulatory approval, or limit their commercial potential, Inventiva faces substantial competition and Inventiva’s and its partners' business, and preclinical studies and clinical development programs and timelines, survey results may not be indicative of broader views and the views expressed in survey results may be inaccurate and/or may change over time, results of prior trials may not be indicative of future trial results, Inventiva’s financial condition and results of operations could be materially and adversely affected by geopolitical events, such as the war in Ukraine and related sanctions, impacts and potential impacts on the initiation, enrollment and completion of Inventiva’s and its partners’ clinical trials on anticipated timelines and the conflict in the Middle East and the related risk of a larger conflict, health epidemics, and macroeconomic conditions, including global inflation, rising interest rates, uncertain financial markets and disruptions in banking systems. Given these risks and uncertainties, 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, 2023 filed with the Autorité des Marchés Financiers on April 3, 2024, as amended on October 14, 2024, and the Annual Report on Form 20-F for the year ended December 31, 2023 filed with the Securities and Exchange Commission (the “SEC”) on April 3, 2024 and the Half-Year Report for the six months ended June 30, 2024 on Form 6-K filed with the SEC on October 15, 2024. Other risks and uncertainties of which Inventiva is not currently aware may also affect its forward-looking statements and may cause actual results and the timing of events to differ materially from those anticipated. All information in this presentation is as of the date of the release. 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. This presentation shall not constitute an offer to sell or the solicitation of an offer to buy any securities, nor shall there be any sale of securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction. This presentation includes information and statements of third parties. Inventiva does not make any representation with respect to the accuracy or otherwise with respect to such third party information.

Management team with extensive global experience across all stages of drug development and commercialization

Frédéric Cren, MA/MBA, CEO and Co-Founder

- Wide expertise within the areas of R&D, marketing, strategy and commercial operations
- Held senior positions at Abbott, Fournier, Solvay Pharma and The Boston Consulting Group
- Former member of both Fournier and Solvay Pharma Executive Committees

Jean Volatier, MA, CFO

- Former Head of controlling at URGO & Financial Director International Operations of Fournier
- Held various positions as CFO
- Started his career with PwC in Paris and Philadelphia

Pascaline Clerc, Ph.D., EVP Strategy and Corporate Affairs

- Held global roles in academia, non-profit organization, government and biotech companies

David Nikodem, Ph.D., VP U.S. Operations

- Former buyside portfolio manager and analyst for +15 years in public equities and VC

Pierre Broqua, Ph.D., CSO and Co-Founder

- Successfully managed numerous research programs leading to the discovery, development and commercialization of innovative compounds, including lanifibranor and Degarelix/ Firmagon®
- Held several senior research positions at Fournier, Solvay Pharma and Abbott

Michael Cooreman, MD, CMO

- Gastroenterologist-hepatologist
- Held global roles in several companies including Takeda Pharmaceuticals, Merck, Mitsubishi Tanabe, ImmusanT and Novartis

Alice Roudot-Ketelers, PharmD, COO

- Previously in charge of all drug development programs and cross-functional teams in Chemistry, CMC, non-clinical and clinical development up to Phase III at one of the major biotech companies in the NASH field

Kristina Meyer, Ph.D., EVP Business Development & Alliance Management

- 20+ years experience in business development in the biotech industry

Lanifibranor well positioned to treat MASH patients with advanced fibrosis and T2D

Best in Class Oral Efficacy Data

Phase IIb demonstrated **18% fibrosis placebo-adjusted improvement at 6 months**

Differentiated profile that **has been observed to improve cardiovascular, glycemic and metabolic markers and reduce insulin resistance**

Differentiated pan-PPAR Agonist

Balanced pan-PPAR agonist activity, once-daily dosing, IP protection through 2040

Differentiated Safety & Tolerability Profile

Differentiated safety profile in the PPAR class

Non-overlapping AE profile with incretin agonists, allowing for combination therapy

Significant Near-Term Commercial Opportunity

Phase III ~95% enrolled; projected **1H25 enrollment completion** and **2H26 Phase III data readout**

A multi-tranche equity financing of $400M+ secured in October 2024 led by New Enterprise Associates, BVF Partners and Samsara BioCapital capitalized Inventiva to execute on the clinical trial through NDA(1)

(1) In October 2024, Inventiva announced a multi-tranche equity financing of up to €348 million, subject to conditions, and up to $30 million in milestone payments. If all tranches close, the proceeds are expected to fully fund the development of lanifibranor through its Phase III trial and potential NDA filing

Clinicians and industry have recognized the value of PPAR agonists

Prescriptions and M&A support the potential of this class of drugs

Physicians continue to prescribe pioglitazone with over 6M scrips written in 2023 in the U.S.

Pioglitazone U.S. Annual TRx

	2022	2023	1H24
ACTOPLUS MET	369	259	113
ACTOPLUS MET XR	1	1	–
ACTOS	1,941	1,340	519
AVANDIA	7	1	1
DUETACT	35	16	2
PIOGLIT/GLIMEPIRID	11,361	10,660	4,819
PIOGLIT/METFORMIN	139,794	119,237	54,056
PIOGLITAZONE HCL	6,025,851	5,882,329	2,861,187
TOTAL	**6,179,359**	**6,013,843**	**2,920,697**

- Pioglitazone is one of the recommended diabetes pharmacotherapy for patients with MASLD F0 to compensated cirrhosis(1)

"It is my opinion that PPAR gamma activation remains most effective in repletion of adiponectin levels and adiponectin is the missing link that connects the health of visceral adipose depot to systemic inflammation."
– Kris Kowdley, Director at Liver Institute Northwest, Washington.

In 2024, the FDA liver division has approved two PPARs in PBC

IQIRVO® elafibranor 80 mg tablets

Livdelzi® seladelpar 10mg Capsules

Gilead acquires Cymabay for $4.3B in February 2024

GILEAD

CYMABAY

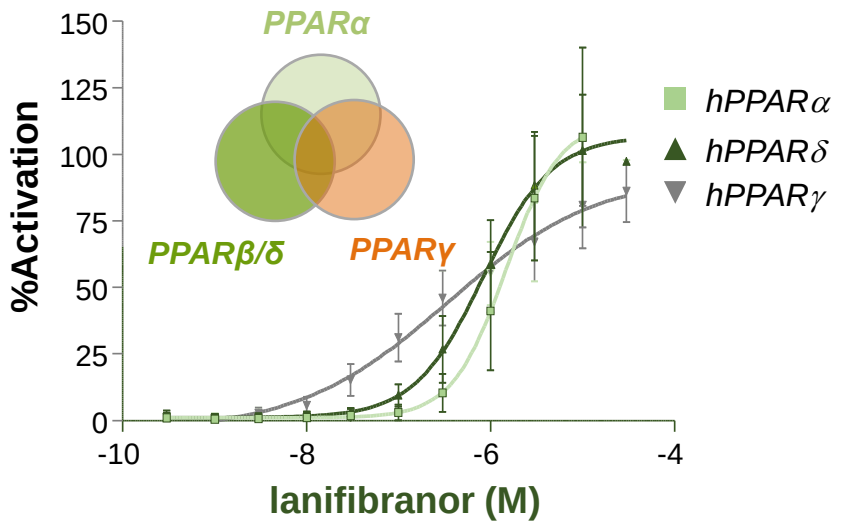
- Cymabay was developing seladelpar, a PPARδ-agonist in PBC, an orphan chronic liver indication
- At time of Cymabay acquisition, results of the Phase III had been published but seladelpar was not yet approved by FDA nor EMA

Source: IQVIA Script Data; KOL Interviews; Inventiva Analysis; (1) 2025 ADA Standard of care

Lanifibranor: a pan-PPAR agonist with differentiated profile

A new chemical entity: not a fibrate, not a TZD

Moderate and balanced pan-PPAR agonist activity



- Small molecule that activates **all three PPAR isoforms** in humans
- **Balanced activity** across the three human PPAR isoforms
- Differentiated chemical structure: not a fibrate or a TZD
- Once daily oral administration
- FDA confirmation that the **non-clinical toxicology package is complete and acceptable for NDA filing**
- In 2020, FDA granted lanifibranor **breakthrough therapy and fast track designation** for the treatment of MASH
- **IP protection** through 2040

Pan-PPAR activity likely required for efficacy across MASH disease drivers

METABOLISM	STEATOSIS	INFLAMMATION AND BALLOONING	FIBROSIS	VASCULAR
PPARα PPARδ PPARγ	PPARγ	PPARα PPARδ PPARγ	PPARδ PPARγ	PPARα PPARγ
↑ Insulin sensitivity	↓ FA uptake	↓ NFkB-dependent gene activation	↓ Stellate cell proliferation and activation	↓ Portal pressure
↑ HDLc	↑ FA catabolism	↓ Inflammasome	↓ Collagen and fibronectin production	↓ LSEC capillarization
↓ Triglycerides	↓ Lipogenesis	↓ Ballooning		↓ Intrahepatic vascular resistance

TZD: Thiazolidinediones

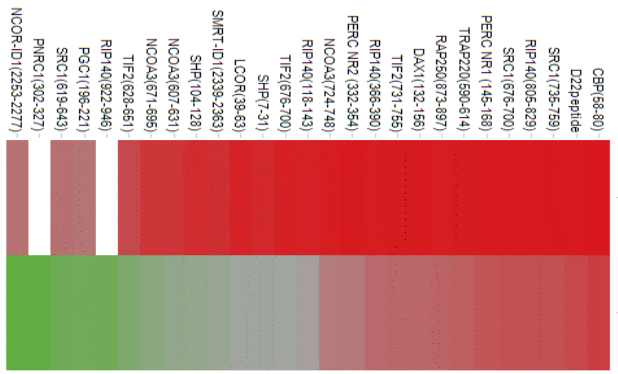
Balanced PPAR activity with differential binding/target engagement

Lanifibranor did not lead to the adverse events and toxicity previously seen in single/dual PPAR agonists

Moderate 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*	*-*

… that engages PPARγ differently



- Induces different coactivator recruitment^^

Adverse events and toxicity previously seen in other single and dual PPAR agonists have not been observed with lanifibranor in preclinical studies

Organ	Isoforms activated	Reported PPAR side effects	Lanifibranor effects
HEART	*PPARγ*	▶ Fluid retention ▶ Cardiac hypertrophy	**Adverse events and toxicity of single / dual PPAR agonists not observed in primate and rodent studies**
SKELETAL MUSCLE	*PPARα*	▶ Myofiber degeneration	
KIDNEY	*PPARα*	▶ > 50% increases in creatinine, degenerative changes in renal tubules	
URINARY BLADDER	*PPARγ*	▶ Proliferative changes in bladder epithelium	

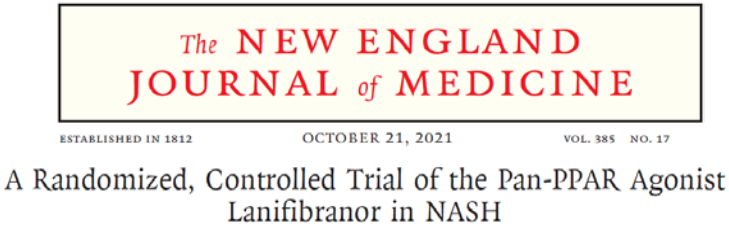
Source: * Company data ** Hanf R et al, Diabetes & Vascular Dis Res 2014 ^ Cymabay company presentation ^^ J Med Chem. 2018 Feb 15. doi: 10.1021/acs.jmedchem.7b01285

NATIVE Phase II Study of lanifibranor in MASH

The Phase IIb NATIVE trial published in NEJM

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

- **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
- **Results published in the New England Journal of Medicine (1) and additional analysis in Nature Communications (2)**


The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 21, 2021 VOL. 385 NO. 17

A Randomized, Controlled Trial of the Pan-PPAR Agonist Lanifibranor in NASH


nature communications

Article https://doi.org/10.1038/s41467-024-47919-9

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

(1) 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

Patient population (I/II)

Parameters (unit) n (%) or mean ± SD	Placebo - N = 81	lanifibranor 800 mg/day N = 83	lanifibranor 1200 mg/day N = 83	Overall - N = 247
Demographics				
Female	41 (51%)	54 (65%)	49 (59%)	144 (58%)
Age (years)	53.4 ± 13.1	55.0 ± 10.4	52.2 ± 13.8	53.6 ± 12.5
White	74 (91%)	80 (96%)	78 (94%)	232 (94%)
Weight (kg)	95.1 ± 17.3	91.6 ± 19.3	93.0 ± 19.9	93.2 ± 18.9
Body Mass Index (kg/m²)	32.8 ± 5.1	32.5 ± 5.5	33.3 ± 5.5	32.9 ± 5.4
Type 2 diabetes	35 (43%)	33 (40%)	35 (42%)	103 (42%)
Liver biopsy characteristics				
SAF Activity score (inflammation + ballooning)	3.3 ± 0.5	3.2 ± 0.5	3.3 ± 0.5	3.3 ± 0.5
NAFLD Activity Score (NAS) ≥6	56 (69.1%)	63 (75.9%)	61 (73.5%)	180 (72.9%)
Fibrosis stage F2/F3	57 (70.4%)	68 (81.9%)	63 (75.9%)	188 (76.1%)

Patient population (II/II)

Parameters (unit) mean ± SD	Placebo - N = 81	lanifibranor 800 mg/day N = 83	lanifibranor 1200 mg/day N = 83
Liver enzymes			
Alanine aminotransferase, ALT (UI/L)	56.9 ± 31.6	64.1 ± 41.4	63.6 ± 43.4
Aspartate aminotransferase, AST (UI/L)	43.3 ± 24.1	53.9 ± 43.4	43.9 ± 24.8
Gamma glutamyl transferase, GGT (UI/L)	67.9 ± 80.4	101.6 ± 146.1	67.1 ± 93.1
Plasma lipid levels			
HDL-Cholesterol (mmol/L)	1.2 ± 0.3	1.3 ± 0.3	1.2 ± 0.3
Triglycerides (mmol/L)	2.0 ± 0.8	1.9 ± 0.9	2.0 ± 0.9
Glucose metabolism for patients with T2D (n= 103)			
Fasting Glucose (mmol/L)	6.9 ± 2.0	7.3 ± 2.2	6.6 ±1.2
HbA1c (%)	6.5 ± 0.7	6.7 ± 0.8	6.6 ± 0.7
Insulin (pmol/L)	222.7 ± 186.5	246.3 ± 213.4	278.5 ± 233.5

Resolution of MASH and fibrosis improvement ≥ least 1 stage

Compares favourably to other oral and injectable compounds

ORAL

PPARs

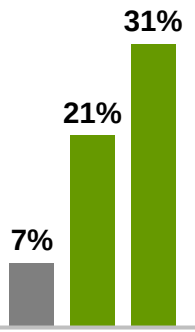
Lanifibranor

Phase II
6 months

N=247

ITT

Effect size 24%*



0.017* <0.001*

THR-β

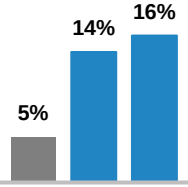
Resmetirom**

Phase III
12 months

N=955

ITT

Effect size 11%



<0.0001* <0.0001*

INJECTABLE

FGF-21

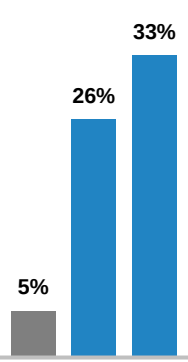
Efruxifermin

Phase IIb
6 months

N=128

ITT

Effect size 28%



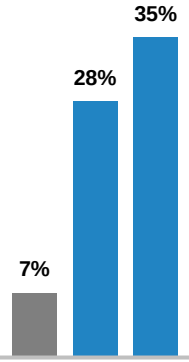
0.009* 0.002*

Phase IIb
24 months

N=126

ITT

Effect size 28%



<0.01* <0.01*

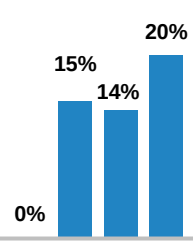
Pegozafermin

Phase II
6 months

N=222

PP

Effect size 20%



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GLP1-RA and GLP1-RA dual agonists

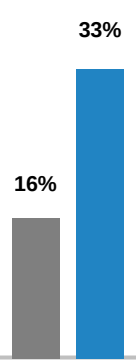
Semaglutide

Phase III
18 months

N=800

PP

Effect size 16.6%



Survodutide

Phase II
12 months

N=223 (F2/F3)

Tirzepatide

Phase II
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 has 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 IIb trial. Lancet Gastroenterology October 2023 ; **Semaglutid**e Phase III 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 II 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 favourably to other oral and injectable compounds

ORAL

PPARs

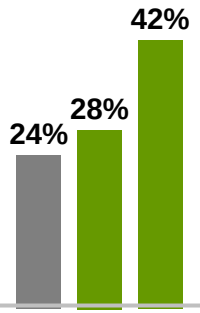
Lanifibranor

Phase II
6 months

N=247

ITT

Effect size 18%



THR-β

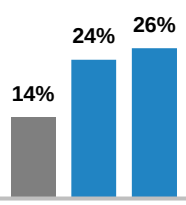
Resmetirom**

Phase III
12 months

N=955

ITT

Effect size 12%



INJECTABLE

FGF-21

Efruxifermin

Phase IIb
6 months

N=128

ITT

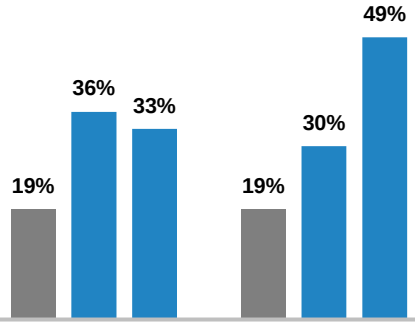
Effect size 14%

Phase IIb
24 months

N=126

ITT

Effect size 20%



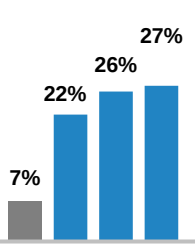
Pegozafermin

Phase II
6 months

N=222

PP

Effect size 20%



GLP1-RA and GLP1-RA dual agonists

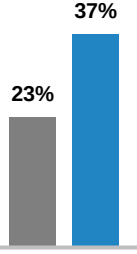
Semaglutide

Phase III
18 months

N=800

PP

Effect size 15%



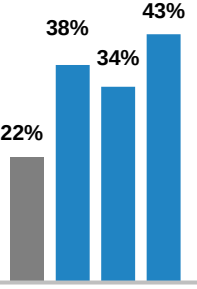
Survodutide

Phase II
12 months

N=293

ITT

Effect size 21%



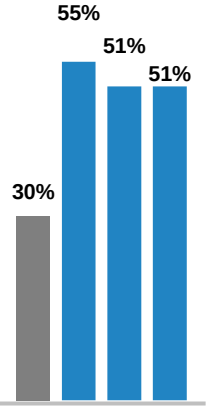
Tirzepatide

Phase II
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 has 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 IIb trial. Lancet Gastroenterology October 2023; corporate presentation of March 2024 pg15; **Semaglutide** Phase III ESSENCE trial of semaglutide 2.4mg in participants with non-cirrhotic non-alcoholic steatohepatitis; Newsome et al.**; Pegozafermin**, 89Bio Phase IIb ENLIVEN Topline Results presentation; **Survodutide** A Phase II 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

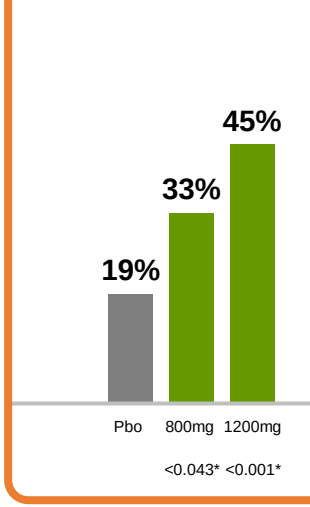
Compares favourably to other oral and injectable compounds

ORAL

PPARs

Lanifibranor (inventiva)

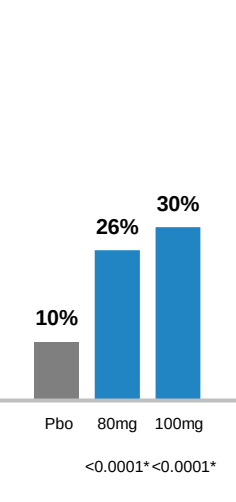
Phase II 6 months	N=247	ITT	Effect size **26%**



THR-β

Resmetirom** (Madrigal Pharmaceuticals)

Phase III 12 months	N=955	ITT	Effect size **20%**

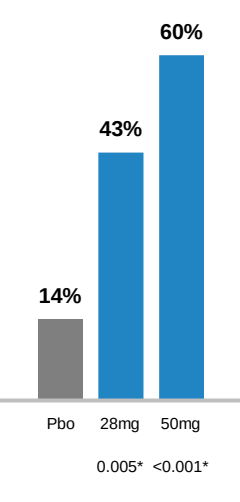


INJECTABLE

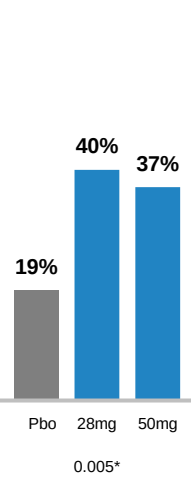
FGF-21

Efruxifermin (akero)

Phase IIb 6 months	N=128	ITT	Effect size **46%**

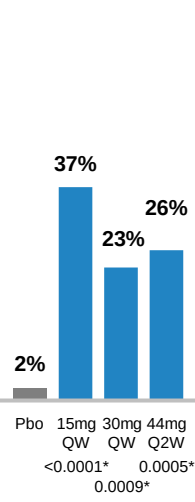


Phase IIb 24 months	N=126	ITT	Effect size **18%**



Pegozafermin (89bio)

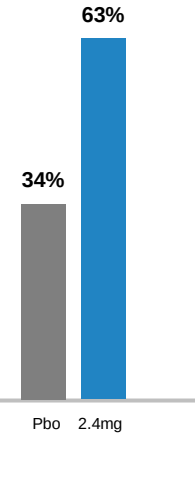
Phase II 6 months	N=222	PP	Effect size **24%**



GLP1-RA and GLP1-RA dual agonists

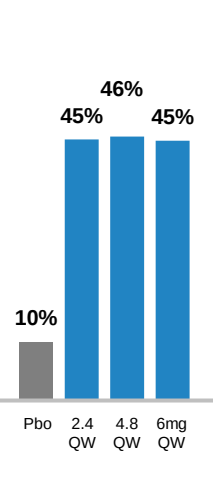
Semaglutide (novo nordisk)

Phase III 18 months	N=800	PP	Effect size **40%**



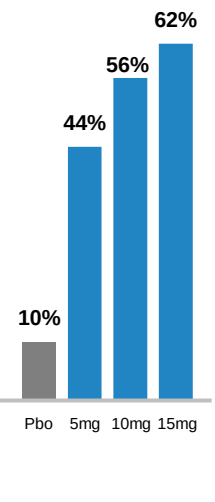
Survodutide (Boehringer Ingelheim)

Phase II 12 months	N=293	ITT	Effect size **35%**



Tirzepatide (Lilly)

Phase II 12 months	N=190	ITT	Effect size **52%**



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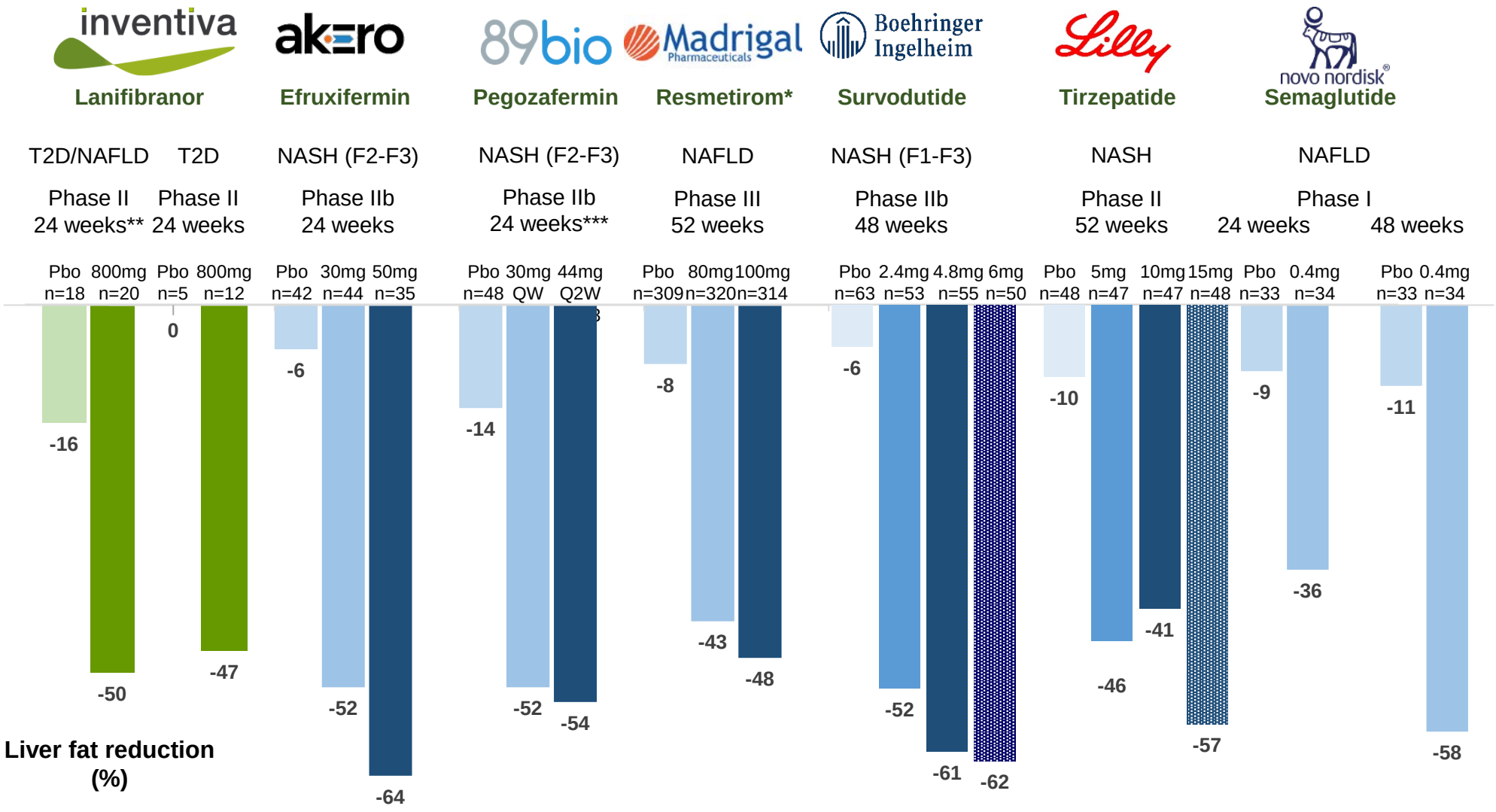
Source: **lanifibranor** native results;; **resmetirom** MAESTRO NASH top-line results webcast Dec. 19 2022, pg 10; resmetirom : Harrison et al, Lancet 2019 ; S0140-6736(19) 32517-6 **Efruxifermin** Safety and efficacy of once-weekly efruxifermin versus placebo in non-alcoholic steatohepatitis (HARMONY): a multicentre, randomised, double-blind, placebo-controlled, Phase IIb trial. Lancet Gastroenterology October 2023; corporate presentation of March 2024 pg15; **Semaglutid**e Phase III ESSENCE trial of semaglutide 2.4mg in participants with non-cirrhotic non-alcolohic steatohepatitis; Newsome et al.**; Pegozafermin**, 89Bio Phase IIb ENLIVEN Topline Results presentation; **Survodutide** A Phase II 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

Reduction in Steatosis measured by MRI-PDFF

Compares favourably to other oral and injectable compounds



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 has been approved under accelerated approval by the FDA
** Results reported among completers
***Reductions reported only for subset of patients with liver fat content ≥10 at baseline

Efruxifermin – Akero's Phase IIb Harmony Study Results presentation (sept. 2022), **Pegozafermin** - 89Bio' Corporate Presentation (May 2023); **Resmetirom** – Madrigal's corporate presentation (May 2023); **Semaglutide** - Flint A, Andersen G, Hockings P, Johansson L, Morsing A, Sundby Palle M, Vogl T, Loomba R, Plum-Mörschel L. Randomised clinical trial: semaglutide versus placebo reduced liver steatosis but not liver stiffness in subjects with non-alcoholic fatty liver disease assessed by magnetic resonance imaging. Aliment Pharmacol Ther. 2021 Nov;54(9):1150-1161. doi: 10.1111/apt.16608. Epub 2021 Sep 27. PMID: 34570916; PMCID: PMC9292692; **Survodutide** A Phase II randomized trial for Survodutide in MASH and fibrosis, The NEJM DOI: 10.1056/NEJMoa2401755 ; **Tirzepatide** Tirzepatide for Metabolic Dysfunction-Associated Steatohepatitis with Liver Firbosis, The NEJM DOI: 10.1056/NEJMoa2401943

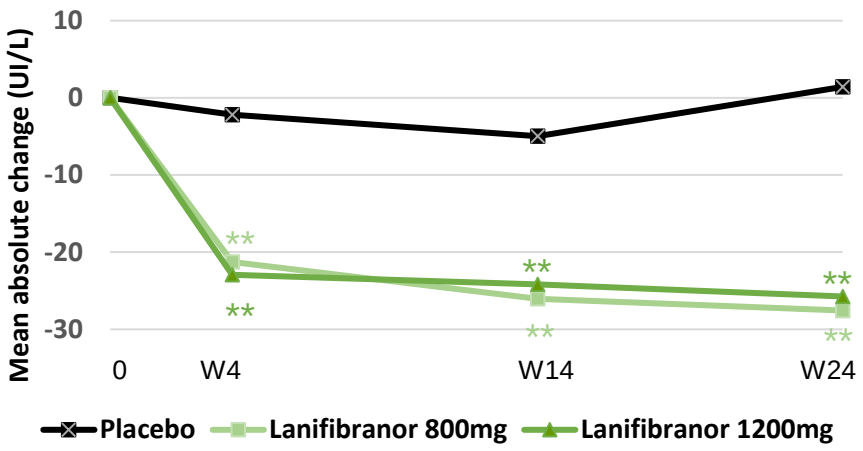
Statistically significant decrease in liver enzymes

Liver biomarkers show rapid and sustained improvement

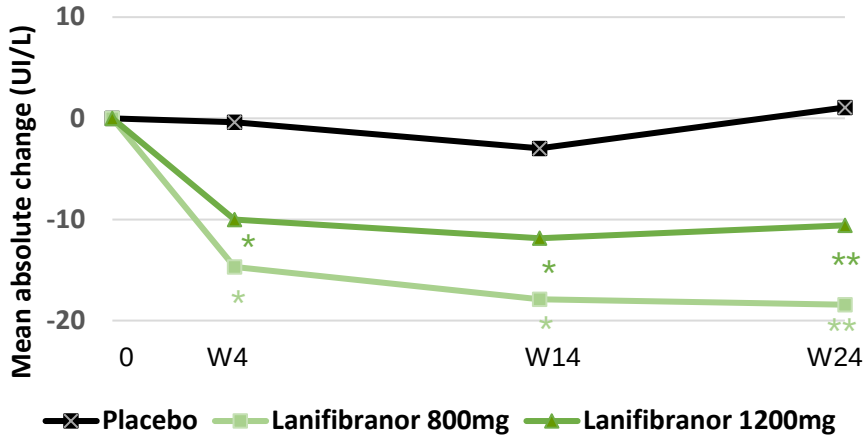
Other secondary endpoints in ITT (N = 247)

SECONDARY ENDPOINTS

Absolute change from baseline in ALT

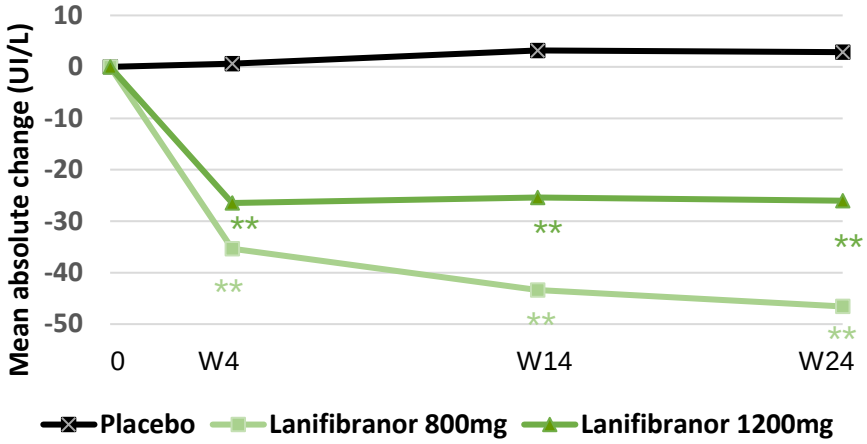


Absolute change from baseline in AST



* p<0.01 **p<0.001

Absolute change from baseline in GGT



A statistically significant decrease of ALT, AST and GGT in both lanifibranor dose groups observed after 4 weeks

Statistically significant change in lipid profile

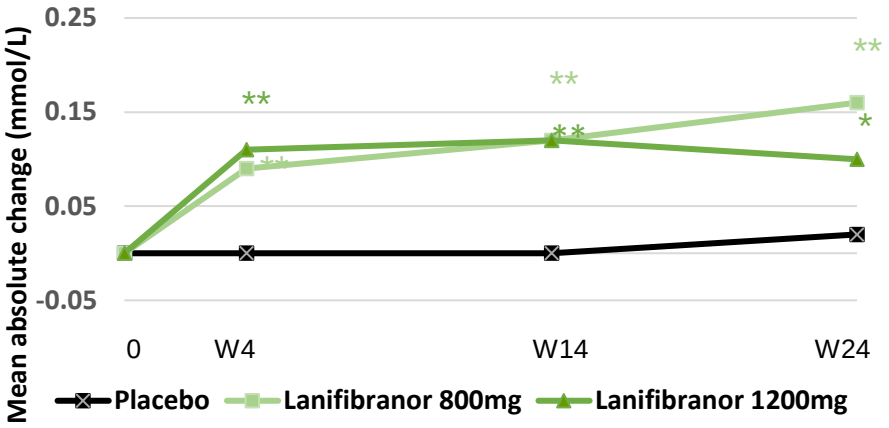
Improvements in HDL-cholesterol & triglycerides without a change in LDL-cholesterol

Other secondary endpoints in ITT (N = 247)

* p<0.01 **p<0.001

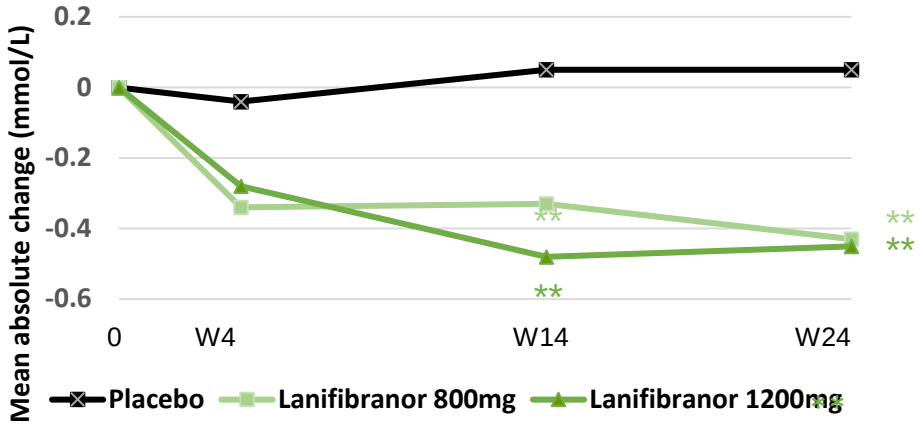
SECONDARY ENDPOINTS

Absolute change from baseline in HDL-C



Statistically significant change in HDL-cholesterol

Absolute change from baseline in triglycerides



A Statistically significant change in triglycerides

- No change in LDL-cholesterol

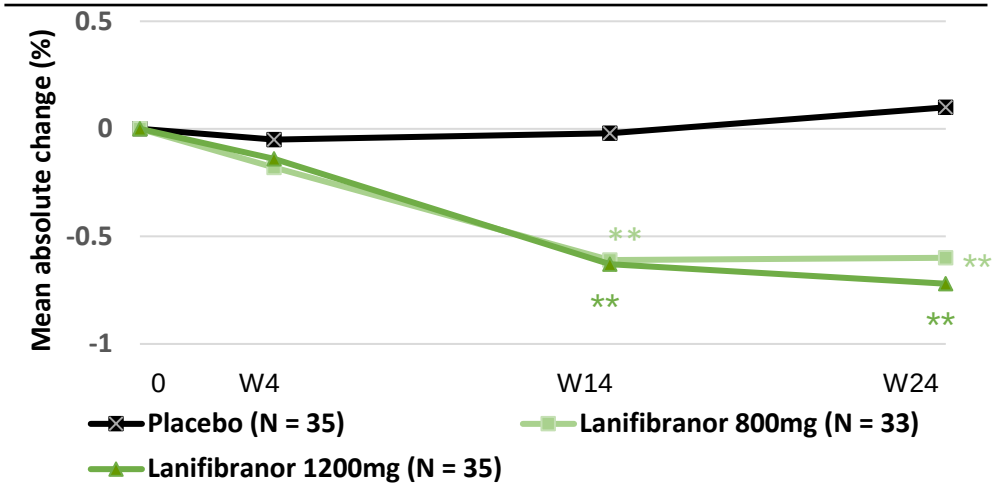
Clear benefit in MASH patients with T2D, across multiple studies

Significant reductions in HbA1c and fasting glucose

Secondary endpoints in patients with NASH/MASH and T2D (N = 103)

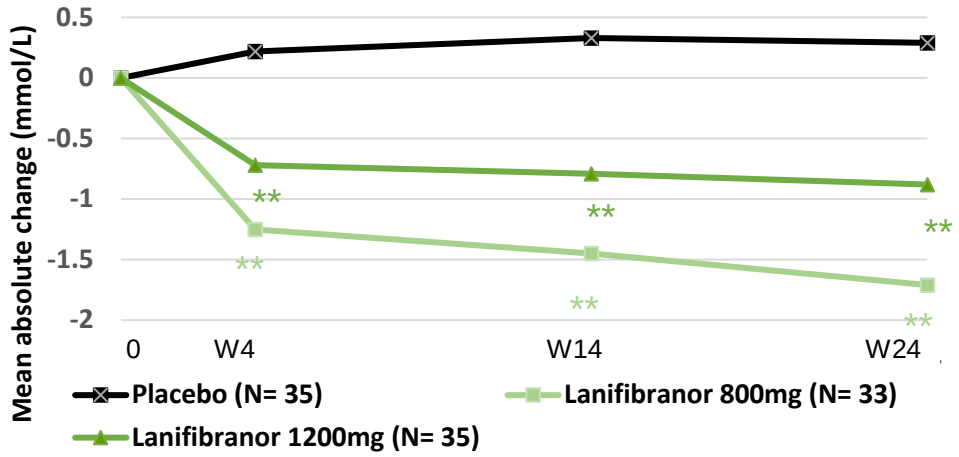
SECONDARY ENDPOINTS

Absolute change from baseline in HbA1c

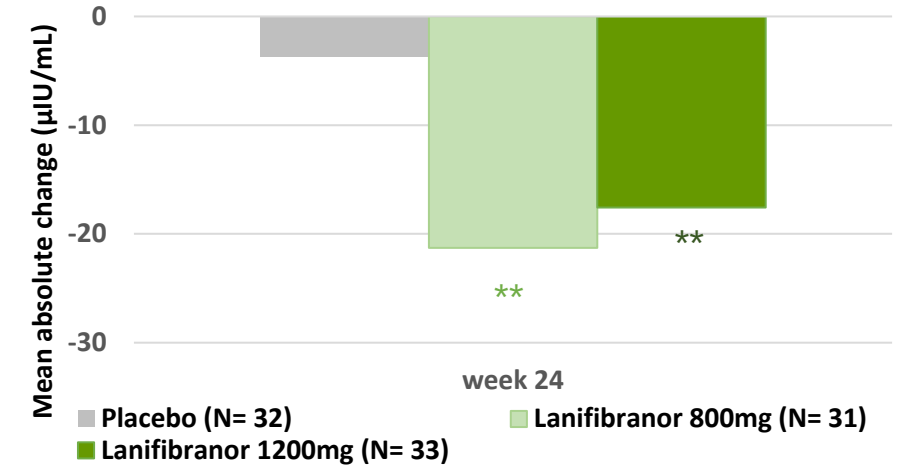


**p<0.001

Absolute change from baseline in fasting glucose



Absolute change from baseline in insulin at W24

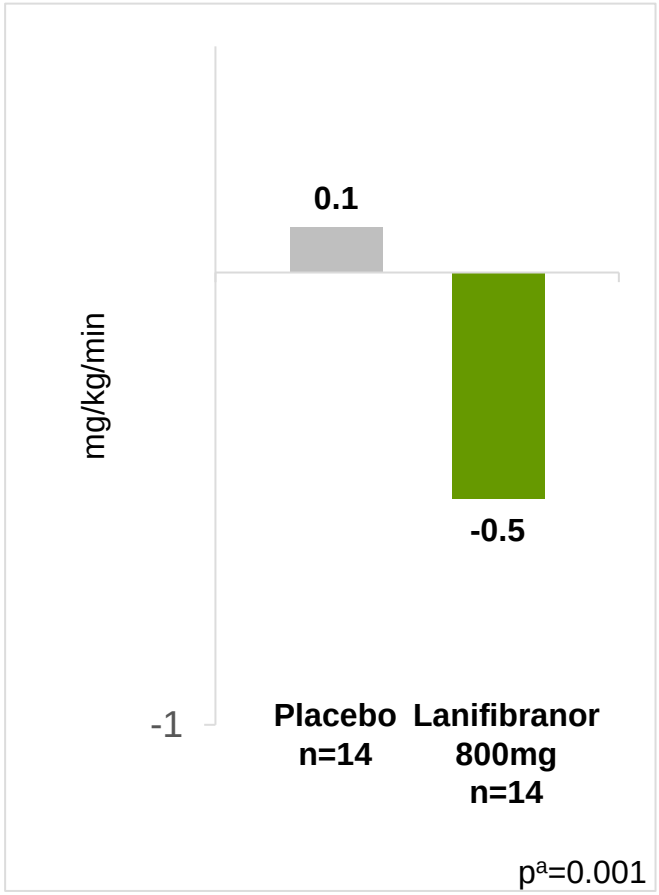


Lanifibranor associated with improvements in insulin sensitivity and glycemic control in MASH patients

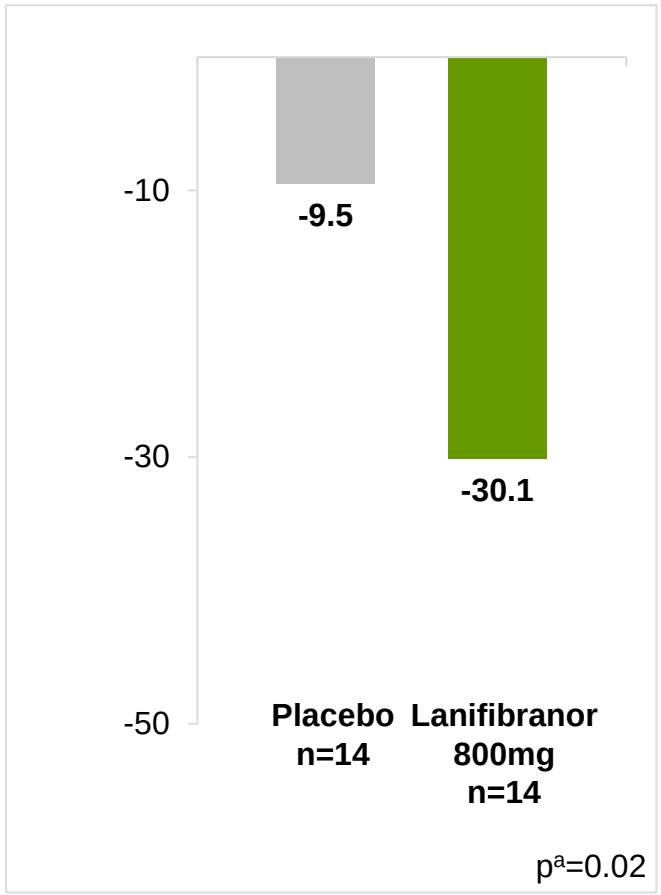
Significant improvements in hepatic and muscular insulin sensitivity(1)

Strong benefit has been observed across multiple studies

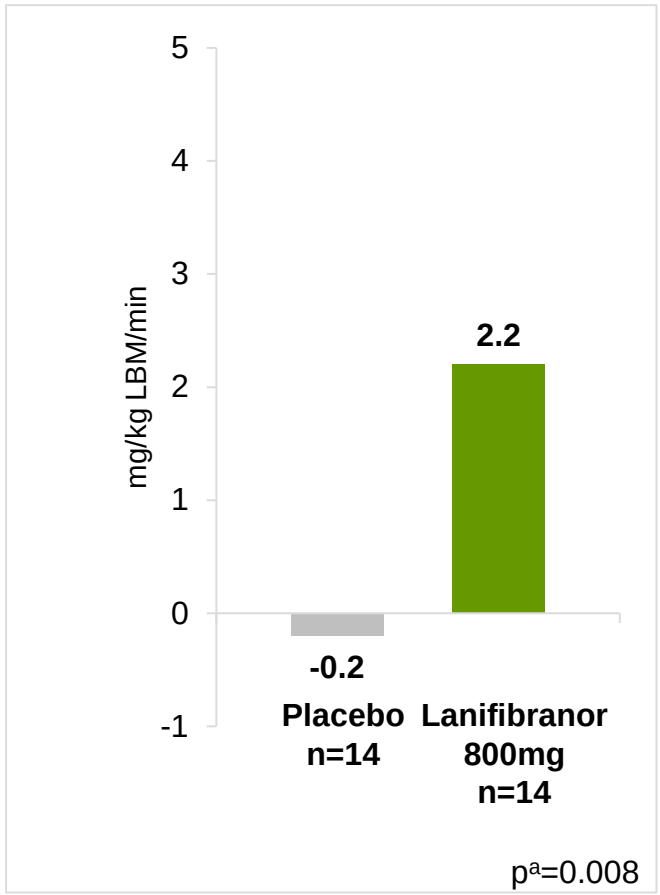
LS mean absolute change from baseline to week 24 in endogenous glucose production (completers N=28)



LS mean absolute change from baseline to week 24 in hepatic insulin resistance index (completers N=28)



LS mean absolute change from baseline to week 24 in insulin-stimulated muscle glucose disposal (completers N=28)



(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

Lanifibranor observed to induce a decrease in serum biomarkers

Increasing use of biomarkers to measure MASH/fibrosis in clinical practice

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

	Median relative change (%)		Placebo	lanifibranor *(Two doses pooled)*	Pvalue
OTHER OUTCOME MEASURES	Fibrosis	Pro-C3	(4.1%)	(13.9%)	*p= 0.005**
		Pro-C3 >14 at baseline(1)	(12.8%)	(20.5%)	*p= 0.017**
		Ratio TIMP-1/MMP-2	(4.6%)	(22.5%)	*p < 0.001**
	Apoptosis	CK18-M30	0.5%	(41.1%)	*p < 0.001**
	Inflammation	Ferritin	(9.1%)	(29.4%)	*p < 0.001**
		hs-CRP	13.0%	(35.5%)	*p < 0.001**

(1) Level where it is estimated that fibrogenesis is active and corresponding to F2/F3 patients
FAS (Full Analysis Set) population with available data at baseline and at week 24
* Statistically significant

Lanifibranor has a favourable safety profile

N (%) patients reporting Adverse Event (AE)	Placebo (N = 81)	800 mg (N = 83)	1200 mg (N = 83)
▶ **Any Treatment-Emergent AE (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)	-	-

Focus of next slide

(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

- 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.

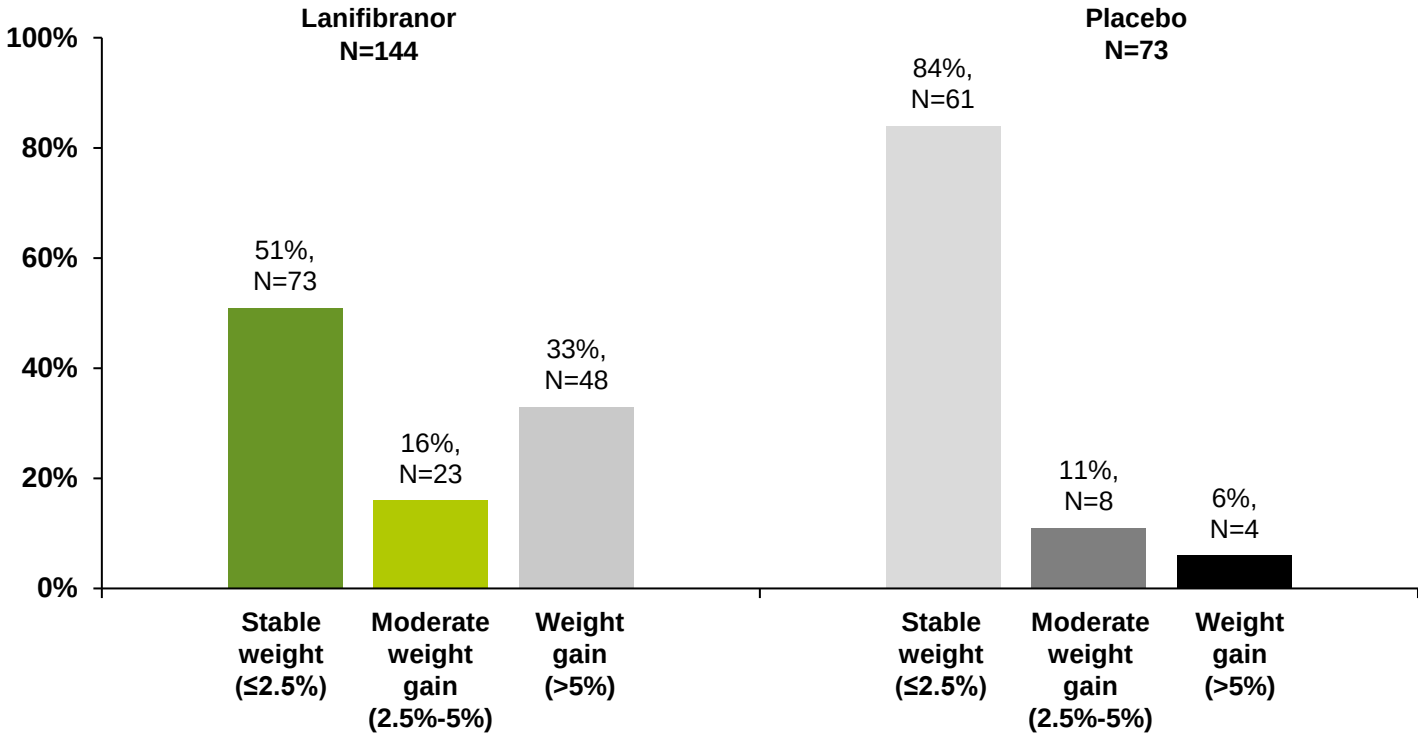
* One AE of severe intensity

A limited number of serious TEAEs occurred

Patients reporting treatment-emergent Serious AE (SAE); N (%)	Placebo (N = 81)	800 mg (N = 83)	1200 mg (N = 83)
Total	3 (3.7%)	3 (3.6%)	7 (8.4%)
Treatment-Emergent Serious AE linked to biopsy procedure			
Post-procedural haematoma/haemorrhage	-	1 (1.2%)	1 (1.2%)
Post-procedural pain	-	-	1 (1.2%)
Pneumobilia (post-procedural)	-	-	1 (1.2%)
Other Treatment-Emergent Serious AE			
Wrist fracture	1 (1.2%)	-	-
Angina unstable	-	-	1 (1.2%)
Cardiac failure	1 (1.2%)	-	-
Gastroenteritis	-	-	1 (1.2%)
Pyelonephritis	-	-	1 (1.2%)
Pancreatitis	-	1 (1.2%)	-
Undifferentiated connective tissue disease	-	1 (1.2%)	-
Urticaria	1 (1.2%)	-	-
Foot operation	-	-	1 (1.2%)

Weight gain is observed in ~50% of patients

Weight changes at end of treatment (week 24) in patients treated with lanifibranor versus placebo



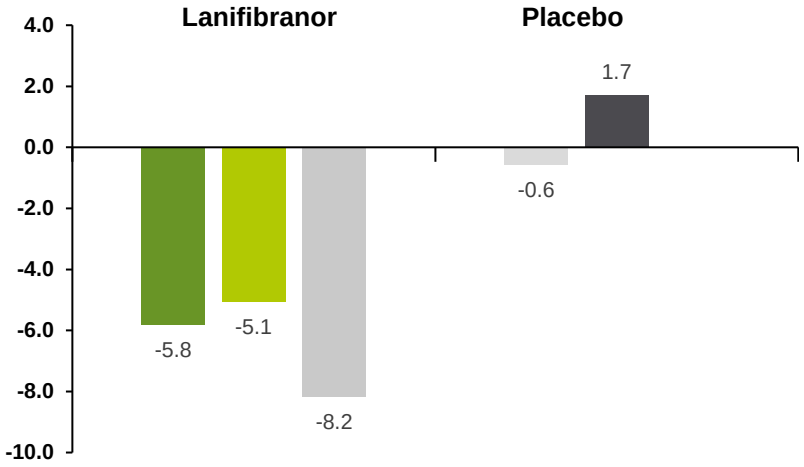
Source: MP. Cooreman, Lanifibranor improves markers of cardio-metabolic health in NASH patients independent of weight change – EASL 2022

Weight gain comes with improvements in metabolic, cardiometabolic, or liver markers (I/II)

Stable weight (≤2.5%) | Moderate weight gain (2.5%-5%) | Weight gain (>5%) | Stable weight (≤2.5%) | Weight gain (>5%)

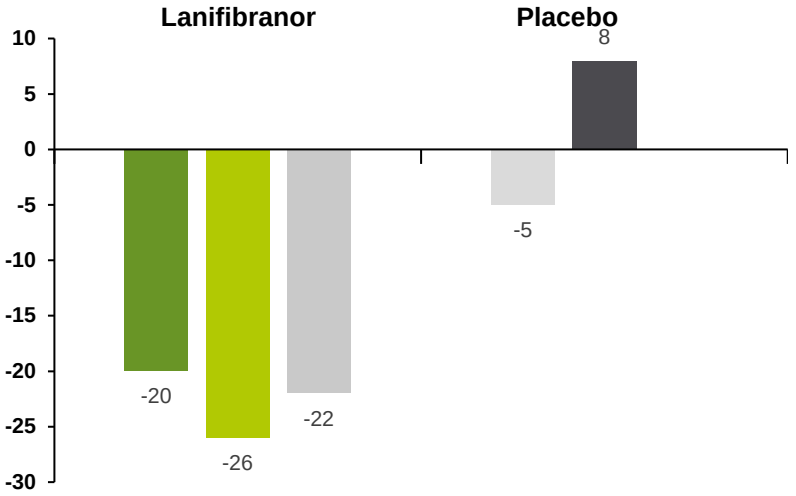
Fasting HOMA-IR

Mean absolute change at Week 24 from baseline



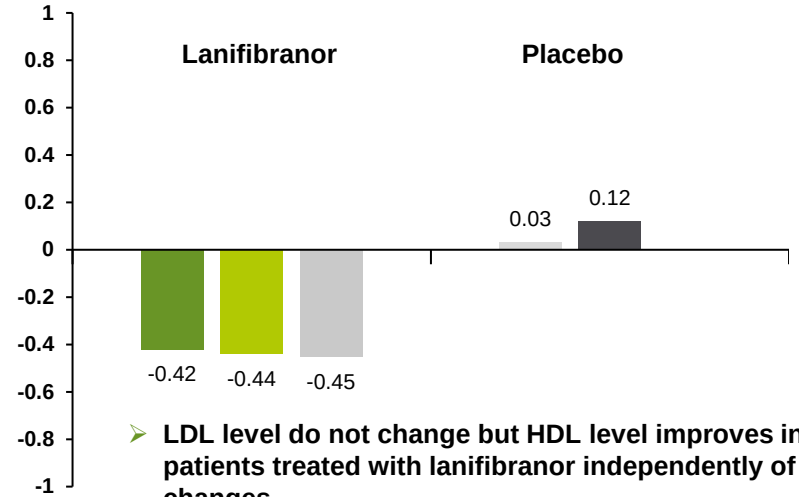
ALT

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



Triglycerides

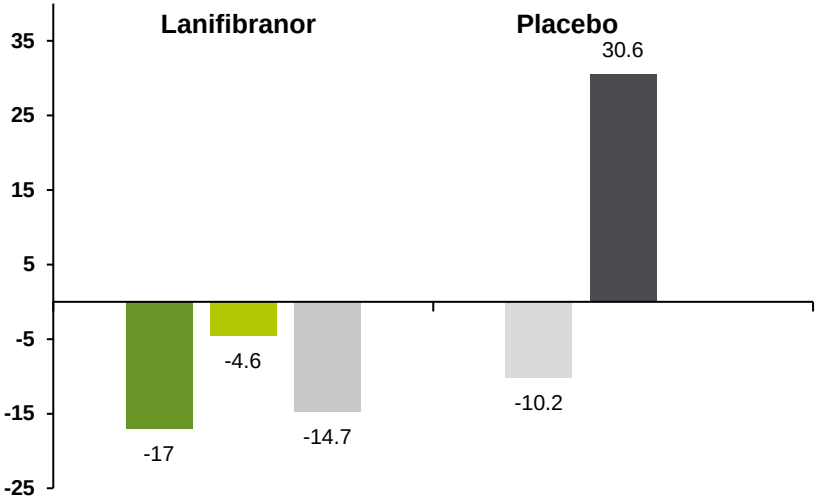
Mean absolute change at Week 24 from baseline (mmol/L)



- **LDL level do not change but HDL level improves in patients treated with lanifibranor independently of weight changes**

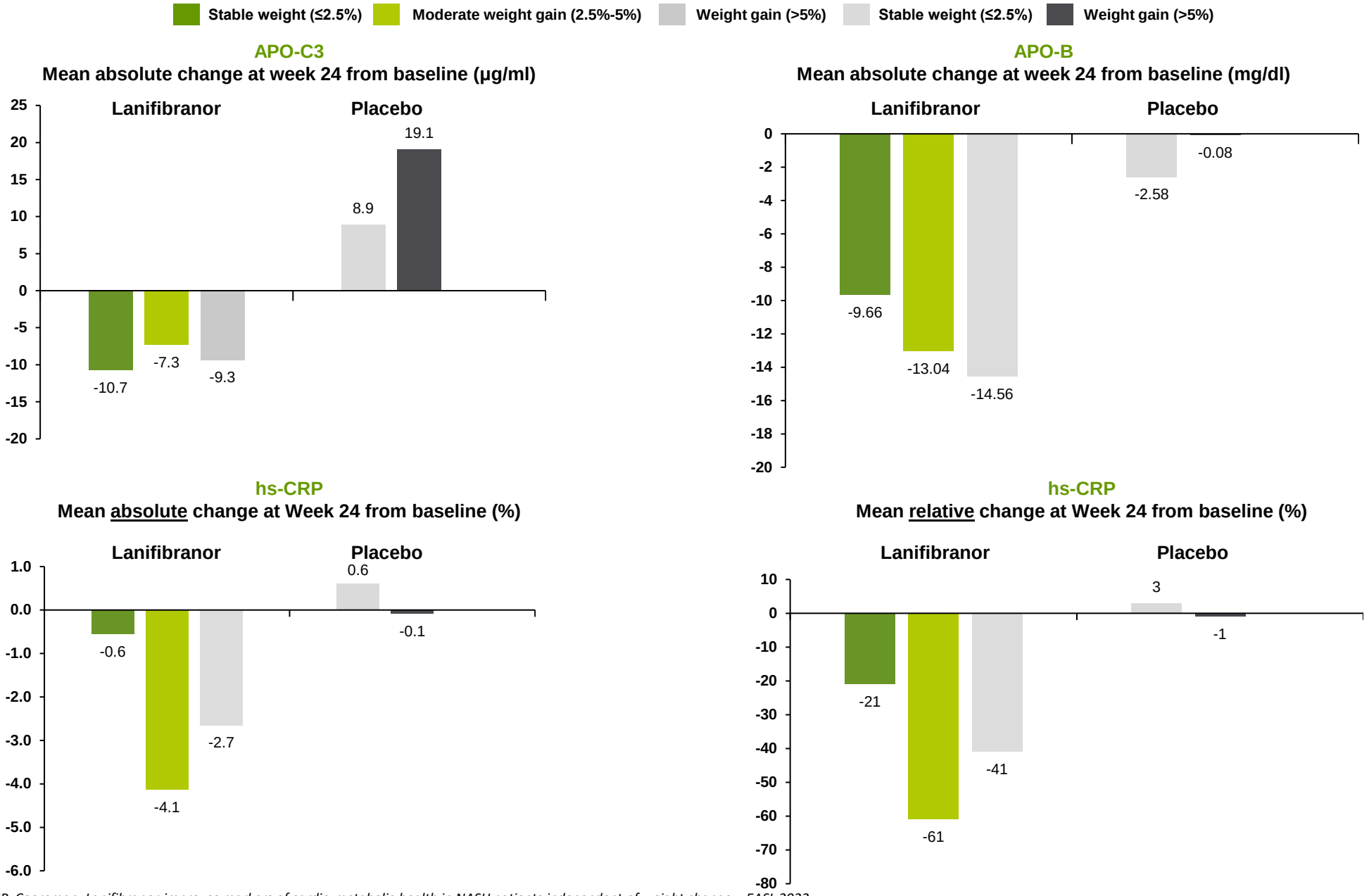
CAP

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



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

Weight gain comes with improvements in metabolic, cardiometabolic, or liver markers (II/II)

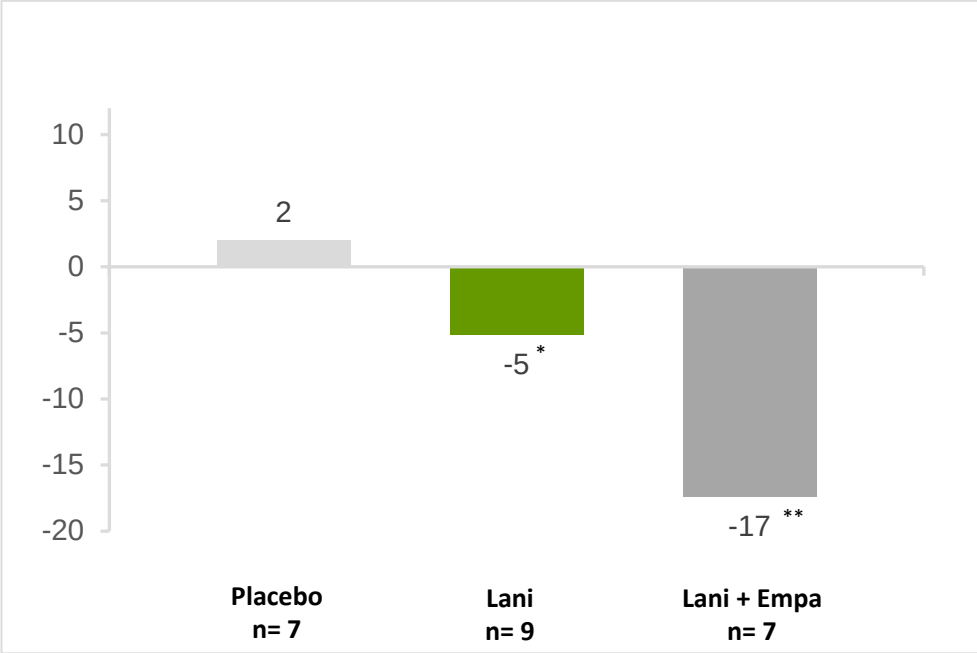


Source: MP. Cooreman, Lanifibranor improves markers of cardio-metabolic health in NASH patients independent of weight change – EASL 2022

Lanifibranor alone and in combination with empagliflozin leads to a shift towards metabolically healthy adipose tissue

Ratio VAT/SAT, N=23

LS Mean Relative change (%) from Baseline to Week 24



SAT=Subcutaneous Adipose Tissue, VAT=Visceral Adipose Tissue

* p=0.08, **p<0.05, versus placebo (ANCOVA)

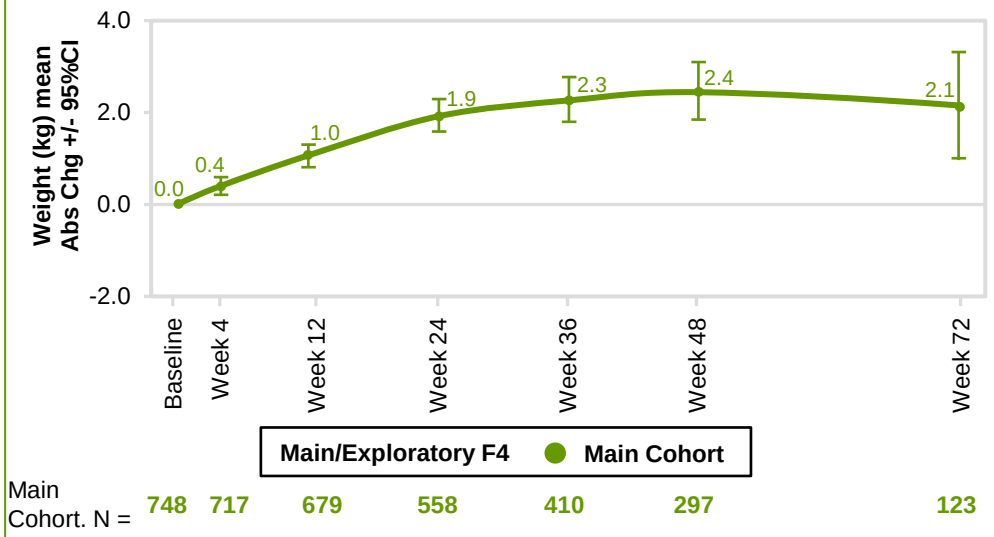
Sixteen patients were not considered in the FAS because of no VAT/SAT values available at Week 24:

- 5 patients under placebo and 1 patient under lani+empa who prematurely stopped before Week 24
- 2 patients under placebo / 3 patients under lanifibranor / 5 patients under lani+empa with missing values at Week 24

Lanifibranor has a differentiated weight gain profile relative to pioglitazone

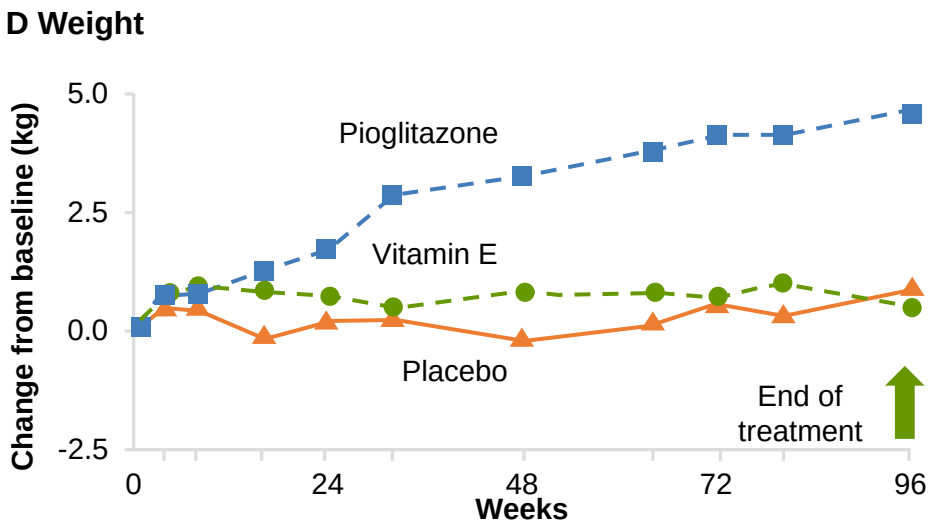
Weight gain plateaus with lanifibranor after 24-36 weeks

Lanifibranor



- In the interim blinded data of the main cohort from NATiV3, **lanifibranor shows a distinct plateau after week 24-36,** consistent with prior data

Pioglitazone



- In PIVENS study, a 96-week randomized trial of pioglitazone vs vitamin E in nondiabetic adults with MASH, mean weight increased 4.7kg
- **Continuous weight gain seen over the full 96 weeks**

While not conclusive, data suggests that lanifibranor weight gain stops after 24-36 weeks

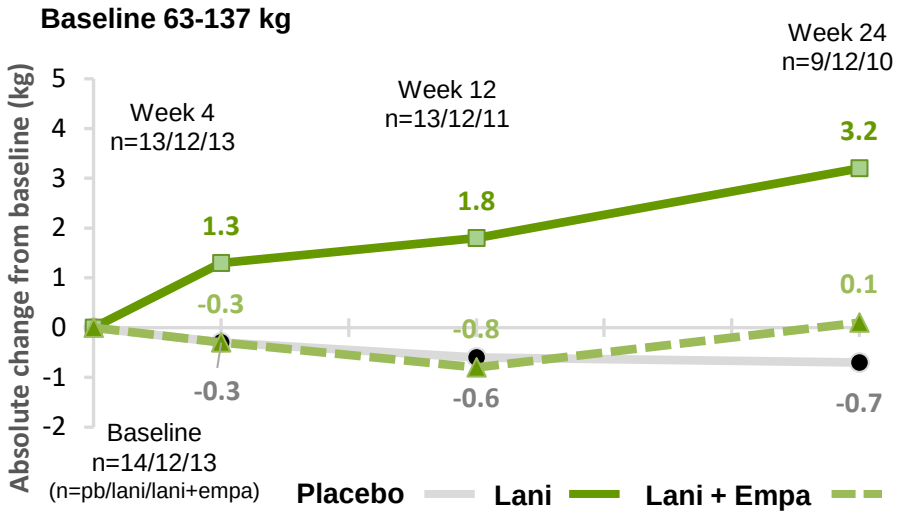
"If you can get PPAR activation without the liabilities it could be a best-in-class drug" – Kris Kowdley

Source: Tan MH et al. Diabetes Care 28:544 –550, 2005; KOL Interviews; Inventiva Analysis.

SGLT2 inhibitor empagliflozin mitigates lanifibranor weight gain

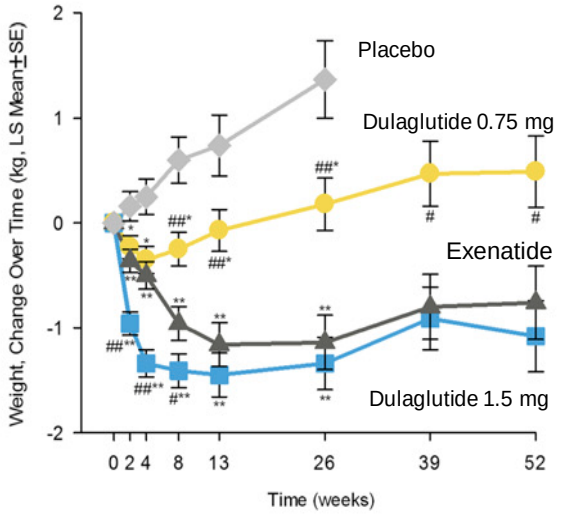
Meta-analysis data suggest that GLP-1s have a similar effect when combined with PPARs

Lanifibranor + empagliflozin



- In the LEGEND trial, albeit with a small n, results suggested that empagliflozin, an **SGLT2i, completely mitigated the lanifibranor weight gain profile over 24 weeks**

Pioglitazone + GLP1 or SGLT2i



- Recently published meta-analyses suggested that pioglitazone with GLP1 or SGLT2i is associated with increased weight loss and reduced risk of heart failure compared with monotherapy

Source: Anson. 2024. Diabetes, Obesity, and Metabolism; KOL Interviews; Inventiva Analysis.

LEGEND Study of lanifibranor in Combination with SGLT2 inhibitor

LEGEND, a study of lanifibranor in combination with empagliflozin

Strong mechanistic rationale for combination of lanifibranor with an SGLT2 inhibitor agent

Lanifibranor in Combination with the SGLT2 Inhibitor empagliflozin in patients with MASH and Type 2 Diabetes

LEGEND Trial

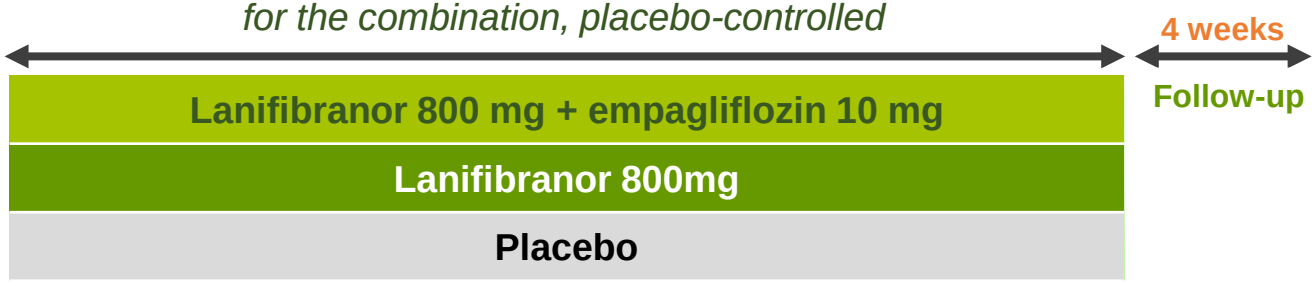
- Clinical data suggest that **lanifibranor** improves insulin sensitivity, lipid and glucose metabolism, inflammation, liver tissue injury (MASH activity) and fibrosis.
- **Empagliflozin** improves glycaemia, insulin sensitivity, has weight reducing and diuretic effects.
- **The combination of lanifibranor + empagliflozin** may
  - Add additional metabolic benefits
  - Address metabolically healthy weight gain observed in some patients on lanifibranor

Key inclusion criteria:

1) Adult patients with **MASH:**
   - historical biopsy with NAS ≥ 4
   - or cT1 ≥ 875 ms
   - or cT1 ≥ 825 ms and MRI-PDFF ≥ 10%
2) **T2D** diagnosed
3) Screening **HbA1c** in 7-10%

24 weeks treatment

Randomized, double-blind for lanifibranor and placebo, open label for the combination, placebo-controlled



Primary outcome measure:

HbA1c reduction at Week 24

Secondary outcome measures:

- Insulin resistance
- Hepatic fat (MRI-PDFF)
- Liver injury markers (AST, ALT)
- Lipid markers

Other outcome measures:

- Body weight
- Body fat composition
- Hepatic inflammation and fibrosis markers

Safety and tolerability

Patient population (I/II)

Parameters (unit) n (%) or mean ± SD	Lanifibranor 800 mg N=12	Lanifibranor + Empagliflozin N=13	Placebo N=14	Total N=39
Disposition				
24-week completed	12 (100%)	12 (92%)	9 (64%)	33 (85%)
Prematurely discontinued	0 (0%)	1 (8%)	5 (36%)	6 (15%)
Demographics				
Female	6 (50%)	8 (62%)	7 (50%)	21 (54%)
Age (years)	55.1 ± 11.4	54.2 ± 13.5	54.7 ± 13.0	54.6 ± 12.4
White	10 (91%)	10 (77%)	9 (69%)	29 (78%)
Weight (kg)	93.3 ± 11.6	103.3 ± 12.4	94.5 ± 21.3	97.1 ± 16.2
Body Mass Index (kg/m²)	33.3 ± 2.3	37.6 ± 4.3	34.5 ± 5.4	35.2 ± 4.6
MASH diagnosis				
Based on LiverMultiScan® (cT1 >= 875 ms or cT1 >= 825 ms and MRI-PDFF≥ 10%)	12 (100%)	12 (92%)	13 (93%)	37 (95%)

Patient population (II/II)

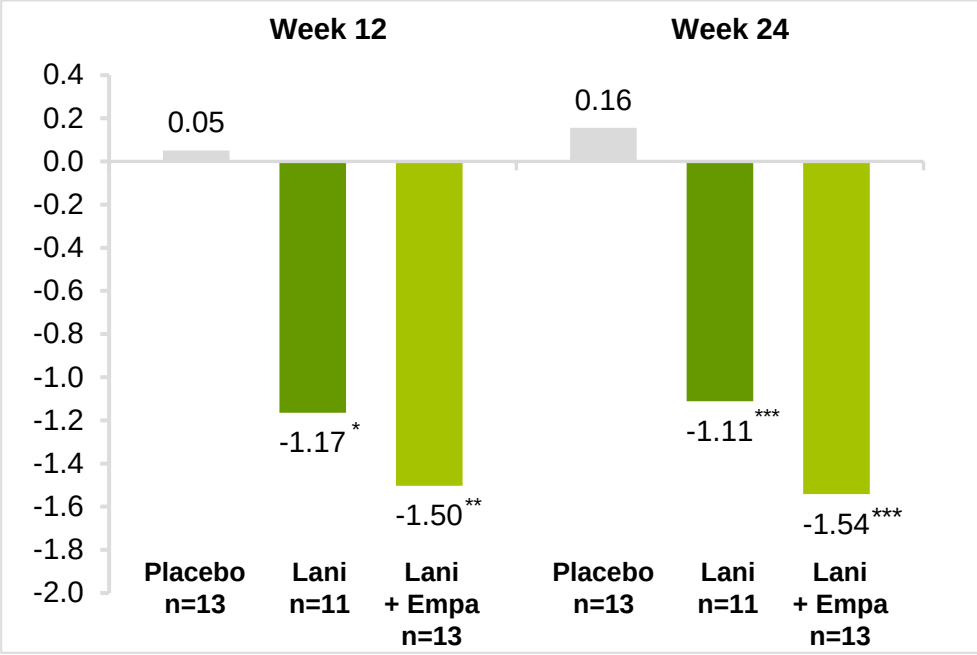
Parameters (unit) mean ± SD	Lanifibranor 800 mg N=12	Lanifibranor + Empagliflozin N=13	Placebo N=14	Total N=39
Liver enzymes				
Alanine aminotransferase, ALT (UI/L)	54.0 ± 36.9	54.8 ± 40.5	38.9 ± 22.2	48.8 ± 33.7
Aspartate aminotransferase, AST (UI/L)	37.3 ± 24.8	35.2 ± 20.5	31.1 ± 15.6	34.4 ± 20.0
Gamma glutamyl transferase, GGT (UI/L)	44.9 ± 26.4	54.9 ± 31.0	63.3 ± 66.1	54.8 ± 45.4
Plasma lipid levels				
HDL-Cholesterol (mmol/L)	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.3
Triglycerides (mmol/L)	3.0 ± 2.6	2.0 ± 0.9	2.2 ± 1.3	2.4 ± 1.7
Glucose metabolism for patients with T2D (n= 103)				
Fasting Glucose (mmol/L)	8.8 ± 2.7	8.7 ± 1.7	9.5 ± 5.0	9.0 ± 3.4
HbA1c (%)	8.0 ± 1.1	8.2 ± 1.0	8.1 ± 1.2	8.1 ± 1.1
Insulin (pmol/L)	174.0 ± 86.3	285.2 ± 175.4	280.6 ± 169.0	249.3 ± 155.7

Primary endpoint was met

Statistically significant reduction in HbA1c with lanifibranor alone and in combination

HbA1c (%) – FAS N=37

LS Mean Absolute Change from Baseline to Week 24



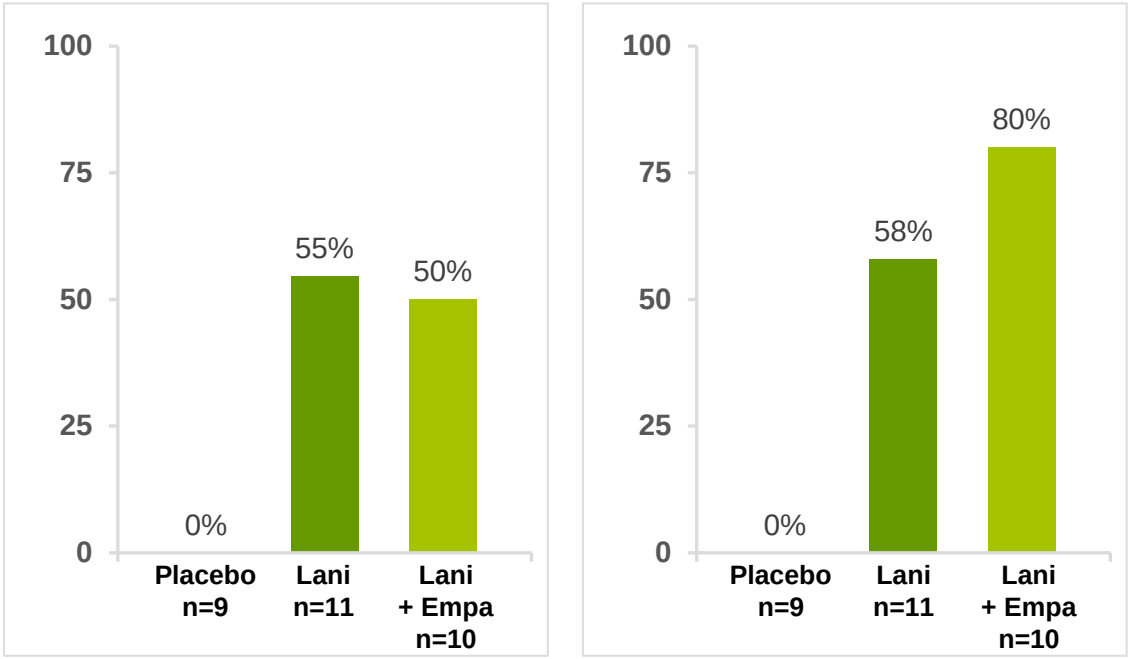
*p<0.05, **p<0.01, ***p<0.001, versus placebo (Mixed Model Repeated Measure [MMRM])

Two patients were not considered in the FAS because not having post-treatment values available:
- 1 patient under placebo who prematurely stopped before Week 4
- 1 patient under lanifibranor who received 'Metformin' as a rescue medication (intercurrent event) before Week 4 (Results were similar including this patient in a sensitivity analysis).

HbA1c < 6.5% Completers, N=30

HbA1c absolute decrease ≥1% Completers, N=30

Percentage of responders at Week 24



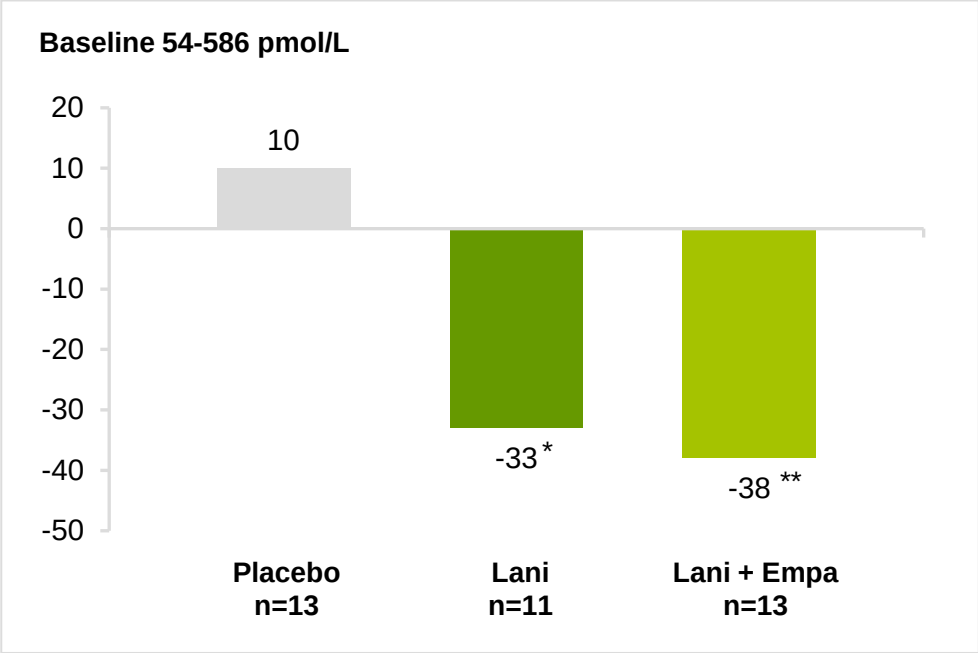
Nine patients were not considered in the Completers set:
- 5 patients under placebo who prematurely stopped before Week 24
- 1 patient under lanifibranor who received 'Metformin' as a rescue medication (intercurrent event) before Week 4
- 1 patient under lani+empa who prematurely stopped before Week 24,1 patient with missing data at Week 24, and 1 patient under lani+empa who significantly modified his/her diet (intercurrent event) before Week 24

Insulin sensitivity was improved, consistent with other studies

Additional improvement was observed in combination with empagliflozin

Insulin – FAS
N=37

LS Mean Relative change (%) from Baseline to Week 24

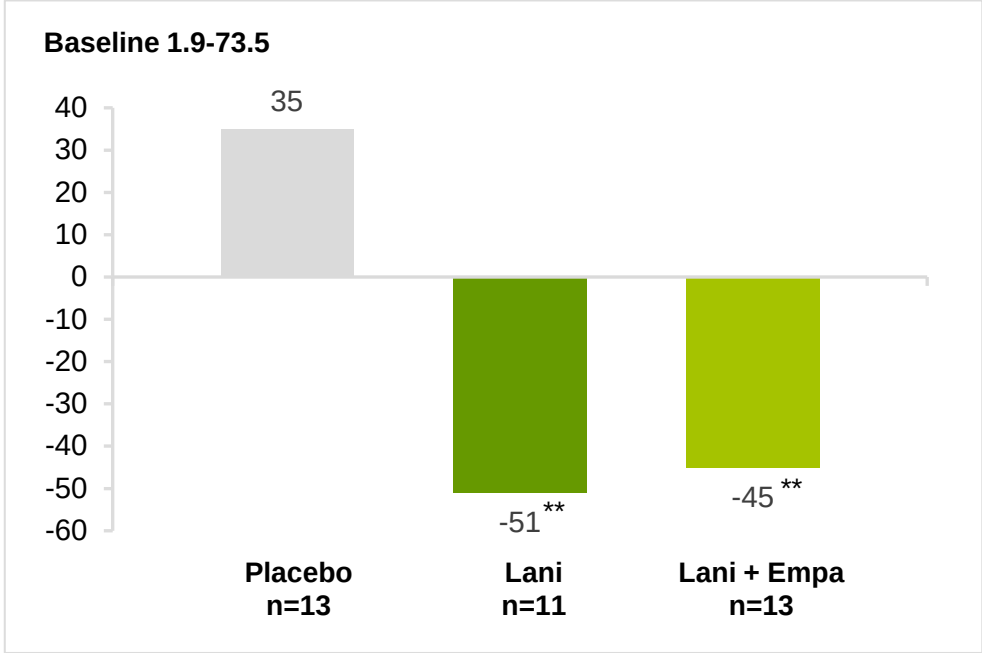


*p<0.1, **p<0.05, versus placebo (MMRM)

Two patients were not considered in the FAS because not having post-treatment values available:
- 1 patient under placebo who prematurely stopped before Week 4
- 1 patient under lanifibranor who received 'Metformin' as a rescue medication (intercurrent event) before Week 4

HOMA-IR – FAS
N=37

LS Mean Relative change (%) from Baseline to Week 24



*p<0.1, **p<0.05, versus placebo (MMRM)

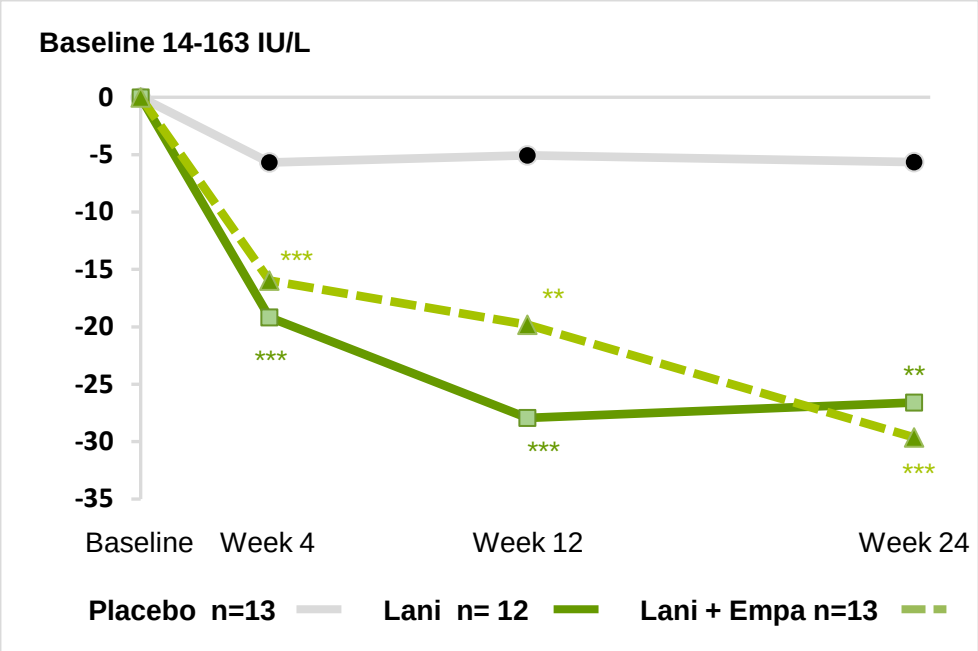
Two patients were not considered in the FAS because not having post-treatment values available:
- 1 patient under placebo who prematurely stopped before Week 4
- 1 patient under lanifibranor who received 'Metformin' as a rescue medication (intercurrent event) before Week 4

Markers of liver injury were significantly improved

Improvement was solely driven by lanifibranor; empagliflozin did not add any additional benefit

ALT – FAS
N=38

LS Mean Relative change (%) from Baseline to Week 24

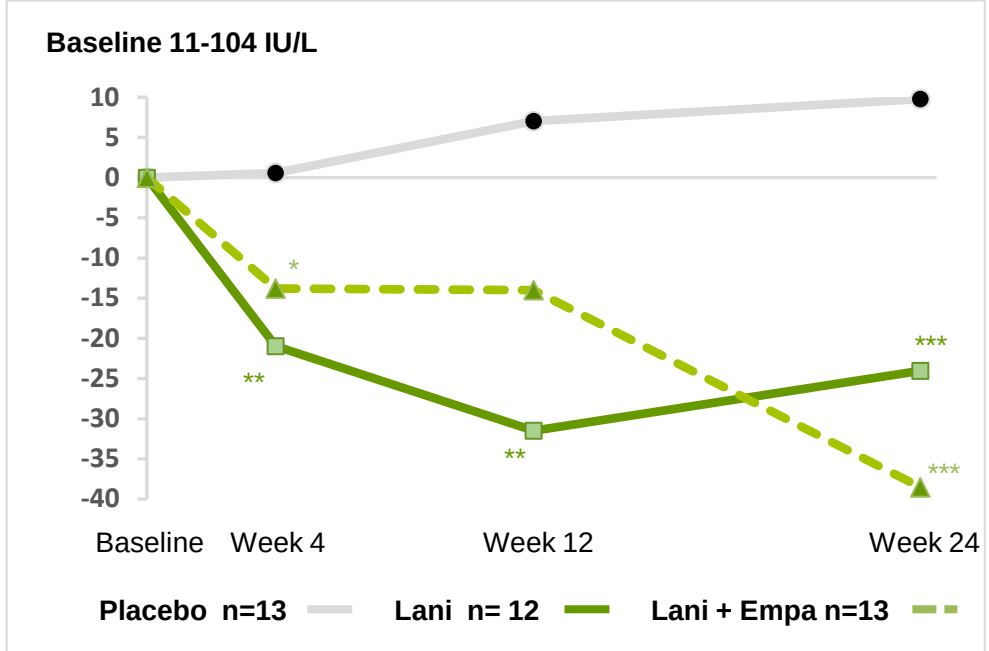


*p<0.05, **p<0.01, ***p<0.001, versus placebo (MMRM)

One patient under placebo was not considered in the FAS because no post-treatment values available (Premature discontinuation before Week 4)

AST – FAS
N=38

LS Mean Relative change (%) from Baseline to Week 24



*p<0.05, **p<0.01, ***p<0.001, versus placebo (MMRM)

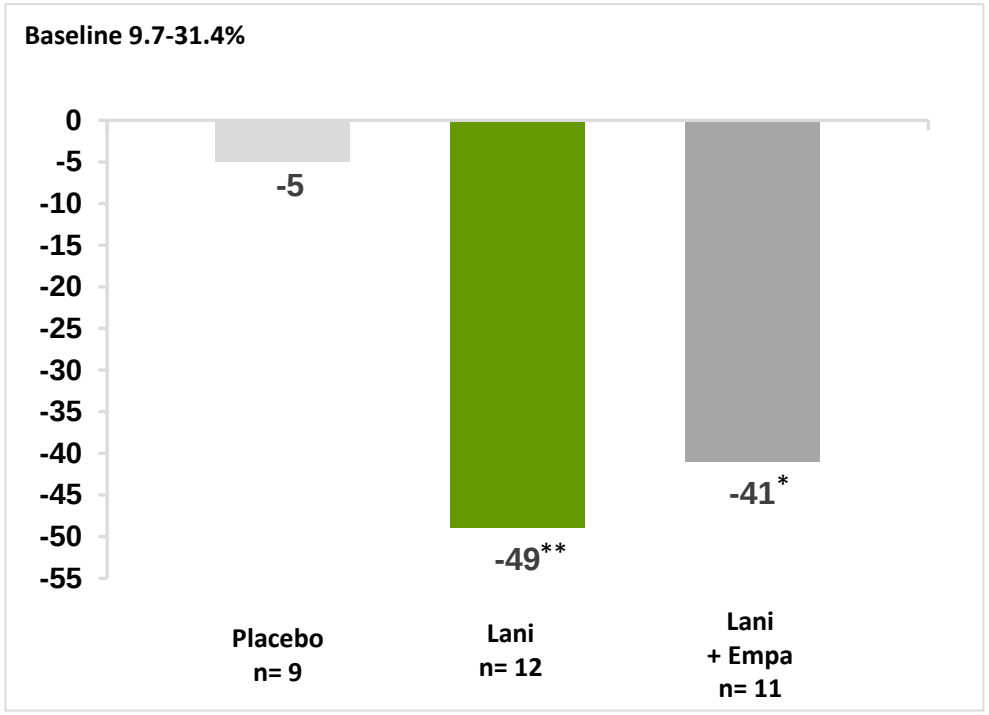
One patient under placebo was not considered in the FAS because no post-treatment values available (Premature discontinuation before Week 4)

Hepatic steatosis measured by MRI-PDFF was reduced significantly

Improvement was observed with lanifibranor alone and in combination with empagliflozin

Liver fat measured by MRI-PDFF, N=32 from Baseline at Week 24

LS Mean Relative change (%)

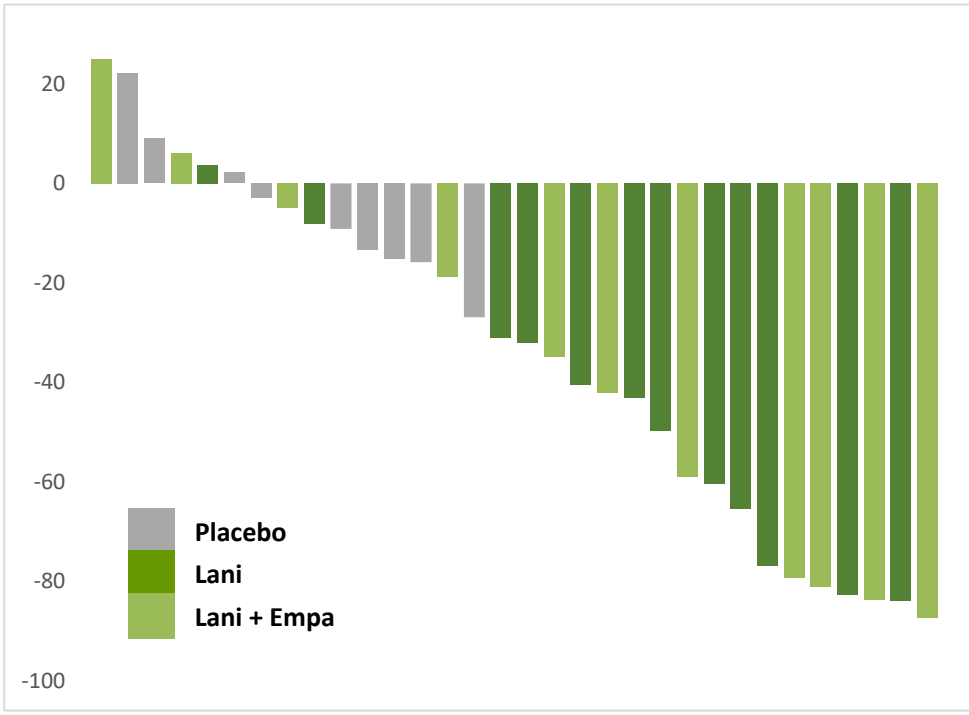


*p<0.05, **p<0.01 versus placebo (ANCOVA – Analysis of Covariance)

Seven patients were not considered in the FAS because no MRI-PDFF values available at Week 24:

- 5 patients under placebo who prematurely stopped before Week 24
- 1 patient under lani+empa who prematurely stopped before Week 24, and 1 patient under lani+empa who significantly modified his/her diet (intercurrent event) before Week 24

Individual Relative changes (%)



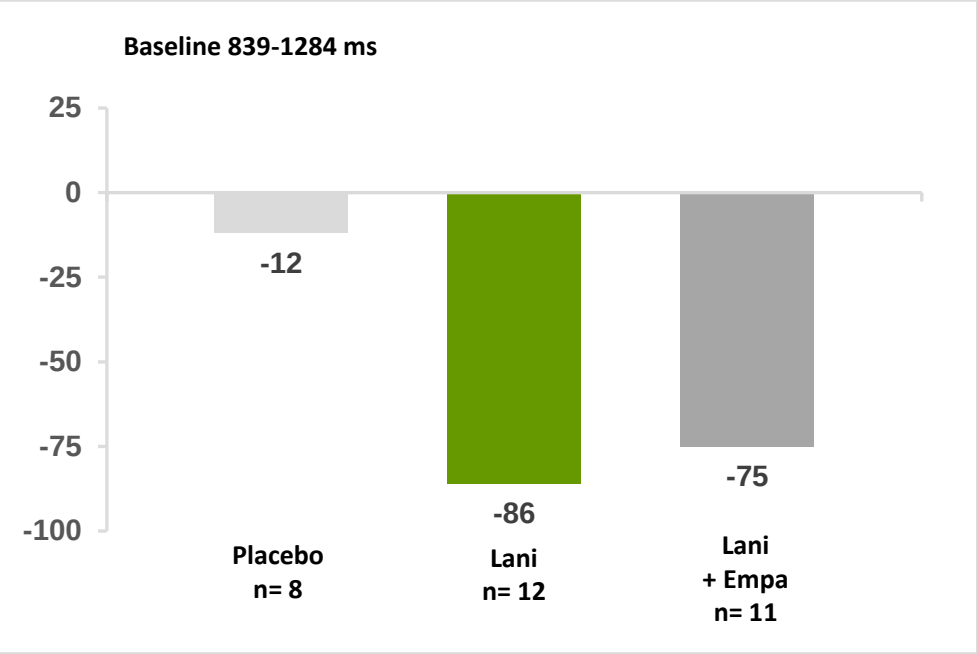
Percentage of responders at Week 24	Placebo (n=9)	Lanifibranor (n=12)	Lanifibranor + empagliflozin (n=11)
Relative reduction ≥ 30%	0%	83%	64%
Absolute reduction of ≥ 5%	11%	67%	64%

Markers of inflammation and fibrosis measured by cT1 were improved

Improvement were similar with lanifibranor alone or in combination with empagliflozin

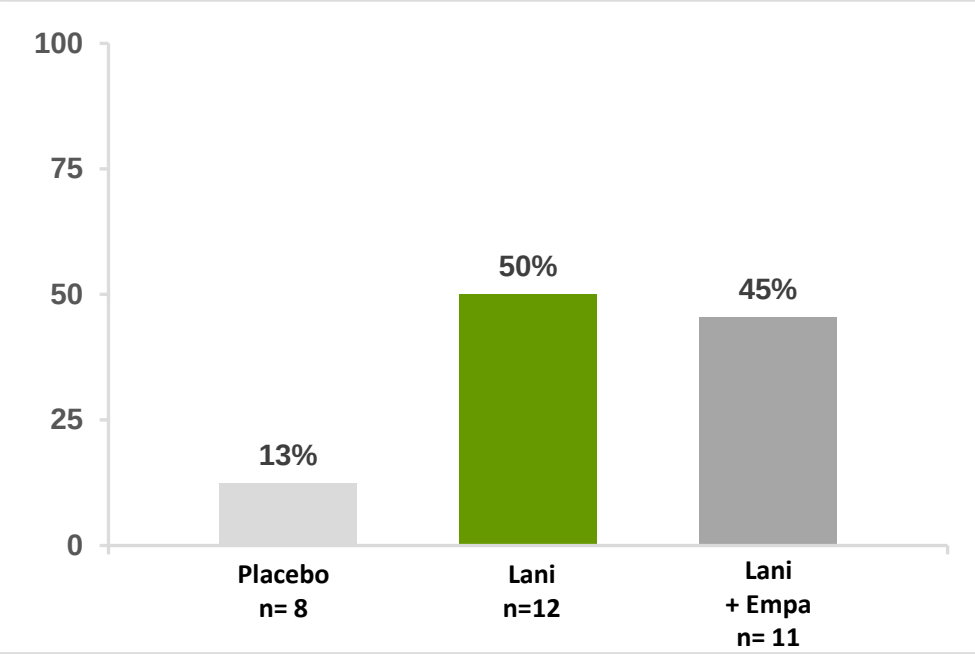
Changes in Inflammation and Fibrosis measured by cT1, N=31

LS Mean Absolute change (ms) from Baseline to Week 24



cT1 Absolute Reduction of >80 ms

Percentage of responders at Week 24



Eight patients were not considered in the FAS because of no cT1 values available at Week 24:

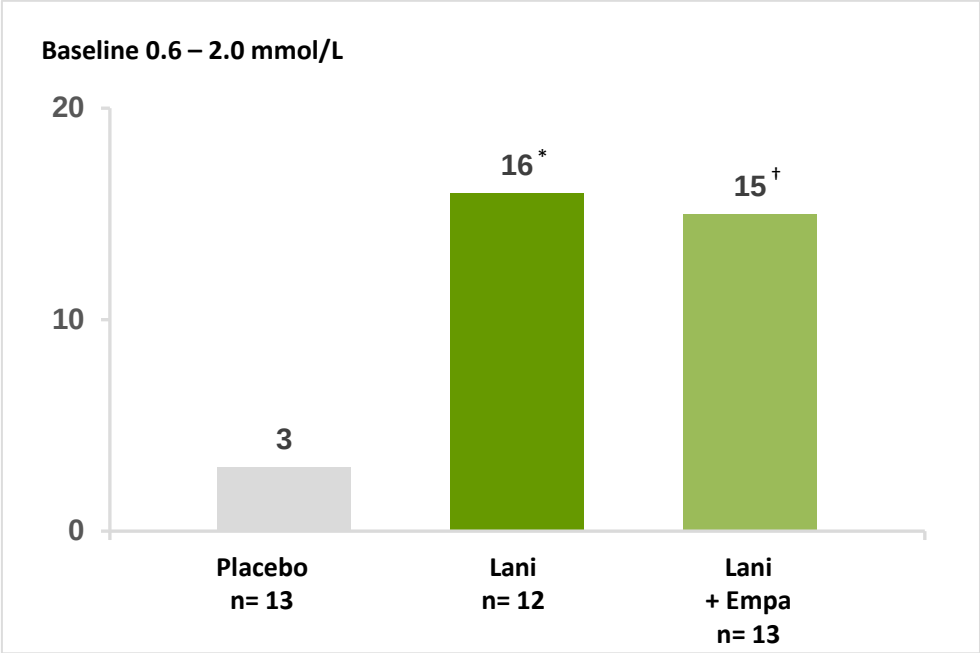
- 5 patients under placebo who prematurely stopped before Week 24 and 1 patient under placebo with a missing value at Week 24
- 1 patient under lani+empa who prematurely stopped before Week 24, and 1 patient under lani+empa who significantly modified his/her diet (intercurrent event) before Week 24

HDL-C and adiponectin improved

Improvement were similar with lanifibranor alone or in combination with empagliflozin

HDL-C, N=38

LS Mean Relative change (%) from Baseline to Week 24

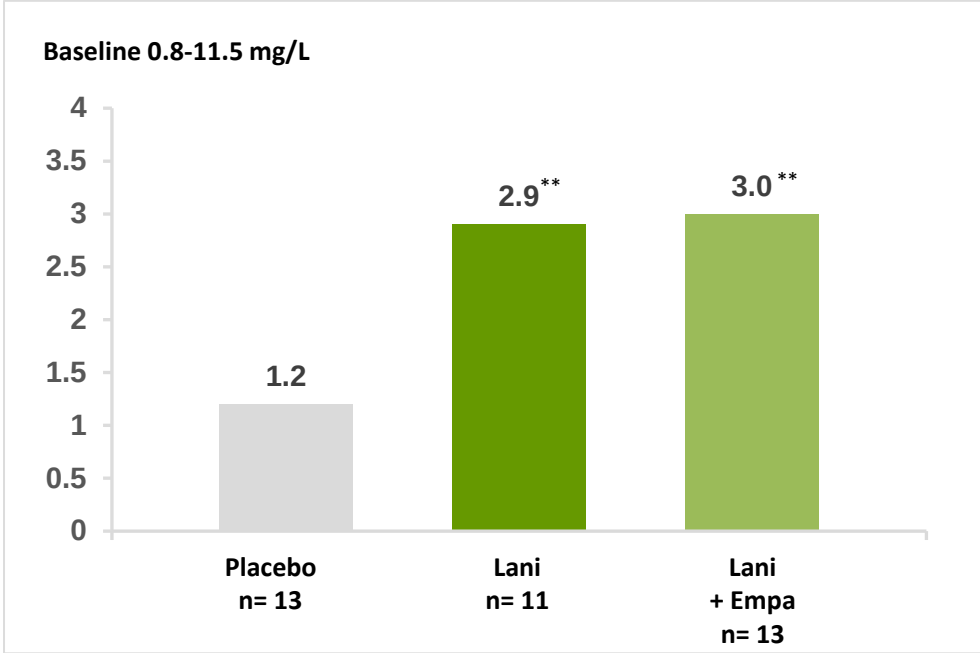


*p<0.10, versus placebo (MMRM) † p<0.01, versus baseline (MMRM)

One patient under placebo was not considered in the FAS because of no post-treatment HDL-C values available (premature discontinuation before Week 4)

Adiponectin, N=37

LS Mean Fold change from Baseline to Week 24



**p<0.01, versus placebo (MMRM)

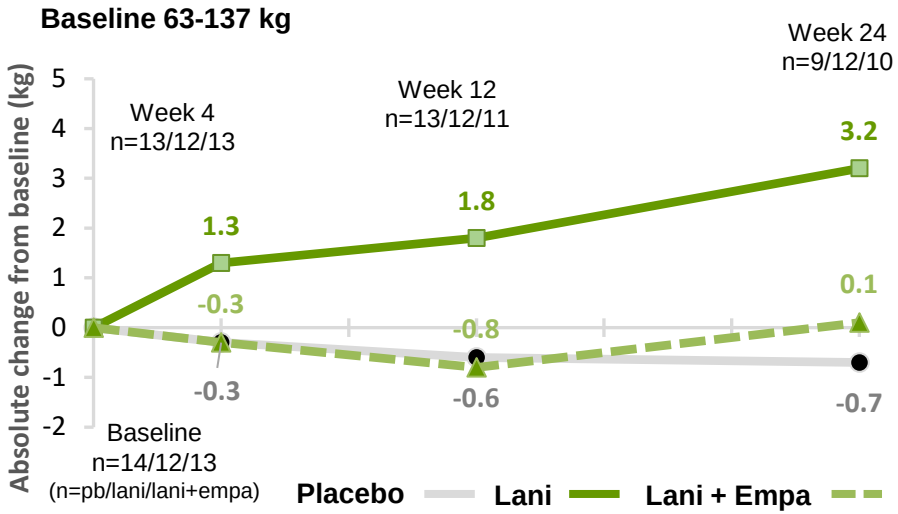
Two patients were not considered in the FAS because not having post-treatment adiponectin values available:

- 1 patient under placebo who prematurely stopped before Week 4
- 1 patient under lanifibranor who received 'Metformin' as rescue medication (intercurrent event) before Week 4

SGLT2 inhibitor empagliflozin mitigates lanifibranor weight gain

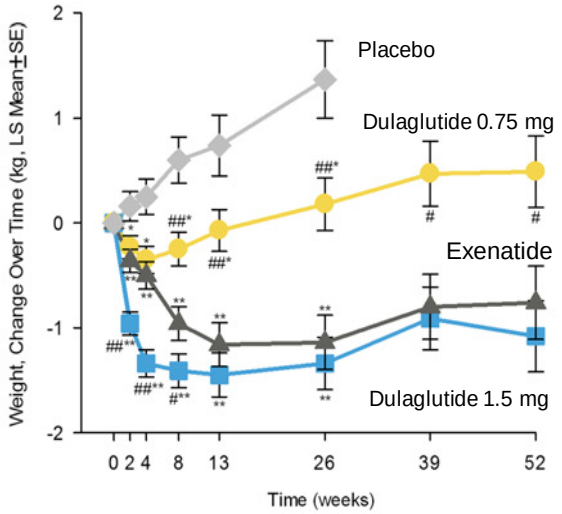
Meta-analysis data suggest that GLP-1s have a similar effect when combined with PPARs

Lanifibranor + empagliflozin



- In the LEGEND trial, albeit with a small n, results suggested that empagliflozin, an **SGLT2i, completely mitigated the lanifibranor weight gain profile over 24 weeks**

Pioglitazone + GLP1 or SGLT2i



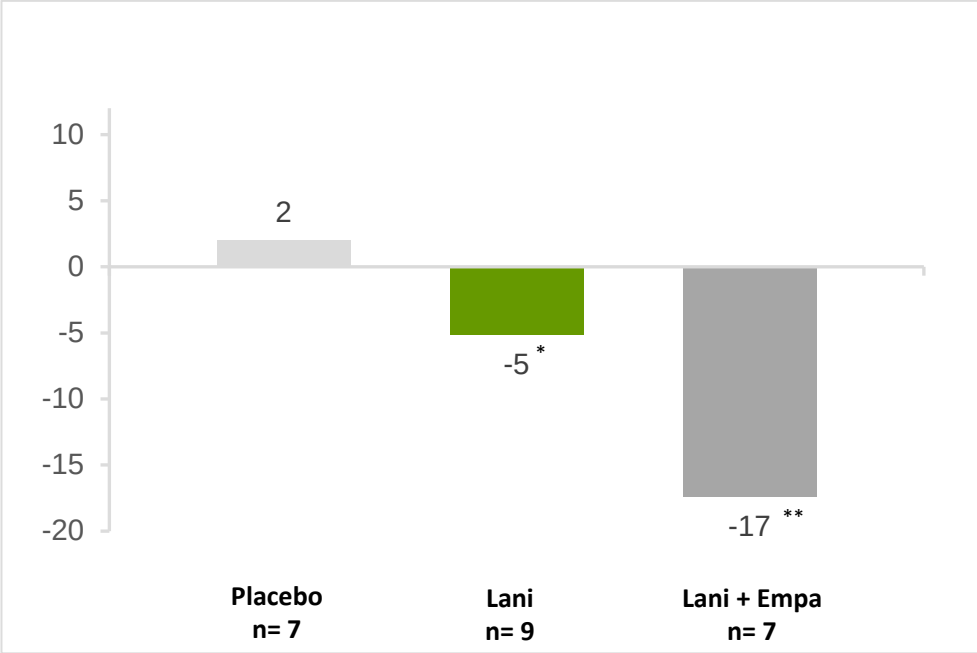
- Recently published meta-analyses suggested that pioglitazone with GLP1 or SGLT2i is associated with increased weight loss and reduced risk of heart failure compared with monotherapy

Source: Anson. 2024. Diabetes, Obesity, and Metabolism; KOL Interviews; Inventiva Analysis.

Lanifibranor alone and in combination with empagliflozin leads to a shift towards metabolically healthy adipose tissue

Ratio VAT/SAT, N=23

LS Mean Relative change (%) from Baseline to Week 24



SAT=Subcutaneous Adipose Tissue, VAT=Visceral Adipose Tissue

* p=0.08, **p<0.05, versus placebo (ANCOVA)

Sixteen patients were not considered in the FAS because of no VAT/SAT values available at Week 24:

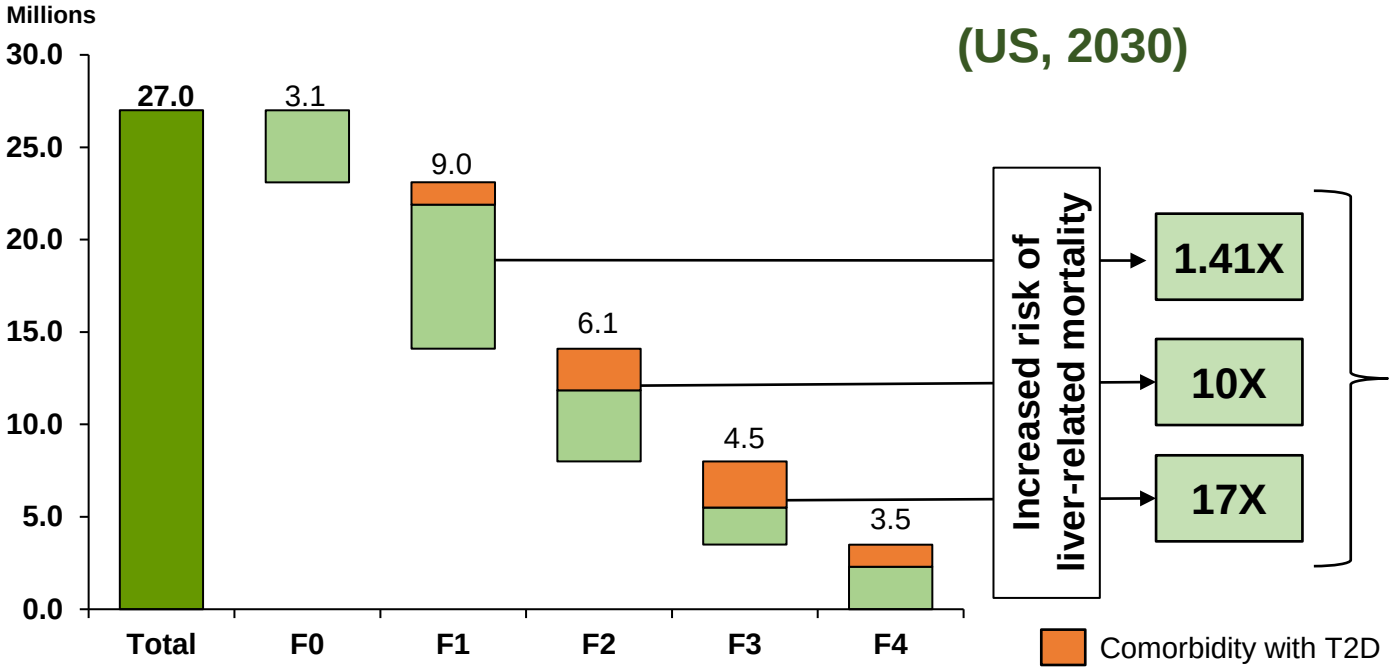
- 5 patients under placebo and 1 patient under lani+empa who prematurely stopped before Week 24
- 2 patients under placebo / 3 patients under lanifibranor / 5 patients under lani+empa with missing values at Week 24

Lanifibranor for the Treatment of MASH

MASH with advanced fibrosis represents a high unmet medical need

Patients with MASH and type 2 diabetes are at higher risk

MASH U.S. Prevalence and Progression Estimates by Fibrosis Stage (US, 2030)



- 22% of patients with F3 fibrosis progress to cirrhosis within 2yrs
- T2D is an independent predictor of fibrosis progression
- T2D is an independent risk factor for mortality in patients with NAFLD

Despite Rezdiffra approval, treatment needs still exist for patients with advanced fibrosis…

- Rezdiffra™ 's published rates of fibrosis improvement are indirect and at best modest with 12% effect size
- Rezdiffra™ has no impact on glycemic parameters
- Rezdiffra™ does not appear to synergize with incretins, where use is growing in obesity
- Pipeline agents targeting FGF21 are injectable and have an unfavorable GI AE profile
- MASH patients need more than one oral option available to them

Source: Estes. 2018. Hepatology; Sanyal. EASL. 2024; Lomanoco Diabetes Care 2021;44(2):399–406; *Angulo P, et al. Gastroenterology. 2015;149:389-397. 2. Loomba R, Adams L. Hepatology. 2019;70(6):1885-1888; Noureddin et al. AASLD 2024; KOL Interviews; Inventiva Analysis.*

NAFLD: Nonalcoholic fatty liver disease; MASH: Metabolic dysfunction-associated steatohepatitis

Lanifibranor is well-positioned in the MASH market

Multiple competitive advantages vs. other therapies

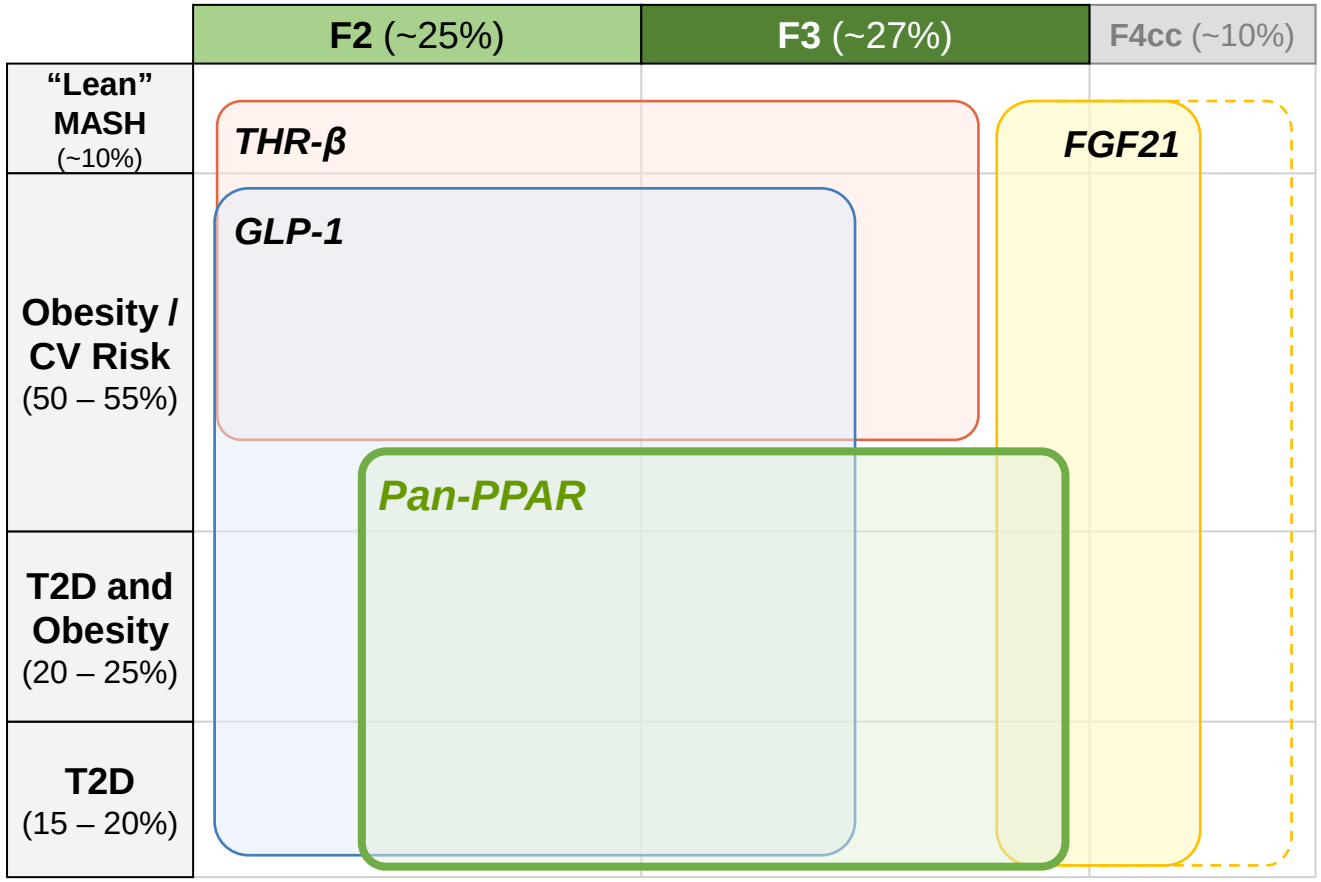
	inventiva	Madrigal / VIKING	akero / 89bio	Boehringer Ingelheim / novo nordisk / Lilly
	pan-PPAR	***THR-β***	***FGF-21***	***GLP-1***
Route of administration	**Oral**	**Oral**	**Injectable**	**Injectable**
Fibrosis improvement	Direct activity seen at 6 months	Indirect seen after 12 months	Direct activity seen at 6 months	Indirect seen with sema. after 18 month. Reported by BI & Lilly after 12 months
MASH resolution	✓	✓	✓	✓
Insulin resistance	✓	✗	✓	✓
Tolerability	Limited dropout Limited GI side effects	Limited dropout GI side effects on initiation	High dropout due to GI side-effects & injections	High dropout due to GI side-effects & injections

Lanifibranor

- Data suggests fibrosis improvement, MASH resolution and cardiometabolic benefits
- Balanced *pan-PPAR* agonists have a favorable insulin sensitivity profile, manageable AEs and oral route of administration making them a promising candidate for patients with advanced fibrosis and/or for combination therapy, particularly in patients with comorbid T2D

Lanifibranor could play a key role in several high unmet need segments in MASH

Priority patient segment based on KOL feedback at time of lanifibranor launch



Pan-PPAR agonists have **strong antifibrotic and insulin sensitivity profile, and the AEs are manageable**

FGF21s ***likely to be used in advanced patients*** due to GI side effects, bone density reduction and injectable RoA

THR-β agonists have modest efficacy best suited for early-stage patients,

GLP-1s are modestly effective anti-fibrotic, but key backbone therapy with cardiometabolic benefits

Source: KOL Interviews; Inventiva Analysis.

Lanifibranor: well positioned in MASH, especially in patients with T2D

Based on patient type, can be used as a monotherapy or in combination with anti-diabetic agents

Lanifibranor Profile

Improvements observed in Fibrosis, CV, and Metabolic Markers

- Superior fibrosis improvement to Rezdiffra™*
- Oral dosing differentiates from FGF21 and incretin agents
- Sustained improvements in hepatic, CV, and glycaemic biomarkers
- Synergy with SGLTs agents

Comprehensive impact on MASH and associated cardiometabolic morbidities

Balanced Safety Profile Without GLP-1 overlapping AEs

- Manageable safety and tolerability issues and no carry-over of AEs and toxicity associated with single and dual PPAR agonists
- Weight gain is limited to one-third of patients with lanifibranor, plateaus after 6-8 months, and did not impact efficacy or metabolic parameters
- Limited overlap of AEs associated with GLP-1s

Clinical results suggest a positive risk-benefit profile

Top-Line Results targeted H2 2026

- $375M multi-tranche financing from existing and new investors in 2024 marks the largest financing of a French biotech and will fully fund Inventiva through NATiV3 TLR if all tranches close
- >90% of patients enrolled in the main cohort, with last patient randomized expected in H1 2025 and Top-Line Data in H2 2026

Lanifibranor could be the second liver-directed therapy approved for MASH

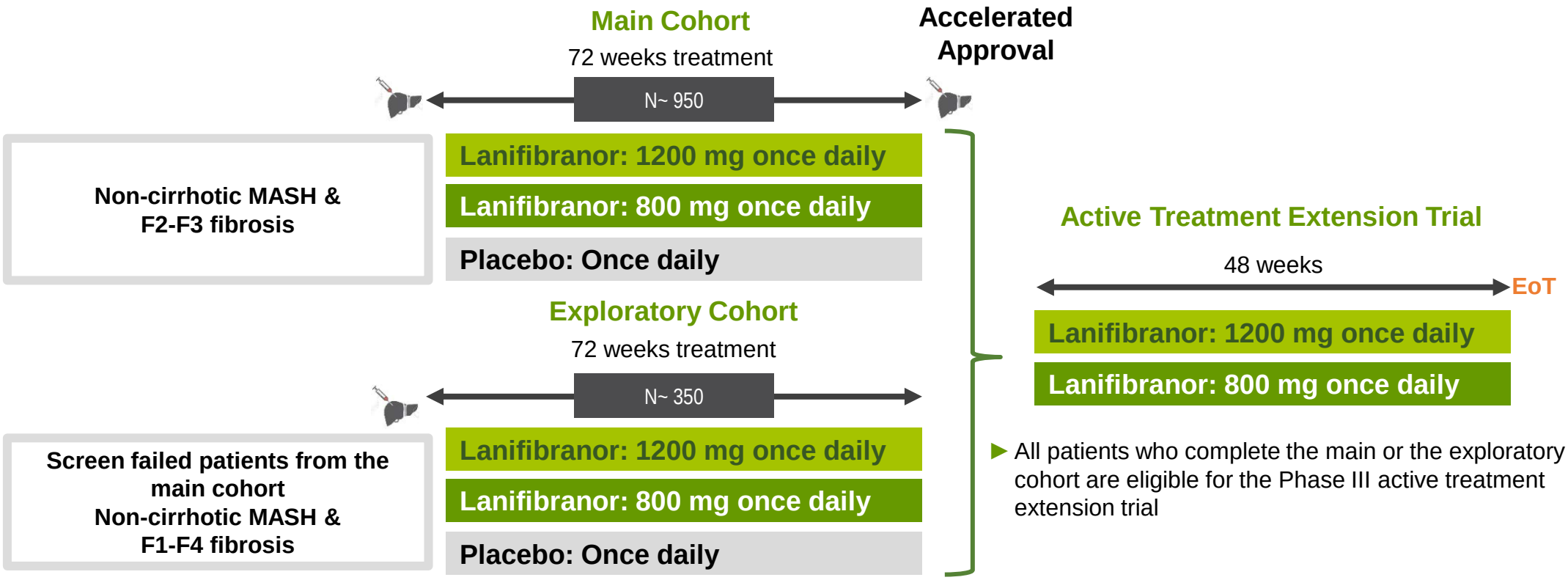
**Not a head to head comparison*

Source: KOL Interviews; Inventiva Analysis.

NATiV3 Phase III Study of lanifibranor in MASH

NATiV3 recruitment is nearly complete

Trial design mirrors the successful Phase IIb study



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

- Primary endpoint: Composite endpoint of patients having both MASH resolution and one stage fibrosis improvement
- Key secondary endpoints: MASH resolution and no worsening of fibrosis, Fibrosis improvement and no worsening of MASH
- GLP1: Patients under a stable dose of GLP1-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
- Over 1200 patients randomized: main cohort ~95% enrolled
- In a blinded analysis conducted comparing Phase IIb and NATiV3, baseline values and magnitude of changes in relevant biomarkers are consistent

Baseline characteristics of NATiV3 versus NATIVE Phase IIb are aligned with expectations

- Status September 10, 2024

		Exploratory N=261	Main N=798	Randomized N=1059	NATIVE N=247
Actual Diabetic status (eCRF)	N	259	795	1054	247
	No	152 (59%)	355 (45%)	507 (48%)	144 (58%)
	Yes	107 (41%)	440 (55%)	547 (52%)	103 (42%)
Actual Fibrosis stage (Perspectum)	N	260	798	1058	-
	1-3	190 (73%)	7 (1%)	197 (19%)	F0: 6 (2%) F1: 53 (22%)
	2	1 (0%)	243 (30%)	244 (23%)	102 (41%)
	3	1 (0%)	547 (69%)	548 (52%)	86 (35%)
	4	68 (26%)	1 (0%)	69 (7%)	0 (0%)
GLP-1 concomitant to Baseline	N	261	798	1059	-
	No	228 (87%)	692 (87%)	920 (87%)	-
	Yes	33 (13%)	106 (13%)	139 (13%)	-
GLP-1 post Baseline	N	261	798	1059	-
	No	252 (97%)	742 (93%)	994 (94%)	-
	Yes	9 (3%)	56 (7%)	65 (6%)	-
SGLT2i concomitant to Baseline	N	261	798	1059	247
	No	233 (89%)	725 (91%)	958 (90%)	240 (97%)
	Yes	28 (11%)	73 (9%)	101 (10%)	7 (3%)
SGLT2i post Baseline	N	261	798	1059	-
	No	259 (99%)	781 (98%)	1040 (98%)	-
	Yes	2 (1%)	17 (2%)	19 (2%)	-

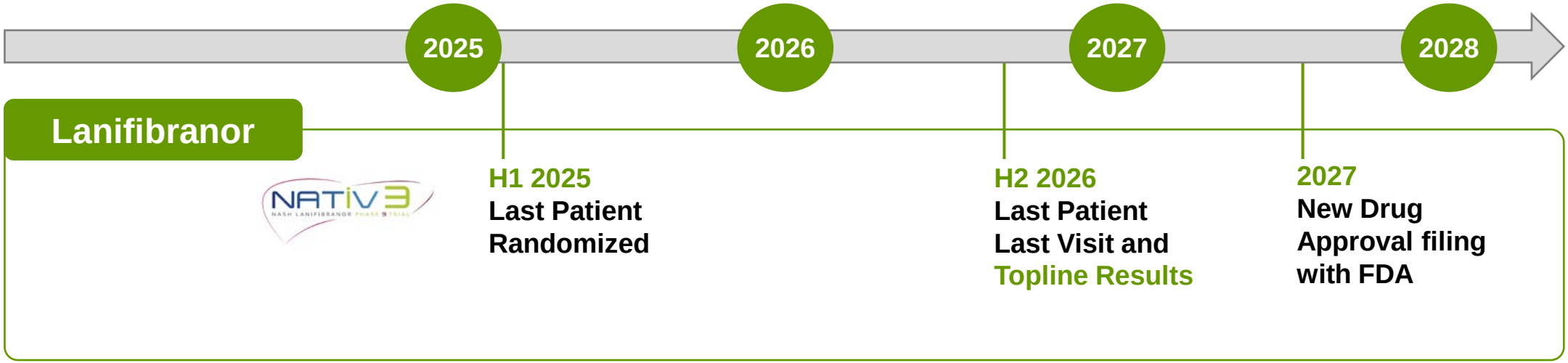
		Exploratory N=261	Main N=798	Randomized N=1059	NATIVE N=247
Weight (kg)	N	261	798	1059	247
	Mean ± SD	94.9 ± 21.3	98.7 ± 23.6	97.8 ± 23.1	93.3 ± 18.8
	Median	95	96	95	92
	Min; Max	44; 163	46; 249	44; 249	50; 147
BMI (kg/m2)	N	260	798	1058	247
	Mean ± SD	34.2 ± 7.0	35.3 ± 7.0	35.0 ± 7.0	32.9 ± 5.4
	Median	33	34	34	32
	Min; Max	20; 64	21; 77	20; 77	21; 45
BMI class	Non obese	65 (25%)	175 (22%)	240 (23%)	86 (35%)
	Obese	195 (75%)	623 (78%)	818 (77%)	161 (65%)

- Higher percentage of patients with T2D in the Phase III versus the Phase IIb: 55% vs 42%. The effect size of lanifibranor in the Phase IIb on the primary efficacy endpoint of NATiV3 (MASH resolution and fibrosis improvement) was higher in patients with T2D: 21% and 26% for lanifibranor 800 and 1200 mg/day in patients with T2D versus 7% and 22% in patients who did not have diabetes
- NATiV3 expected to generate data of lanifibranor in combination with GLP1 and with SGLT2 inhibitors
- Blinded analyses of Phase III data suggest preliminary biomarkers in line with Phase IIb NATIVE study results

NATiV3 data is expected in 2026

Lanifibranor could be the second oral liver-directed agent for the treatment of MASH if approved

Targeted timeline for anticipated catalysts



Financing	Targeted Timeline to Potential Launch
A $400M+ Financing in October 2024 capitalized Inventiva to execute on the clinical trial through to NDA[1]	***Lanifibranor could be the second oral, liver-targeted agent on the market in 2028*** *if NDA is filed and approved.* *Best-in-class fibrosis, cardiovascular, and metabolic benefits.*

(1) In October 2024, Inventiva announced a multi-tranche equity financing of up to €348 million, subject to conditions, and up to $30 million in milestone payments. If all tranches close, the proceeds are expected to fully fund the development of lanifibranor through its Phase III trial and potential NDA filing.

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