Developing innovative therapies in NASH and MPS

Corporate Presentation

November 2021

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DISCLAIMER

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this presentation, including statements regarding our future financial condition, results of operations, business strategy and plans, and objectives of management for future operations, as well as statements regarding industry trends, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential" "predict," "project," "should," "target," or "will" or the negative of these terms or other similar expressions.

We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, among other things: the success, cost and timing of our product development activities and clinical trials; our expectations about the timing of achieving regulatory approval and the cost of our development programs; our ability to obtain funding for our operations, including funding necessary to complete further development of our product candidates; the commercialization of our product candidates, if approved; our plans to research, develop and commercialize our product candidates; our ability to attract collaborators with development, regulatory and commercialization expertise; our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates; future agreements with third parties in connection with the commercialization of our product candidates; our ability to maintain, expand, protect and enforce our intellectual property portfolio; our ability to operate our business without infringing, misappropriating or otherwise violating the intellectual property rights of third parties; the size and growth potential of the markets for our product candidates, and our ability to serve those markets; the rate and degree of market acceptance of our product candidates; regulatory developments in the United States, Europe and other jurisdictions; our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately; the success of competing therapies that are or may become available; and our ability to attract and retain key scientific or management personnel.

For additional information in relation to such factors, risks and uncertainties, please refer to the Universal Registration Document for the year ended December 31, 2020 filed with the Autorité des Marchés Financiers on March 15, 2021, the Annual Report on Form 20-F for the year ended December 31, 2020 filed with the Securities and Exchange Commission on March 15, 2021, Amendment No. 1 to the Annual Report on Form 20-F for the year ended December 31, 2020 filed with the Securities and Exchange Commission on March 24, 2021, as well as the half-year financial report for the six months ended June 30, 2021 as well as our other documents or reports that we may file with or furnish to the SEC from time to time, available at www.sec.gov. New risk factors emerge from time to time and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements. You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this presentation, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

Inventiva in a nutshell

- Clinical stage biotech with focus on **oral small molecules for the treatment of NASH, MPS, and other diseases with high unmet medical needs**

- **Two unencumbered late stage assets**
  - **Lanifibranor:** only pan-PPAR agonist in clinical development for NASH; **positive Phase IIb topline data** announced in June 2020 and **Breakthrough Therapy Designation granted by FDA** in October 2020. **Pivotal Phase III initiated in Q3 2021**
  - **Odiparcil:** potential for first orally available therapy for MPS; **positive Phase IIa trial results** in adult patients with MPS VI published in December 2019

- **A clinical stage collaboration with AbbVie**
  - Cedirogant RORγ program with potential in several auto-immune indications
  - In Phase Ib study, **cedirogant achieved clinical proof of concept** as an oral psoriasis agent and AbbVie plans to move the asset forward to a **Phase IIb dose-ranging study planned to start in November 2021**
  - Inventiva eligible to receive milestone payments and sales royalties

- **Compelling early stage pipeline**
  - YAP-TEAD oncology program in pre-clinical stage, approaching clinical candidate selection

- **R&D capabilities** including wholly-owned 'pharma scale' discovery facilities with a **discovery engine** focused on nuclear receptors, transcription factors and epigenetic targets
  - compound library of 240,000 molecules, 60% of which are proprietary

- **Strong U.S. and European shareholder base and experienced senior management** team

- Cash position currently allowing a **runway through Q1 2023**

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

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

Jean Volatier, MA, CFO

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

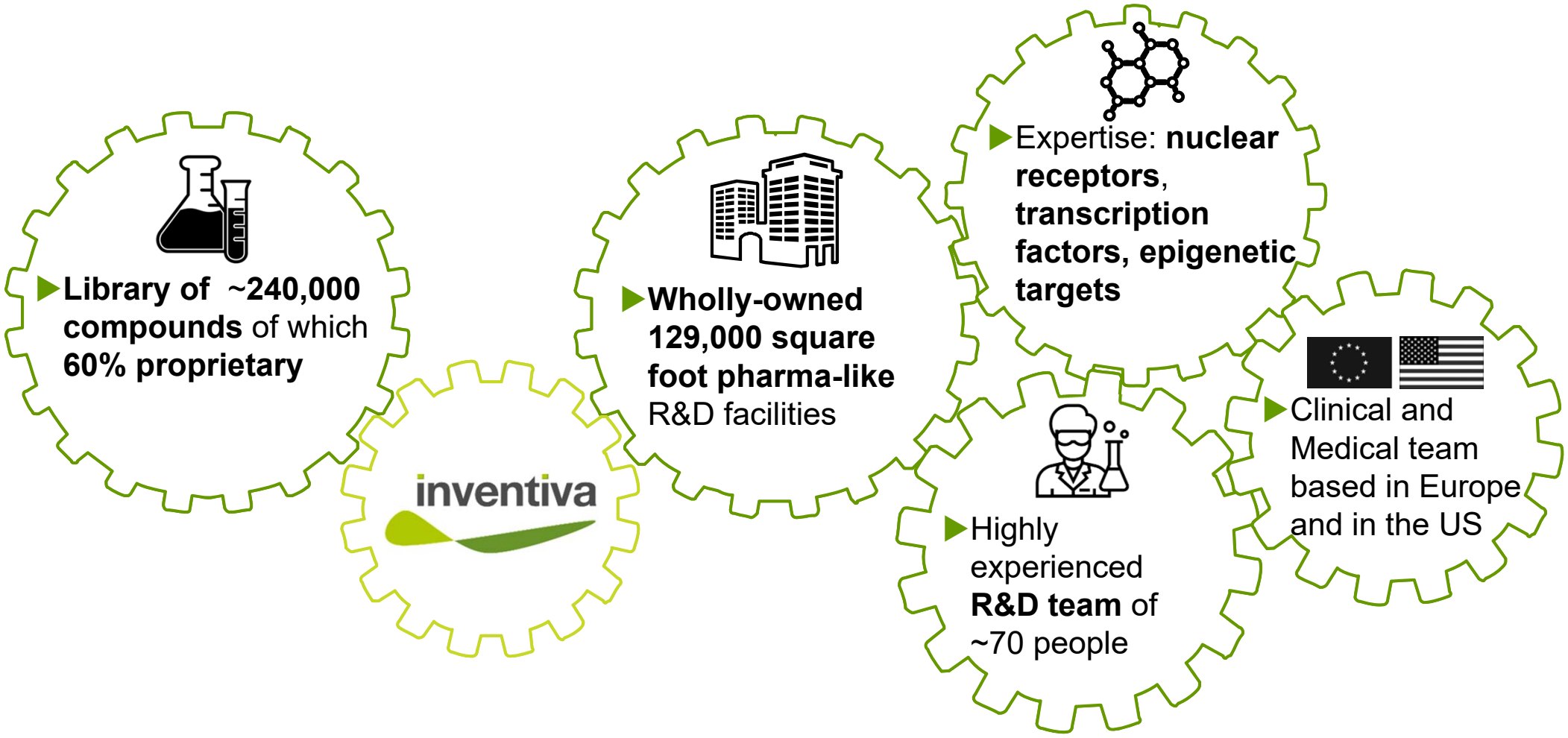
Michael Cooreman, MD, CMO

- Gastroenterologist-hepatologist with numerous U.S.-based positions as CMO and Executive Director in global roles at leading pharmaceutical and biotechnology companies, including Takeda Pharmaceuticals, Merck, Mitsubishi Tanabe, ImmusanT and Novartis, covering the four major regulatory regions U.S., EU, Japan and China
- U.S. based

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

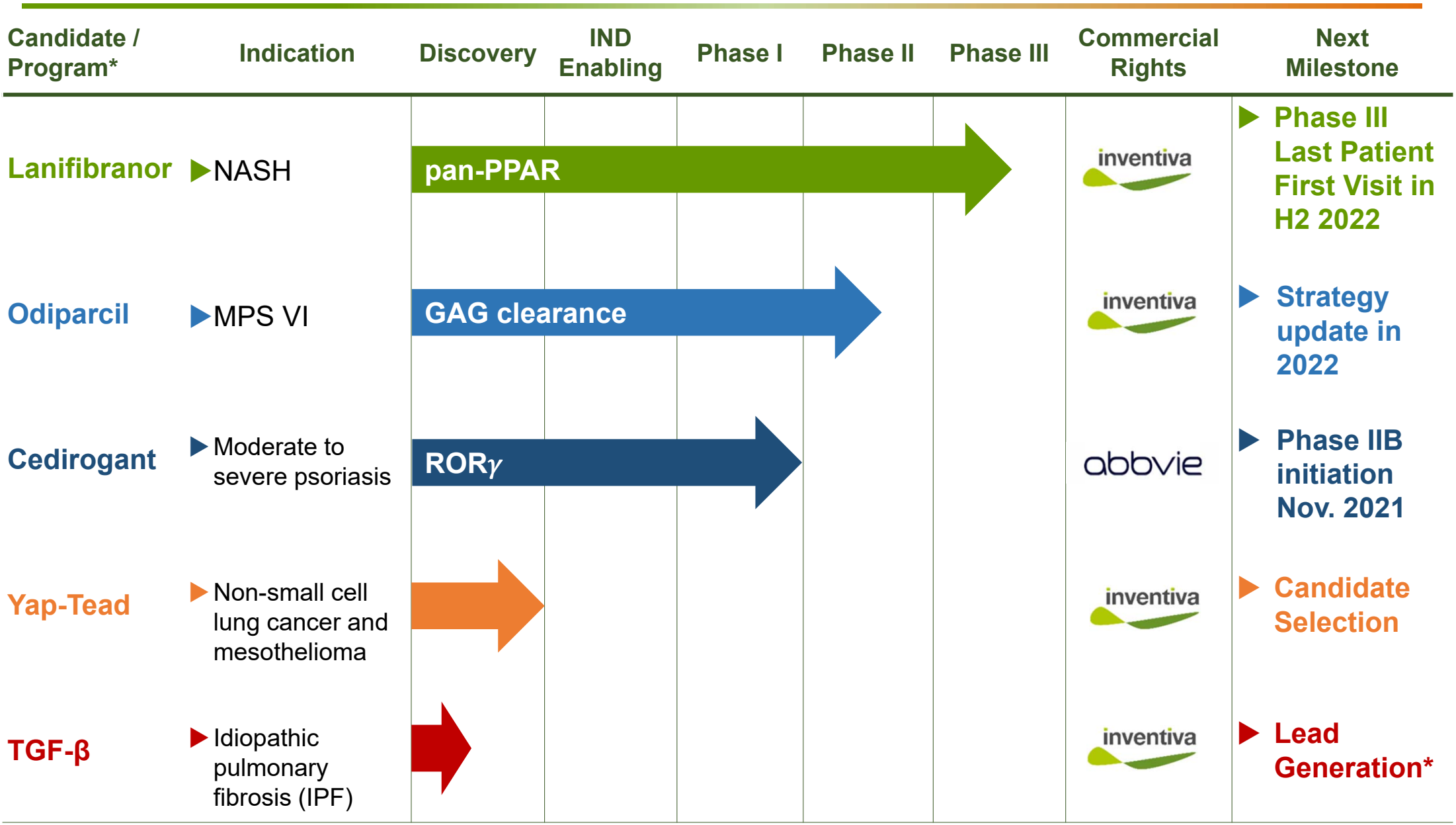
- Former buyside portfolio manager and analyst for +15 years in public equities and VC
- U.S. based

Oral small molecule-focused discovery engine targeting nuclear receptors, transcription factors and epigenetic modulation



Power of discovery engine underpins deep pipeline of clinical and discovery stage assets

Deep pipeline



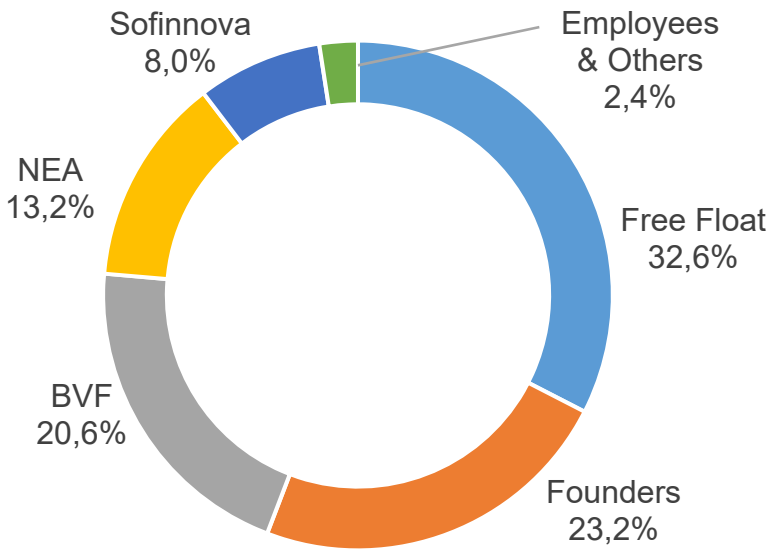
* Lead generation means identifying molecules in anticipation of selecting candidates

Key financials and shareholder base

Key financials

ISIN code	FR0013233012 / US46124U1079
Market	Euronext Paris / Nasdaq GM
Shares outstanding	40 873 551
Market cap (November 1, 2021)	Euronext Paris: €527m Nasdaq Global Market: $611m
Cash position (as of June 30,2021)	€93.6m (vs €105.7m as of December 31, 2020)(1) Current expected cash runway through Q1 2023 (including the $30m ATM executed Sept. 23)
Revenues (H1 2021)	€0.1m compared to €0.2m in H1 2020
R&D expenditures (H1 2021)	€19.1m compared to €12.6m in Q1 2020

Shareholder base



Analyst coverage

Jefferies	L. Codrington / M. J. Yee
Guggenheim	S. Fernandez / T. Soni
HC Wainwright	E. Arce
Roth Capital	Z. Jallah
LifeSci Capital	P. Dolezal
KBC	L. Van Steenhuyse
Société Générale	D. Le Louët
Bryan Garnier	JJ. Lefur
Portzamparc	M. Kaabouni

(1) The cash position as of December 31, 2020 amounted to €113.7 million published in the press releases on March 4, 2021, May 12, 2021 and July 28, 2021 included cash and cash equivalents as well as short-term deposits which were included in the category "other current assets" in the IFRS statement of financial position. Under IFRS, the variation of short-term deposits and its related exchange effects are reflected in the line items "net cash flows from investing activities" for €5.9 million and "exchange gains (losses)" for €1.4 million, respectively.

Lanifibranor in Nonalcoholic Steatohepatitis (NASH)

Lanifibranor: the only pan-PPAR agonist in clinical development for the treatment of NASH

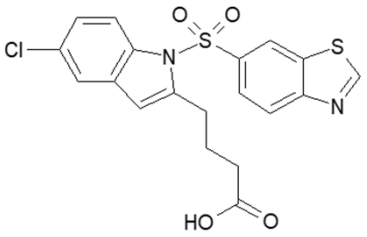
- **Moderate and balanced pan-PPAR agonist activity** (PPARα, PPARγ and PPARδ) with differentiated chemical structure
- **Once daily oral administration**
- **Effects observed** on insulin-sensitivity, dyslipidemia, steatosis, ballooning, inflammation, hepatic fibrosis and cirrhosis in pre-clinical models
- **Phase IIa(1) trial demonstrated pan-PPAR agonist activity,** supporting dose selection for NASH Phase IIb clinical trial
- **Positive Phase IIb trial topline results announced in June 2020** and published by the New England Journal of Medicine
- **Favorable tolerability profile** observed in:
  - 24-months rodent and 12-month monkey studies leading to **PPAR class clinical hold lifted** by FDA
  - **Non-clinical toxicology package considered by FDA as complete and acceptable to support NDA filing** for the treatment of NASH and improvement of liver fibrosis
  - Phase I trials with more than **200** healthy volunteers(2) and Phase IIa trial with **47** TD2M patients
  - Over **250** patients treated for 24 or 48 weeks in Phase IIb clinical trials in NASH and other indications
  - In connection with these trials, lanifibranor underwent a total of **7 DSMB reviews without changes recommended to the different trial protocols**
- Composition of matter patent delivered in 55 countries and method of use patent granted in the U.S., China and in the EU: **limit of exclusivity in the U.S. is 2035**
- **FAST Track** (including in NASH patients with compensated cirrhosis) **and Breakthrough Therapy** designations granted by FDA

(1) Conducted by Abbott prior to our founding; (2) Including 125 healthy volunteers in the Phase I conducted by Abbott prior to our founding

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

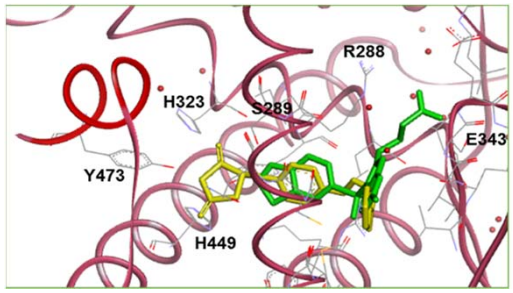
LANIFIBRANOR

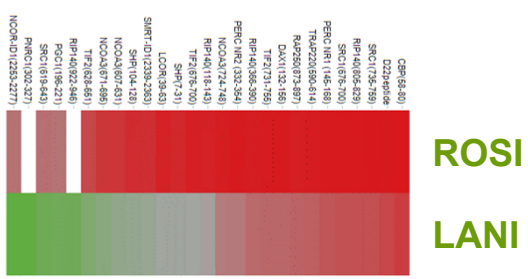
Differentiated oral small molecule …



- Small molecule that activates all three PPAR isoforms
- Differentiated chemical structure with once daily oral administration
- Offered in two dosage forms (800 mg, 1200 mg)

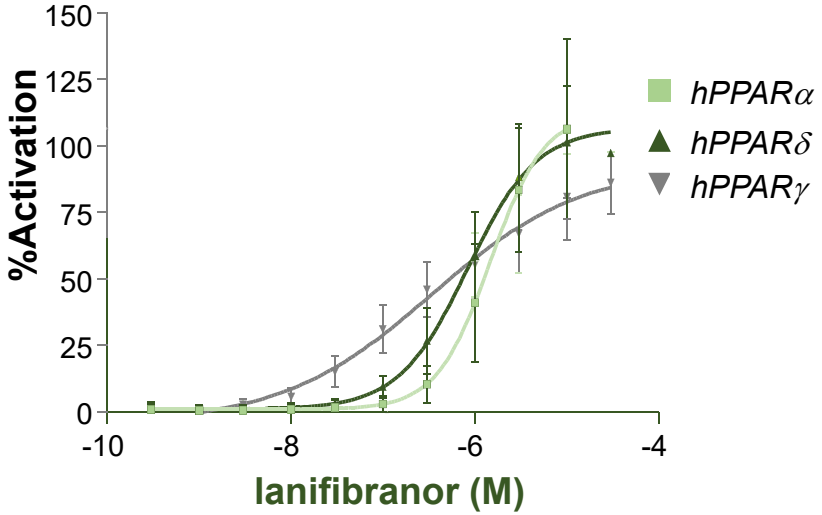
… that binds differently than glitazone to PPARγ





- Induces different coactivator recruitment^^

Moderate and balanced pan-PPAR agonist activity



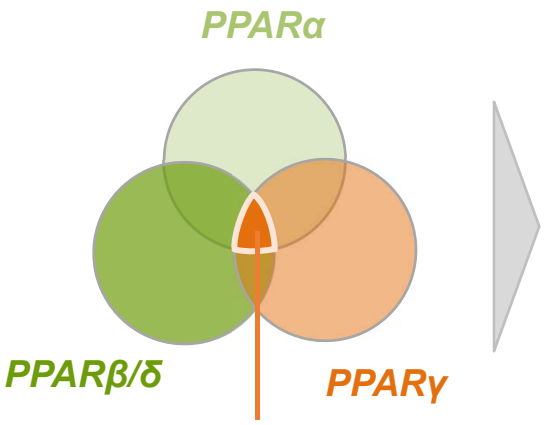
Compound	PPARα EC50 (nM)	PPARδ EC50 (nM)	PPARγ EC50 (nM)
Lanifibranor*	**1630**	**850**	**230**
Fenofibrate	*2400*	*-*	*-*
Pioglitazone	*-*	*-*	*263*
Rosiglitazone	*-*	*-*	*13*
*Elafibranor***	*10*	*100*	*-*
*Seladelpar^*	*-*	*2*	*-*

*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*

Lanifibranor's activation of the three PPAR isoforms addresses the key features of NASH

LANIFIBRANOR

Pan-PPAR activity expected to ensure improved efficacy



LANIFIBRANOR

METABOLISM

PPARα PPARδ PPARγ

- ↑ Insulin sensitivity
- ↑ HDLc
- ↓ Triglycerides

STEATOSIS

PPARγ

- ↓ FA uptake
- ↑ FA catabolism
- ↓ Lipogenesis

INFLAMMATION AND BALLOONING

PPARα PPARδ PPARγ

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

FIBROSIS

PPARδ PPARγ

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

VASCULAR

PPARα PPARγ

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

Adverse events and toxicity previously seen in other single and dual PPAR agonists are not observed in lanifibranor

SAFETY

Organ	Isoforms activated	Reported PPAR side effects	lanifibranor effects
HEART	*PPARγ*	▶ Fluid retention ▶ Cardiac hypertrophy	NOT OBSERVED
SKELETAL MUSCLE	*PPARα*	▶ Myofiber degeneration	
KIDNEY	*PPARα*	▶ > 50% increases in creatinine, degenerative changes in renal tubules	
URINARY BLADDER	*PPARγ*	▶ Proliferative changes in bladder epithelium	

Adverse events and toxicity of single / dual PPAR agonists not observed in primate and rodent studies

FAVOURABLE TOLERABILITY PROFILE in a 12-month monkey study …

- No adverse clinical signs observed at any dose-level tested
- No effects on body and heart weight, no haemodilution or creatinine increase
- Electrocardiography and clinical pathology investigations did not reveal any undesirable effects

… and in two-year **CARCINOGENITY STUDIES** performed in rat and mice

- Rat: no observed neoplastic change or increase in tumor types commonly associated with single PPARγ and dual PPARα/γ agonists (liver, adipose, bladder, renal and skin)
- Mice: no observed neoplastic changes of human relevance

Confirmation by FDA that the non-clinical toxicology package is complete and acceptable to support NDA filing in NASH

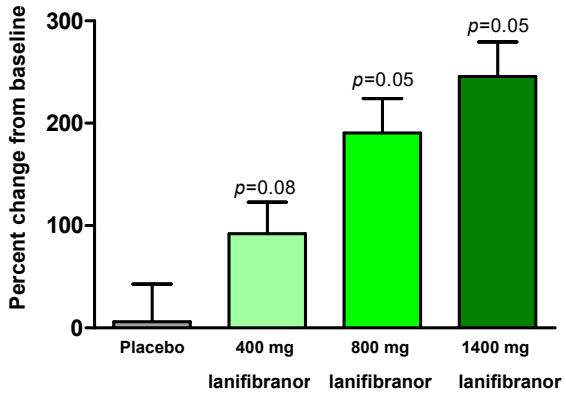
Source: Company data

Phase I and Phase IIa clinical trials* in type 2 diabetes patients: beneficial changes in key metabolic markers

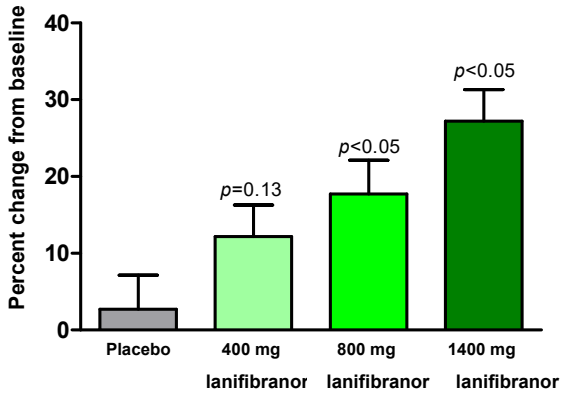
PHASE I AND IIa

Lanifibranor metabolic markers in type II diabetic patients

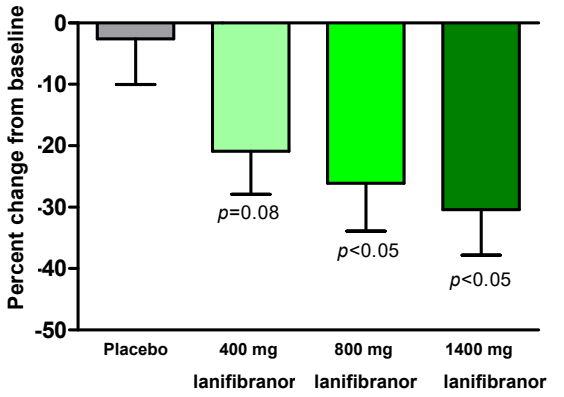
Adiponectin (PPARγ)**



HDL Cholesterol (PPARα/δ)^



Triglycerides (PPARα/δ) ^^



Phase I and IIa* clinical findings support the favorable tolerability of lanifibranor

- Good overall tolerance and no major safety findings
- No increases of creatinine, LFTs, or CPK
- No changes in blood pressure
- No signal of fluid overload or haemodilution
- No clinically relevant weight gain

*Note: * Conducted by Abbott; ** Adiponectin is associated with PPARg activation; ^ HDL-C is associated with PPARa and d activation; ^^ Triglycerides are associated with PPARa and d activation;*
Source: Company data

Improvements in metabolic parameters and liver histology with anti-fibrotic activity have been demonstrated in animal models

LANIFIBRANOR

ANIMAL MODELS, BY MODEL TYPE

METABOLIC	NASH & NAFLD	FIBROSIS	CIRRHOSIS
Diet induced obesity high fat / high sucrose	Methionine Choline Deficient diet (MCD)	Carbon tetrachloride (CCL4)	Thiocetamide (TAA)
Foz / Foz model			
	Choline-deficient amino-acid and high fat diet		

In vivo models

Hepatoma and muscle cells biology	Macrophages biology	Hepatic Stellate Cells (HSC) biology	
			Endothelial biology

In vitro models

OBSERVED EFFECTS, BY MODEL TYPE

- Improvements in
  - Insulin resistance
  - Non fasting glucose
  - Homa-IR
  - Lipid profile
- Maintenance of body weight

- Improvements in
  - Steatosis
  - Inflammation
  - Ballooning
- Improvements in NAS score

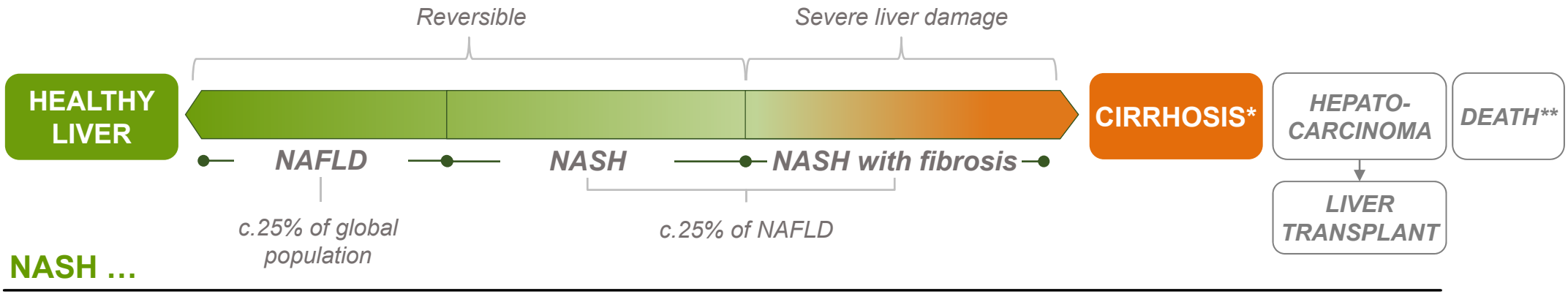
- Improvement of fibrosis
- Inhibition of stellate cell activation

- Reductions in
  - Portal pressure
  - Established fibrosis

NASH is a chronic progressive disease with no currently approved treatment options

NASH OVERVIEW

Chronic disease that may progress to cirrhosis



NASH …

… can be classified based on histologic features

FIBROSIS STAGE

F0 F1 F2 F3 F4

NAS SCORE

Reflects disease activity; composite of three features (steatosis, inflammation, ballooning)

SAF SCORE

Semi-quantitative score of steatosis, activity, fibrosis

… is associated with type 2 diabetes (T2DM)

T2DM patients tend to present with more severe and faster progressing NASH

… is currently mainly diagnosed through liver biopsy

Liver biopsy is currently the gold standard; broader adoption of non-invasive tests and launch of disease-modifying therapies may make diagnosis easier

… is characterised by high unmet needs

KEY UNMET NEED F2 F3

Treatment targeting both NASH resolution and fibrosis

KEY UNMET NEED F4

Treatment of cirrhosis

*Note: * More than 20% of patients with NASH progress to cirrhosis within a decade of diagnosis; ** Compared to the general population patients with NASH have a ten-fold greater risk of liver-related mortality*
Source: PanNASH; NASH Market, Allied Market Research 2016 ; Deutsche Bank Markets Research; HCV Trials; Duseja (2019) L.E.K. interviews, research, and analysis

The overall development plan builds on the successful outcomes of the NATIVE Phase IIb trial

CLINICAL DEVELOPMENT

Phase I → Phase IIa → Phase IIb (NATIVE) → F2-F3 Phase III → Registration

IIb DESIGN

- *24 weeks*
- *800 mg and 1200 mg once-daily lanifibranor*

IIb EFFICACY

- *First candidate to achieve statistically significant results on the two Phase III FDA and EMA primary endpoints*

IIb SAFETY

- *Favourable profile*

III OVERVIEW

- *72 week Part 1 + Part 2 extension period*
- *Inclusion criteria and patient profile in line with NATIVE Phase IIb*
- *Primary composite endpoint combining NASH resolution and fibrosis improvement*

Lani Phase II in NAFLD patients with TD2M

Lani + SGLT2i Phase II in NASH patients with TD2M

Phase II/III in NASH patients with compensated cirrhosis

Completed clinical trials

Ongoing clinical trials

Potential clinical trials

The Phase IIb NATIVE trial studied 800 mg and 1200 mg once-daily lanifibranor across 247 patients

PHASE IIb **DESIGN** **OVERVIEW**

Screening
▶ **Liver biopsy**

24-week treatment + 4-week follow-up
Double blind, randomized, placebo-controlled

End of treatment
▶ **Liver biopsy**

- **Placebo**
- **lanifibranor, 800 mg once daily**
- **lanifibranor, 1200 mg once daily**

- Randomisation 1/1/1
- Stratification on type 2 diabetes mellitus (T2DM)

Patient population	# patients	Definition
Safety / Intention-to-Treat (ITT)	247	Patients randomized having received at least one dose of lanifibranor/placebo
Per Protocol (PP)	194	Patients with paired biopsies and without deviation impacting efficacy results

▶ **Main inclusion criteria**: patients with biopsy-proven NASH 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 on**:

The NEW ENGLAND JOURNAL of MEDICINE

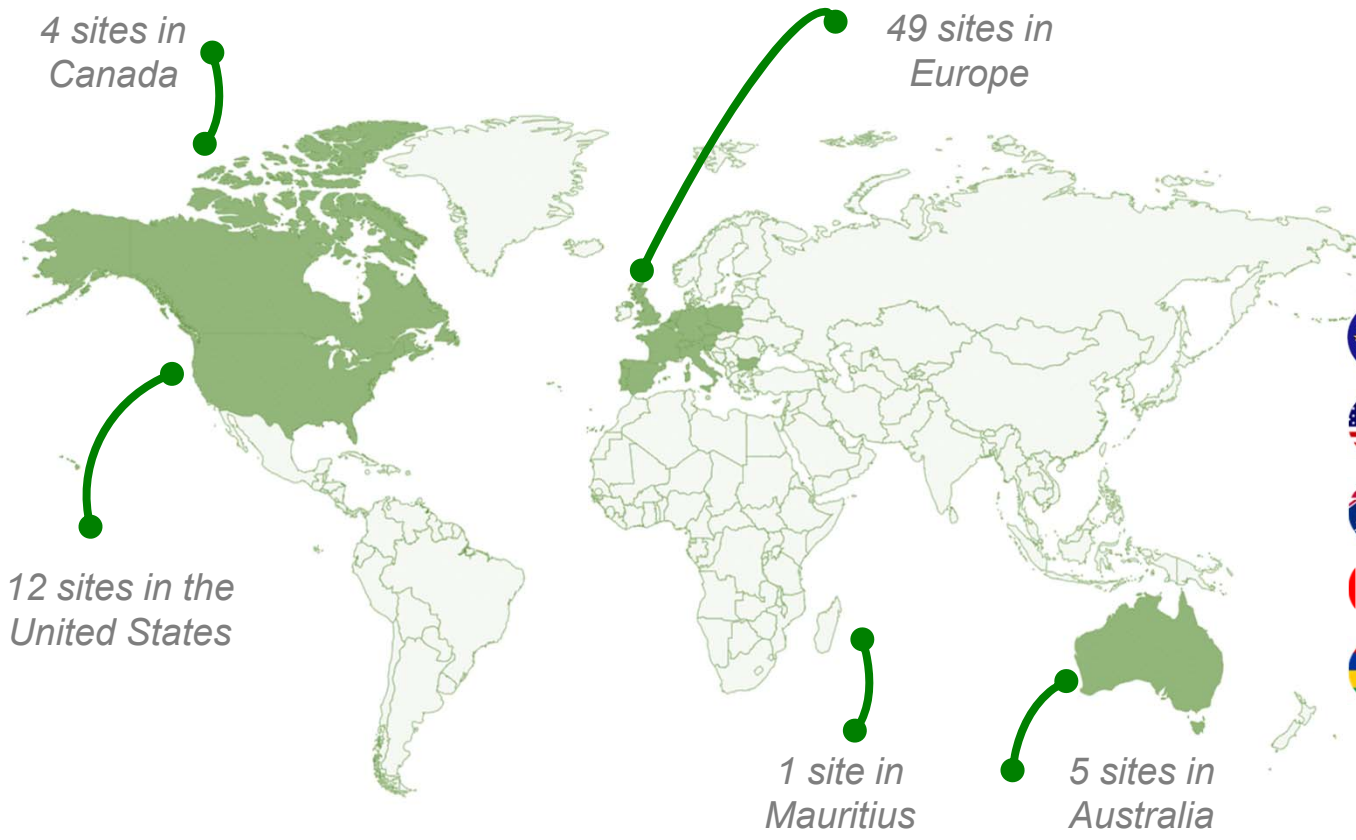
ESTABLISHED IN 1812 OCTOBER 21, 2021 VOL. 385 NO. 17

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

More information on: http://www.native-trial.com/

247 patients were randomised across 71 sites worldwide, with the majority of patients based in Europe

PHASE IIb | DESIGN | SITE SELECTION



Country	Patients randomized
Europe	183 (74%)
U.S.	36 (15%)
Australia	13 (5%)
Canada	8 (3%)
Mauritius	7 (3%)
Total	247 (100%)

16 countries worldwide (number of sites having randomized at least 1 patient)

- Europe: Austria (1), Belgium (5), Bulgaria (5), Czech Republic (3), France (13), Germany (5), Italy (4), Poland (3), Slovenia (1), Spain (4), Switzerland (2), United Kingdom (3)
- North America: United States (12), Canada (4)
- Australia (5)
- Mauritius (1)

The majority of patients successfully completed the 24-week treatment

PHASE IIb | DESIGN | TREATMENT ARMS

247 patients randomised and treated

Placebo N = 81	Ianifibranor 800 mg/day N = 83	Ianifibranor 1200 mg/day N = 83
74 (91%) patients completed the 24-week treatment	77 (93%) patients completed the 24-week treatment	77 (93%) patients completed the 24-week treatment
7 (9%) patients prematurely withdrawn: - Adverse events (n=3) - Withdrawal by patient (n=2) - Forbidden concomitant medication (n=2)	6 (7%) patients prematurely withdrawn: - Adverse events (n=3) - Lost to follow-up (n=1) - Withdrawal by patient* (n=1) - Non-compliance (n=1)	6 (7%) patients prematurely withdrawn: - Adverse events (n=3) - Lost to follow-up (n=1) - Withdrawal by patient (n=2)

*Note: * And adverse event as secondary reason*

Patient population included 58% of female and 42% of patients with T2DM at baseline

PHASE IIb | DESIGN | BASELINE

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%)

A number of liver enzyme, plasma lipid level and glucose metabolism parameters were recorded at baseline

PHASE IIb | DESIGN | BASELINE

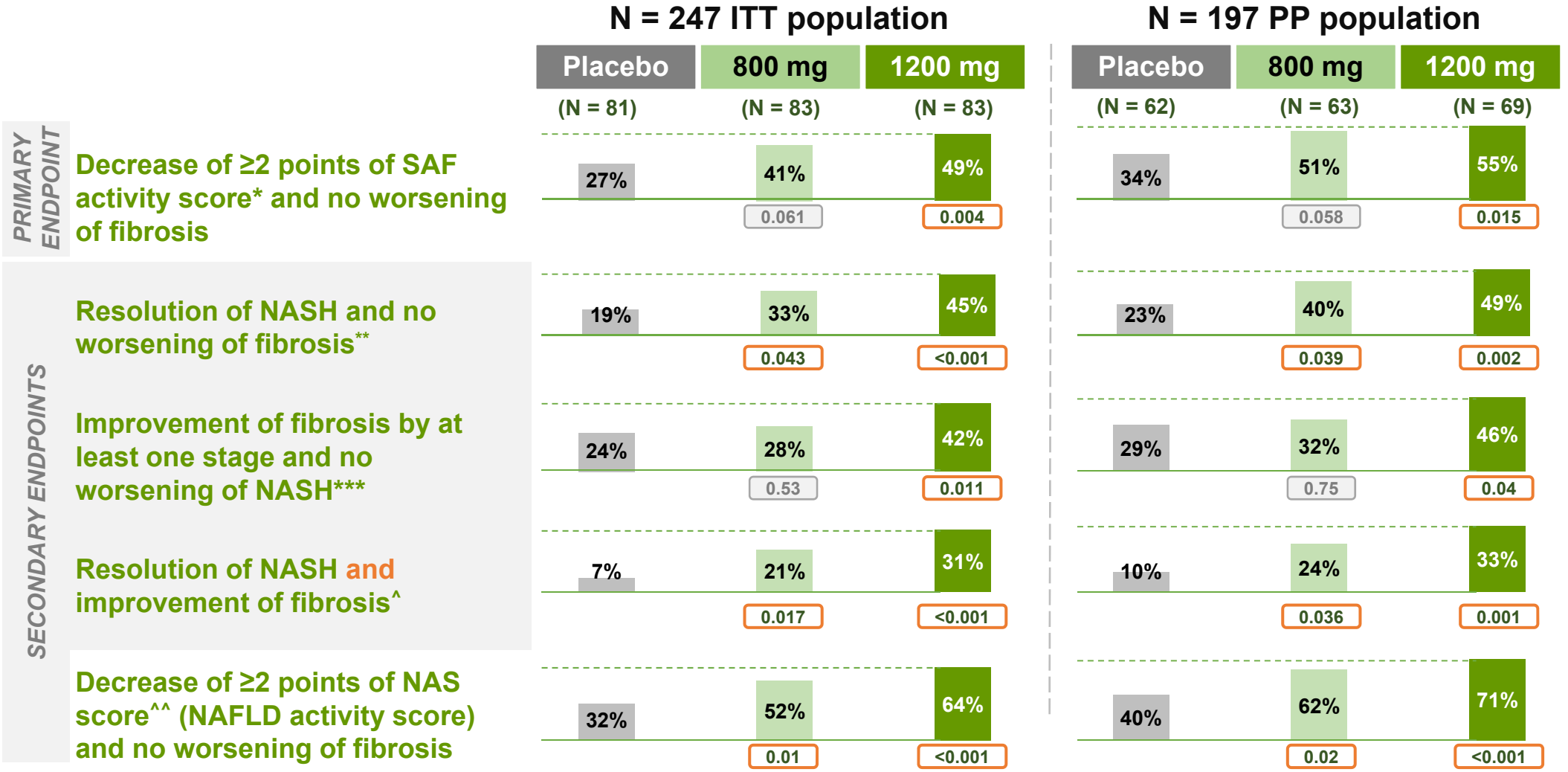
Parameters (unit) mean ± SD	Placebo - N = 81	lanifibranor 800 mg/day N = 83	lanifibranor 1200 mg/day N = 83
Liver enzymes			
Alanine aminotransferase, ALT (UI/L)	56.9 ± 31.6	64.1 ± 41.4	63.6 ± 43.4
Aspartate aminotransferase, AST (UI/L)	43.3 ± 24.1	53.9 ± 43.4	43.9 ± 24.8
Gamma glutamyl transferase, 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 diabetic patients (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

Lanifibranor is the first candidate to achieve statistically significant results on the two Phase III FDA and EMA primary endpoints

PHASE IIb | EFFICACY | KEY ENDPOINTS

xx Statistically significant xx Non-statistically significant

Key Phase IIb results by endpoint



** Response is defined as a decrease from baseline to week 24 of at least 2 points of the SAF Activity score (SAF-A) with no worsening of the NAS Fibrosis score (NAS-F). No worsening means that score remains stable or decreases ; ** Resolution of NASH and no worsening of fibrosis at week 24: NAS-I = 0 or 1 (NAS-Inflammation), NAS-B = 0 (NAS-Ballooning) and no worsening of NAS-F from baseline; *** Improvement of liver fibrosis ≥ 1 stage and no worsening of NASH at week 24; ^ Resolution of NASH and improvement of fibrosis at week 24: NAS-I = 0 or 1, NAS-B = 0 and an improvement of NAS-F ≥ 1 stage; ^^ NAS score is a commonly accepted, semi-quantitative evaluation of biopsy results that assesses the severity of steatosis, inflammation and ballooning in the liver.*

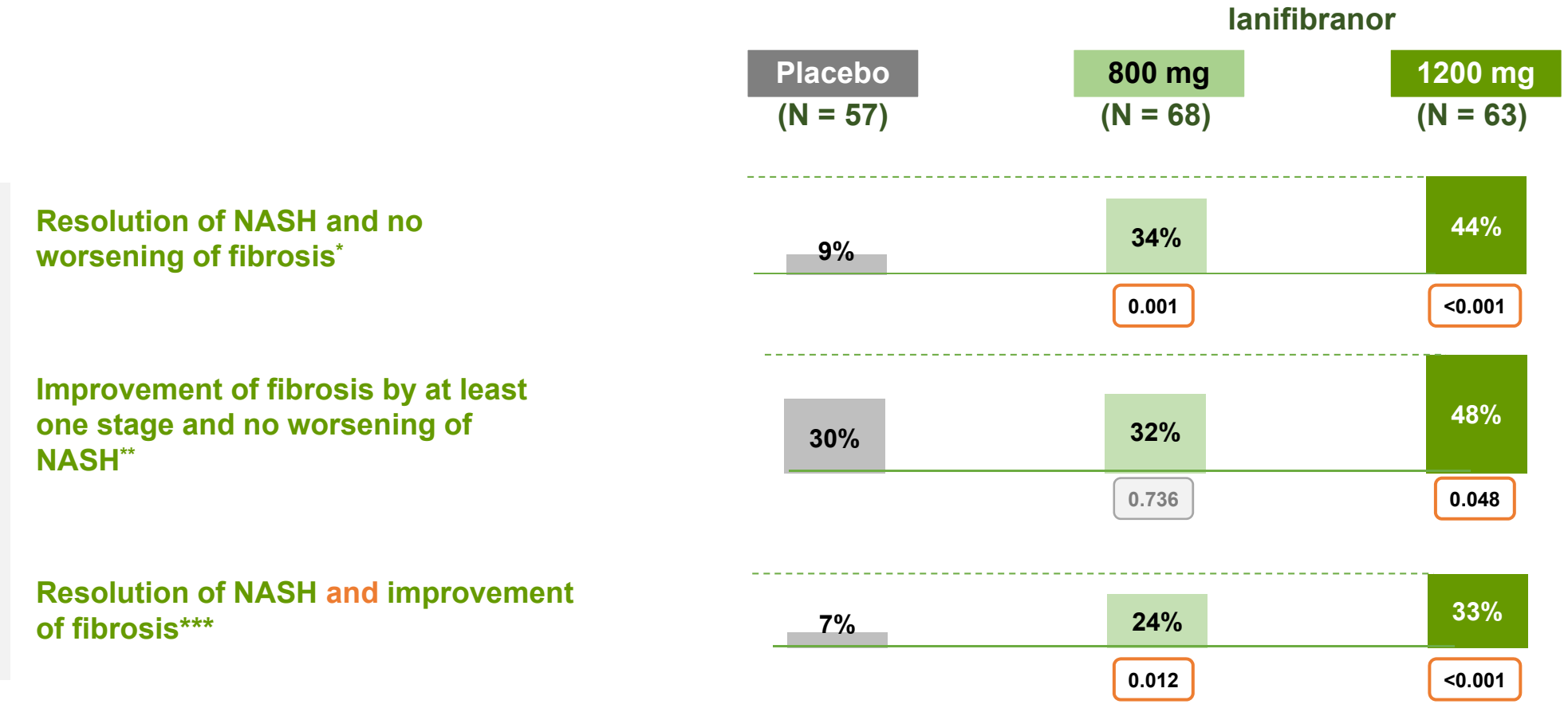
In F2-F3 patients, statistical significance was demonstrated for the main key histological secondary endpoints

PHASE IIb | EFFICACY | F2-F3 POPULATION

xx Statistically significant xx Non-statistically significant

Key secondary endpoints in FAS F2 F3 patients (N=188)

SECONDARY ENDPOINTS

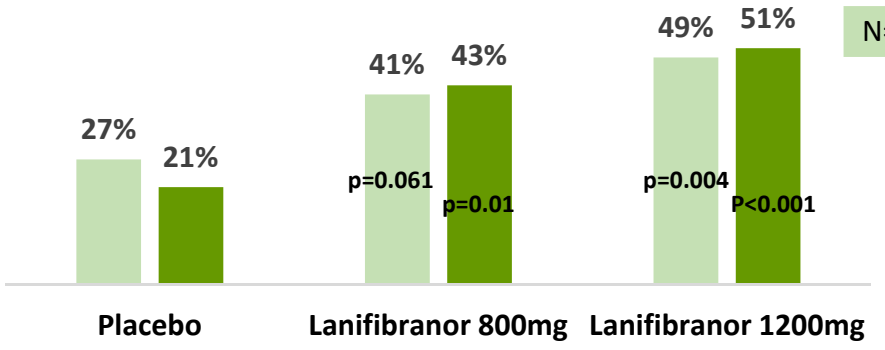


- Similar results in the PP population
- Consistent response in diabetic and non-diabetic patients

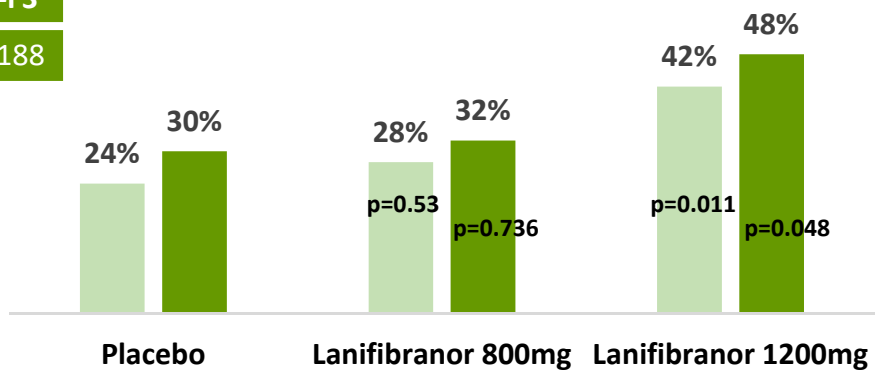
** Resolution of NASH and no worsening of fibrosis at week 24: NAS-I = 0 or 1 (NAS-Inflammation), NAS-B = 0 (NAS-Ballooning) and no worsening of NAS-F from baseline; ** Improvement of liver fibrosis ≥ 1 stage and no worsening of NASH at week 24; *** Resolution of NASH and improvement of fibrosis at week 24: NAS-I = 0 or 1, NAS-B = 0 and an improvement of NAS-F ≥ 1 stage*

Effect of lanifibranor therapy on histological endpoints, in the overall population and the subgroup of F2-F3

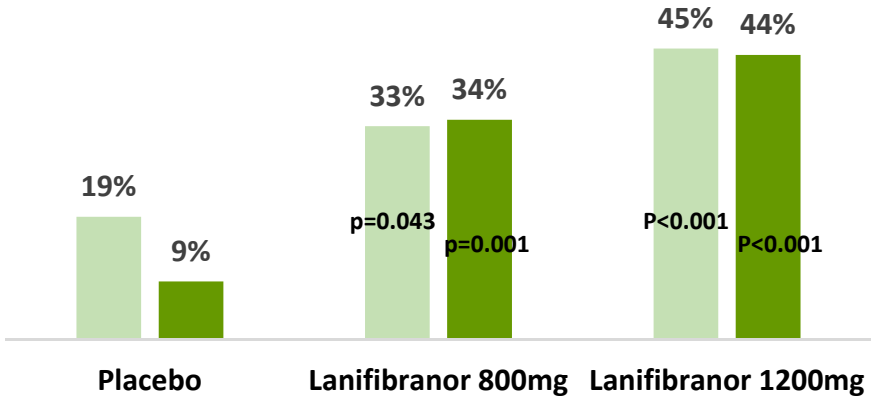
Reduction of 2 points of SAF Activity Score and no worsening of fibrosis



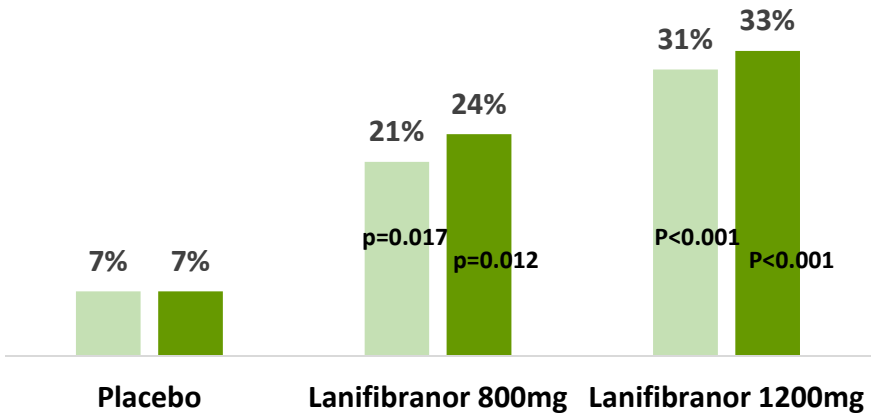
Fibrosis improvement w/o worsening of NASH



NASH resolution w/o worsening of fibrosis



NASH resolution AND Improvement of fibrosis



Effect is higher in the F2-F3 subpopulation

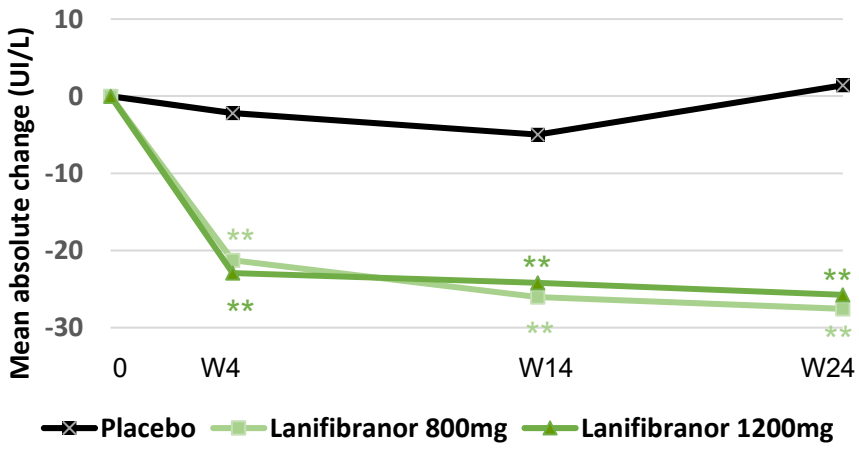
A statistically significant decrease in liver enzymes was observed

PHASE IIb | EFFICACY | OTHER

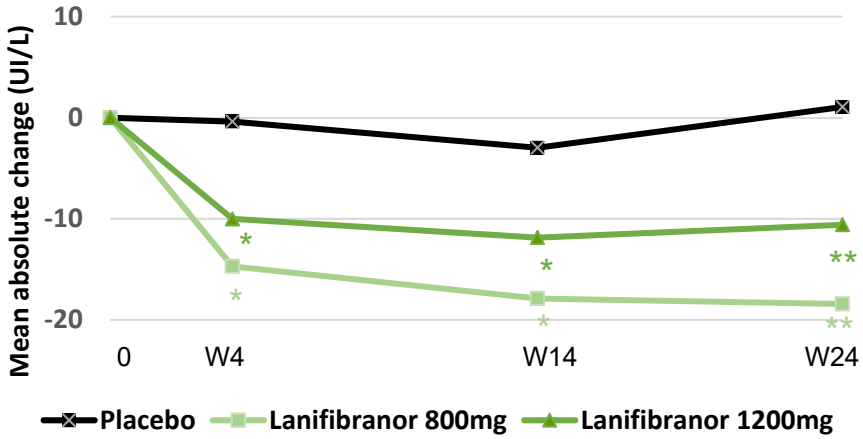
SECONDARY ENDPOINTS

Other secondary endpoints in ITT (N = 247)

Absolute change from baseline in ALT

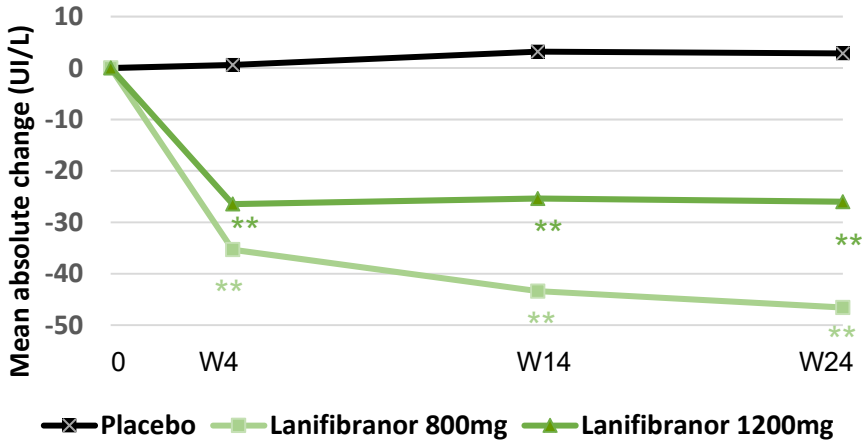


Absolute change from baseline in AST



* p<0.01 **p<0.001

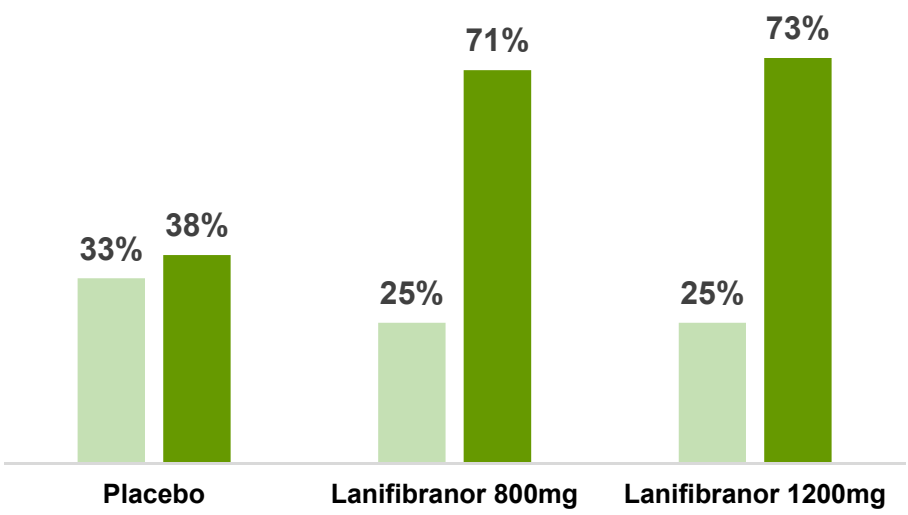
Absolute change from baseline in GGT



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

Effect of lanifibranor therapy on liver enzymes

Percentage of patients with normal ALT values

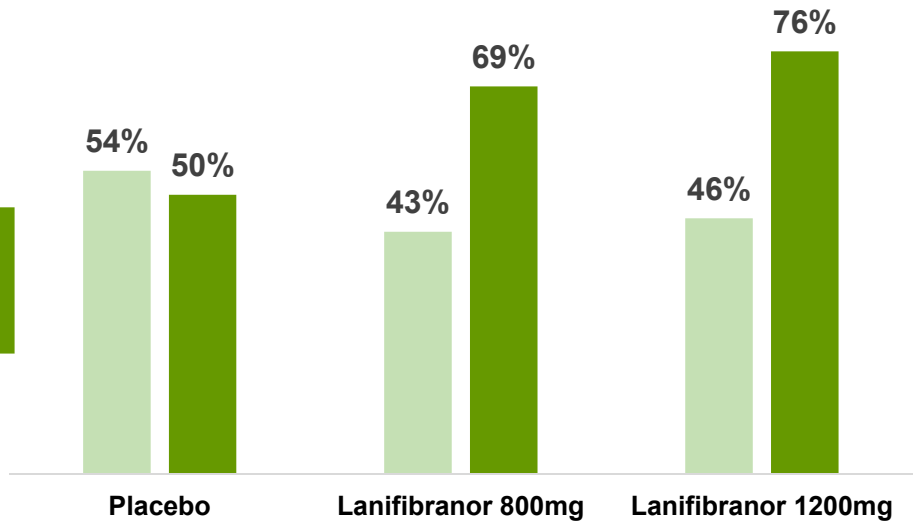


Lower Limit of Normal (LLN)= 0 U/L, Upper Limit of Normal (ULN)= 41 U/L for males, 33 U/L for females

Baseline

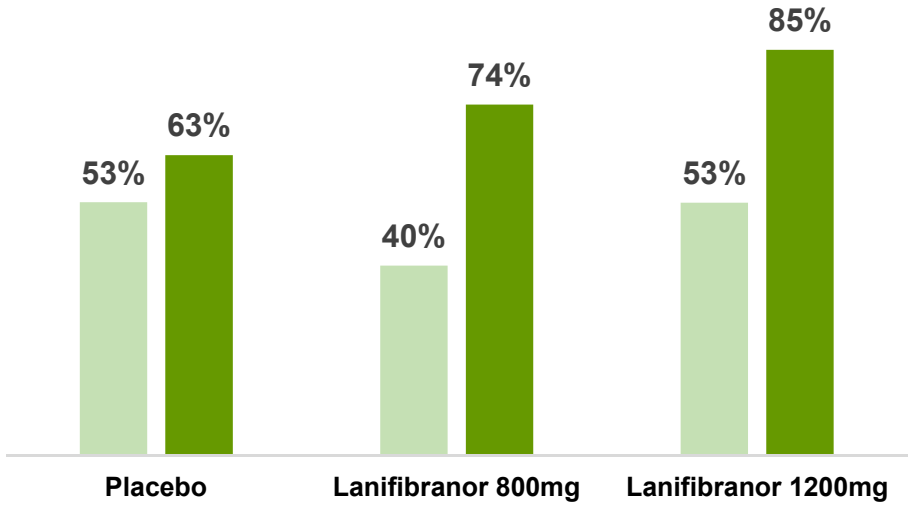
End of treatment (Week 24)

Percentage of patients with normal AST values



LLN= 0 U/L, ULN= 40 U/L for males, 32 U/L for females

Percentage of patients with normal GGT values



LLN= 8 U/L for males, 5 U/L for females; ULN= 61 U/L for males, 36 U/L for females

Significant higher percentage of patients under lanifibranor treatment reach normal liver enzymes at end of treatment

A statistically significant change in HDL-cholesterol and triglycerides was seen, without a change in LDL-cholesterol

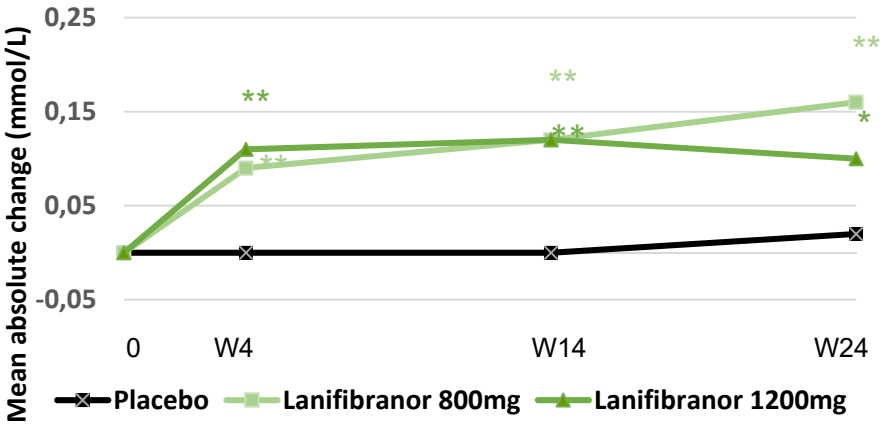
PHASE IIb | EFFICACY | OTHER

SECONDARY ENDPOINTS

Other secondary endpoints in ITT (N = 247)

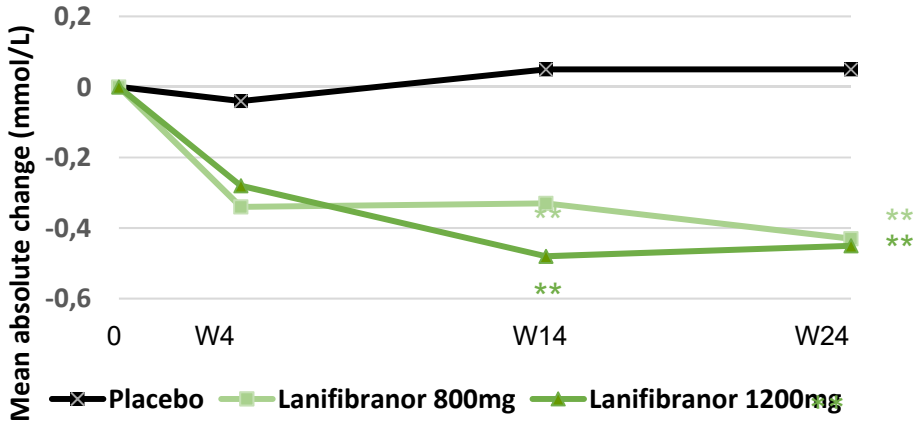
* p<0.01 **p<0.001

Absolute change from baseline in HDL-C



Statistically significant change in HDL-cholesterol

Absolute change from baseline in triglycerides



Statistically significant change in triglycerides

- No change in LDL-cholesterol

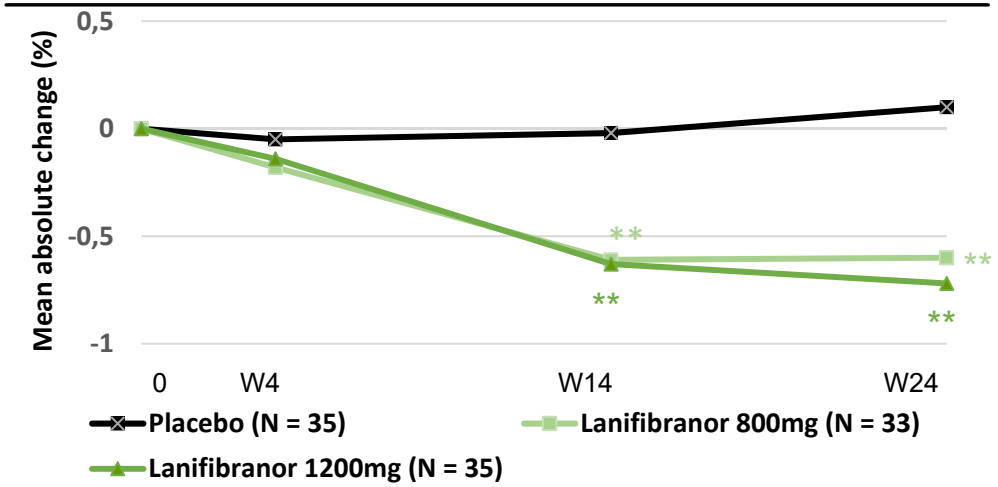
In patients with NASH and T2DM, statistically significant reductions of fasting glucose and insulin, HbA1c were observed

PHASE IIb | EFFICACY | OTHER

Secondary endpoints in patients with NASH and T2DM (N = 103)

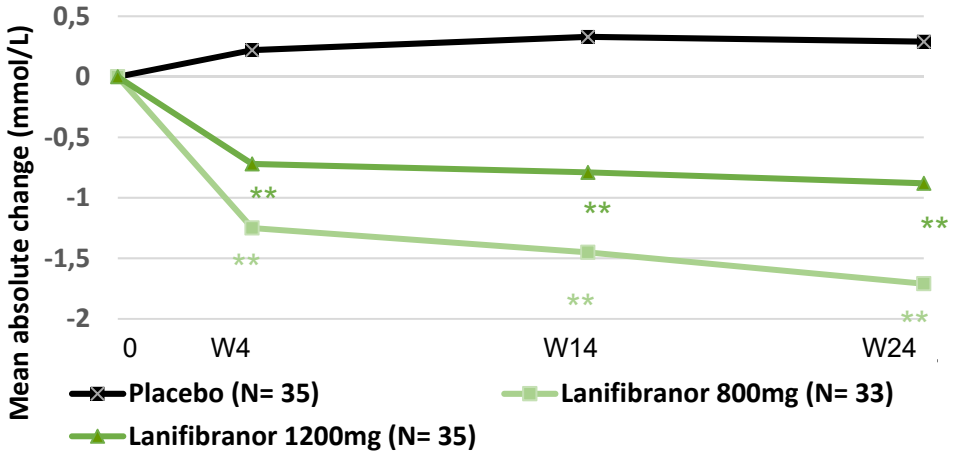
SECONDARY ENDPOINTS

Absolute change from baseline in HbA1c

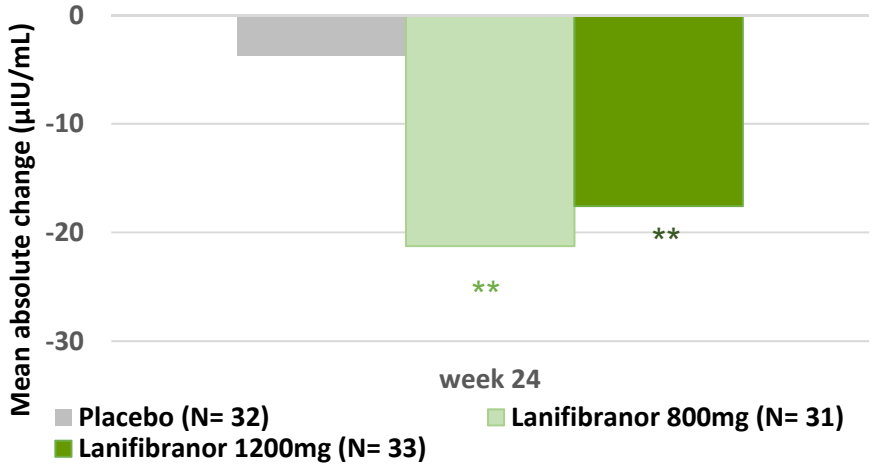


**p<0.001

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 NASH patients

A significant decrease in circulating biomarkers was observed under lanifibranor treatment after 24-weeks

PHASE IIb | EFFICACY | OTHER

OTHER OUTCOME MEASURES

Median relative change (%)		Placebo	lanifibranor *(Two doses pooled)*	Pvalue
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*

Addtional analysis on NATIVE phase 2b results have enlarged lanifibranor spectrum of efficacy

EFICACY: Sub-analysis

AASLD November 13-16, 2020 The Liver Meeting®

- Presentation during the plenary session of **NATIVE phase 2b trial**
- Presentation selected in the Best of Liver Meeting presentation

EASL 2021 The International Liver Congress™ 23-26 June 2021

- Lanifibranor **effect on histology endpoints is higher in the F2-F3 patients** where lanifibranor improves markers of lipid metabolism, insulin resistance, liver injury and fibrosis
- Lanifibranor **has beneficial effects on cardiovascular risk** biomarkers with positive effects on **lipids** (significant effect on HDL and TG and no effect on LDL), **lipid and inflammatory markers** (significant decrease in APO-B, APO-B/APO-A1, APO-C3 and Hs-CRP), **glucose metabolism** (significant decrease of HbA1c, fasting glucose, insulin) and **blood pressure** (no significant change in systolic BP and significant decrease in diastolic BP)
- Preclinical data showing the **combination of lanifibranor and firsocostat**, an ACC inhibitor from Gilead, reached greater efficacy than monotherapy on hepatic lipid content, steatosis, fibrosis and total scoring

AASLD Nov. 12-15, 2021 The Liver Meeting®

- Lanifibranor improves **markers of glucose metabolism in prediabetic patients**
- Analysis showing a **decrease in lanifibranor treated patients of steatosis measured by CAP/Fibroscan**(1)
- Following treatment with lanifibranor **NASH resolution responders were significantly more likely to also be fibrosis improvers**. Correlation seen also with ballooning and fibrosis improvement
- Lanifibranor showed **reduction in LSEC**(2) **capillarization** measured by CD34 immunostaining which reached a dose dependent significance in the periportal area.
- Preclinical data demonstrating that **lanifibranor improves NASH, fibrosis and diastolic dysfunction** in a hamster model of diet-induced NASH and diastolic dysfunction

(1) CAP: Controlled Attenuation Parameter (2) *Liver Sinusoidal Endothelial Cell*

Lanifibranor has continued to show a favourable safety profile

PHASE IIb | SAFETY | OVERALL

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: 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%)

* One AE of severe intensity

A limited number of serious TEAEs occurred

PHASE IIb | SAFETY | SERIOUS TEAE

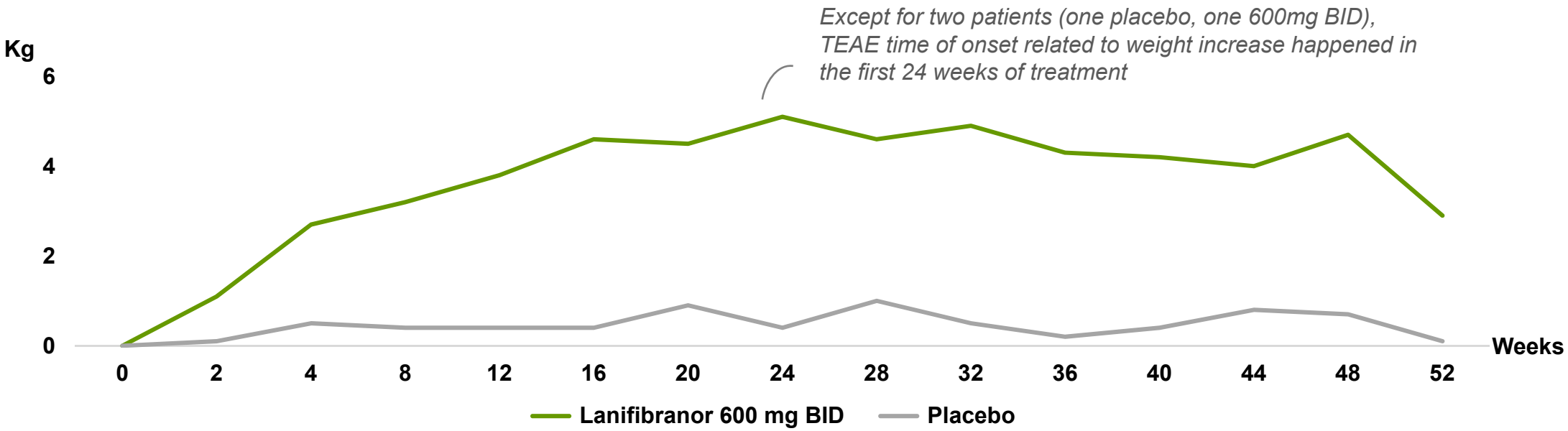
Patients reporting treatment-emergent Serious AE (SAE); N (%)	Placebo (N = 81)	800 mg (N = 83)	1200 mg (N = 83)
Total	3 (3.7%)	3 (3.6%)	7 (8.4%)
Treatment-Emergent Serious AE linked to biopsy procedure			
Post-procedural haematoma/haemorrhage	-	1 (1.2%)	1 (1.2%)
Post-procedural pain	-	-	1 (1.2%)
Pneumobilia (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%)

Phase II results have demonstrated modest weight increase with no impact on efficacy

PHASE IIb | SAFETY | WEIGHT GAIN

- **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
- According to a six month study with pioglitazone in patients * with NASH body weight gain is likely attributed to an **INCREASE IN ADIPOSE TISSUE** and **NOT WATER RETENTION**
- Based on a 52-week lanifibranor trial in systemic sclerosis (SSc) patient weight gain is expected **TO REACH A MAXIMUM BY WEEK 24**

SSc lanifibranor study: weight (kg) relative change from baseline over 52 weeks (Observed cases under treatment – FAS population)



*Note: * Pioglitazone treatment increases whole body fat but not total body water in patients with non-alcoholiv steatohepatitis ; Balas, Belfort, Harrison et al. ; Journal of Hepatology 47 (2007) 565-570*

Peripheral edemas were not flagged as a concern by study investigators

PHASE IIb | **SAFETY** | **PERIPHERAL OEDEMA**

#	Treatment group	Verbatim of AE edema peripheral	Intensity	Action taken or Corrective treatment	Relationship to treatment
1	**Placebo**	edema in the lower leg and knees	Moderate	IMP interrupted + Meloxicam	Unlikely
2		bilateral lower extremity edema	Mild	No actions taken	Unlikely
3	**800 mg**	*bilateral lower extremity edema*	Mild	No actions taken	*Unrelated*
4		*edema in bilateral feet*			*Unlikely*
5		peripheral edema bilateral			Possible
6		right and left ankle swelling			Possible
7		*foot edema bilateral*	*Moderate*	*Bioflavonoids*	*Unrelated*
8	**1200 mg**	*leg edema - both legs*	*Mild*	*Torasemid*	*Unrelated*
9		*edema in the 2 ankles*		*No actions taken*	*Unrelated*
10		*edema lower leg, both sides*			*Unrelated*
11		*peripheral edema , both ankles*			*Unrelated*
12		bilateral edema leg			Probable
13		*bilateral postural extremities edema*	*Moderate*	*IMP stopped*	*Unrelated*
14		legs edema	Severe	IMP interrupted	Possible

Peripheral edemas were not flagged as a concern by study investigators and were:

- Limited
- Transient
- Mostly mild
- Majority unrelated and not requiring treatment

Compared to key competitors, lanifibranor is the only asset that addresses all key features of NASH

EFFICACY

	Lanifibranor *(PPAR)*	Ocaliva *(FXR)*	Resmetirom *(THR-β)*	Aramchol *(Other)*	Efruxifermin *(FGF)*	Semaglutide *(GLP-1)*
STATUS	Phase III	CRL	Phase III	?	Phase II	Phase III
ROUTE OF ADMINISTRATION	Oral	Oral	Oral	Oral	Injectable	Injectable
INSULINO-RESISTANCE	✓	✗	✗	✗	✓	✓
STEATOSIS	✓	✗	✓	✓	✗	✓
NECRO-INFLAMMATION	✓	✗	✓	Unclear	✓	✓
FIBROSIS	✓	✓	Unclear	✗	✓	✗

Source: Newsome et al., 2020; Company websites

Lanifibranor compares favourably in its ability to target both fibrosis improvement and NASH resolution

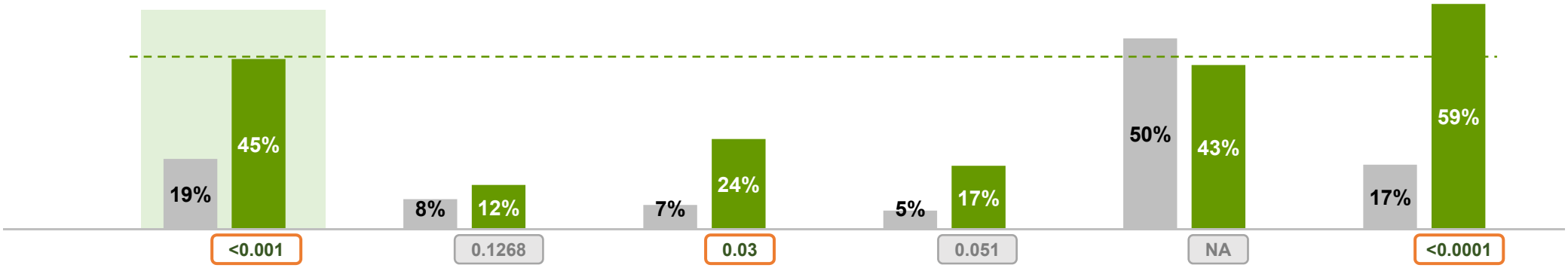
EFFICACY — Active | Placebo | xx Statistically significant | xx Non-statistically significant

Only drug achieving statistical significance on both endpoints

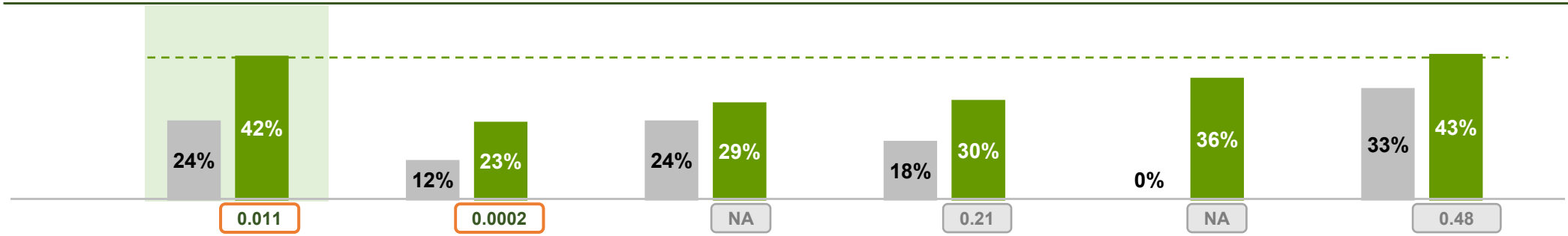
Injectables

	Lanifibranor	Ocaliva	Resmetirom	Aramchol	Efruxifermin*	Semaglutide
Time point of data collection	Phase IIb 6 months	Phase III 18 months	Phase IIb 9 months	Phase IIb 12 months	Phase IIa 4 months	Phase IIb 18 months
# of patients	247	931	125	247	80	320

NASH resolution with no worsening of fibrosis



Fibrosis improvement with no worsening of NASH



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.
**** Efruxifermin 70mg results only. Placebo N = 2. No information available regarding statistical significance of trial results; histology results reported only for patients achieving a ≥30% reduction of hepatic fat at week 12***

Source: lanifibranor native results 1200 mg/day, ITT population; ocaliva 25mg : REGENERATE Phase II trial: company press release February 19, 2019; Newsome et al., 2020: Ratziu et al, Gastorenterology 2016; 150:1147-1159 ; resmetirom 80mg ± 20mg: Harrison et al, Lancet 2019 ; S0140-6736(19) 32517-6; Aramchol 600mg :AASLD 2018 presentation

Physicians are positive about anifibranor's value proposition, noting its ability to target both fibrosis and NASH resolution

EFFICACY

Physicians valued Lanifibranor's efficacy on multiple endpoints

- **The benefits of a pan-PPAR targeting multiple isoforms are clear to most physicians**, who comment positively on lanifibranor's efficacy on fibrosis and NASH resolution whilst also improving glycaemic control and insulin sensitivity

"… This product is a dream come true, it targets all the things I would want it to; it resolves the NASH, the fibrosis and you get improvement of glycaemic control and insulin resistance …" Physician #1, US

"… You have to attack both NASH and fibrosis because if you reverse fibrosis and still have NASH, that's going to lead to more fibrosis …" Physician #2, US

"… It is attractive, I do like that it has an effect on HbAC1 as the most common co-morbidity is T2DM …" Physician #3, US

- **Physicians confirm F2-F3 is a correct patient population** to target, noting lanifibranor's MoA (targeting multiple metabolic pathways) makes it highly suited to the F2-F3 population
  - clinicians also want to treat the disease at its asymptomatic stage prior to complications occurring; some prefer this population over F4, as the latter is considered irreversible
  - some also suggested they would like to use it in F0-1 if possible, in order to slow or prevent progression to F2-F3

A once a day oral is considered optimal

- Lanifibranor's oral administration is considered attractive, **highlighting a once-daily oral pill** will increase ease of use to the patient

"… It is a once a day oral drug so compliance will be as good as you can get. At this point it would all be about education – it is important to educate the patient that they need to take this product, even if they are asymptomatic …" Physician #5, US

Source: L.E.K. Interviews, research and analysis (dated August 2020)

Physicians perceive weight gain due to lanifibranor as manageable, with the risk profile viewed positively

SAFETY

Weight gain appears acceptable and manageable, with limited concerns expressed around edemas

- Physician express differing views on the importance of weight gain
  - the majority of physicians believed that given lanifibranor's efficacy profile the **risk-benefit ratio was acceptable**, and with proper patient counselling around weight loss some of the weight gain could be offset
  - some suggested combination therapy could be used to **manage or reduce weight gain** (e.g., GLP-1, SGLT2)

"…Weight increase can be limiting, but I don't think it be a problem if we can find something to use in combination to offset potential increase in fat tissue …" – Physician, U.S., August 2020

"… I am surprised by the weight gain but I do not see it as a big concern. It would only become an issue if the weight gains happens continuously, for example if you increase 2-3kgs every 2 months… Physician, DE, August 2020

- Physicians express **less concerned about oedema** noting the majority are mild

"… The mechanism of edema determines how bad it is, it is not alarming…" – Physician, FR, August 2020

"… edema is not relevant …" Physician, DE, August 2020

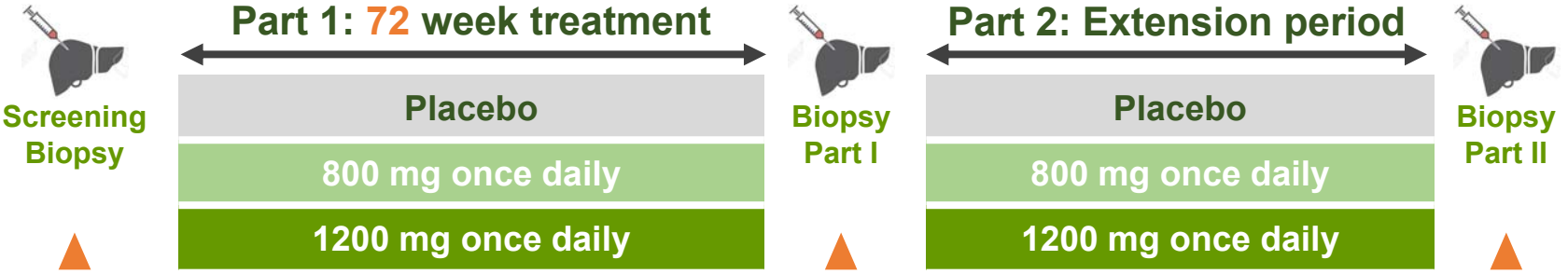
Source: L.E.K. Interviews, research and analysis (dated August 2020)

The F2-F3 Phase III consists of two parts, with inclusion criteria and patient profile in line with the NATIVE Phase IIb trial

PHASE III | **F2 F3 Patients**

A randomized, double-blind, placebo-controlled, multicenter, Phase III study evaluating long-term efficacy and safety of lanifibranor in adult patients with NASH with liver fibrosis

Main inclusion criteria **ALIGNED TO** Phase IIb NATIVE trial



PRINCIPAL INVESTIGATORS

- Prof. Francque and Prof. A. Sanyal

INCLUSION CRITERIA

- Adults ≥18 years of age diagnosed with NASH using SAF scoring (steatosis ≥1, activity ≥3 and fibrosis score of F2-F3)

RANDOMISATION AND STRATIFICATION

- Randomisation 1:1:1
- Stratification on T2DM and F2/F3 patients
- At least 30% of U.S. patients

STATISTICAL POWERING: 90% considered for sample size

CENTRAL BIOPSY review done by two pathologists

PRIMARY ENDPOINT *week 72, c.900 patients*

- Composite endpoint of patients having both NASH resolution and fibrosis improvement of at least one stage

KEY SECONDARY ENDPOINTS

- NASH resolution and no worsening of fibrosis
- Fibrosis improvement and no NASH worsening

SECONDARY ENDPOINTS

- Glycaemic parameters at week 12 and 24 in patients with T2DM not well controlled: proportion of patients with HbA1c back to normal
- Composite endpoint of diabetic patients having both NASH resolution and fibrosis improvement
- Improvement in renal function
- Reduction of cardiovascular risk
- Quality of life

- Endpoints based on time to first clinical event on c.2,000 patients
  - histological progression to cirrhosis
  - all cause mortality
  - hepatic decompensation events
  - MELD score ≥15
  - liver transplant

Eligible for **U.S. ACCELERATED APPROVAL** and **EU CONDITIONAL APPROVAL**

Potential for **FULL APPROVAL** in **U.S.** and **EU**

The primary endpoint combining NASH resolution and fibrosis improvement will help differentiate from key competitors

PHASE III **EFFICACY**

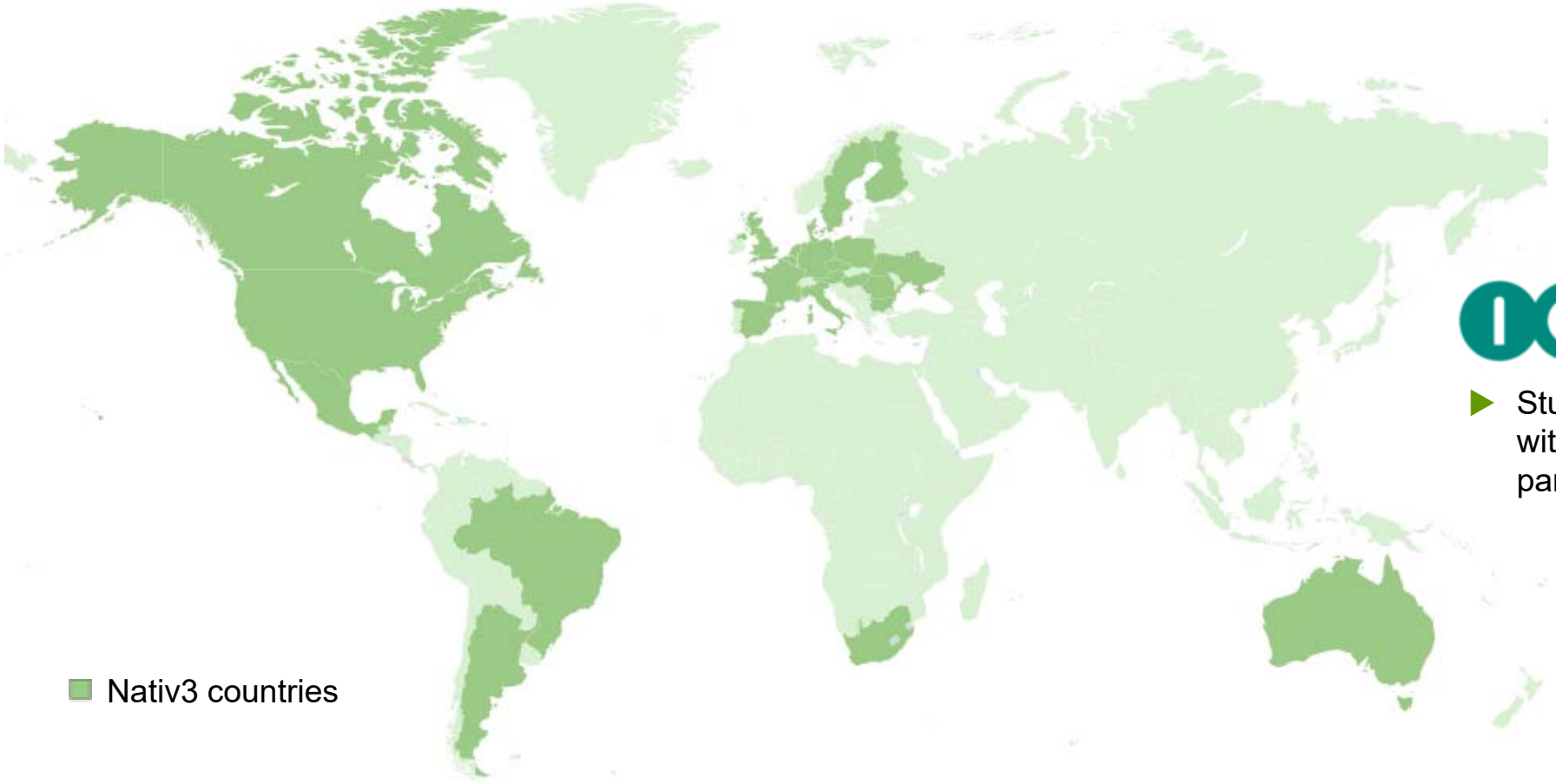
- The primary endpoint "resolution of NASH and improvement of fibrosis" addresses the major pathways of the disease: achieving both of these histological outcomes reflects a stronger impact on disease modification compared with improvement in either steatohepatitis or fibrosis alone
- If met, **a label for the treatment of NASH and the improvement in liver fibrosis** in adult non-cirrhotic NASH patients will be requested

Phase III study	lanifibranor (800 - 1200mg) At W72	Obeticholic acid (10 - 25mg) At W72	Resmetirom (80 - 100mg) At W52
Resolution of NASH and improvement of fibrosis	**Primary**	Secondary (not met)	/
Fibrosis improvement and no worsening of NASH	**Key secondary**	**Primary** (met)	Secondary
NASH resolution and no worsening of fibrosis	**Key secondary**	**Primary** (not met)	**Primary** *(with reduction of at least 2 pts of NAS)*
NASH resolution and fibrosis improvement in patients with diabetes	**Secondary**	/	/

Note: / : information not available*

The Phase III patients will be randomised across approximately 300 sites worldwide

PHASE III | DESIGN | SITE SELECTION



Nativ3 countries

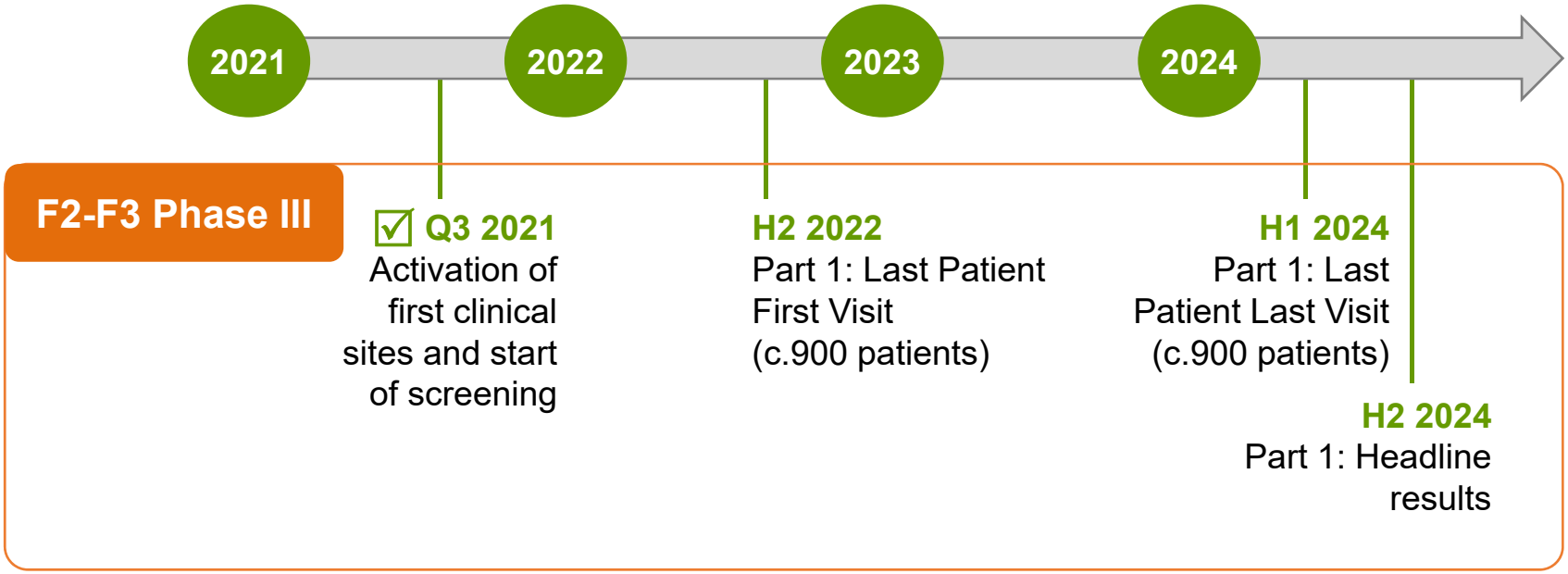
ICON

- Study conducted with our global partner ICON

25 countries worldwide with more than 330 sites expected to participate

Key milestones of the Phase III study in NASH (Part 1)

PHASE III **MILESTONES**



Lanifibranor clnical trial in patients with NAFLD and T2DM

PHASE II **NAFLD T2DM TRIAL**

Objective: Establish safety, efficacy and mechanism of action of lanifibranor in patients with T2DM and NAFLD. Specifically determine if lanifibranor decreases IHTG(1), improves hepatic insulin sensitivity, endogenous (hepatic) glucose production, gluconeogenesis and DNL(2)

Principal investigator

- Prof. Kenneth Cusi (University of Florida)

Randomisation

- Randomized (1:1), double-blind, placebo-controlled
- N=34 and 10 healthy non-obese as "normal" controls for all the metabolic and imaging tests
- Sample calculated assuming a 35% relative reduction of IHGT

Status

- Results expected for H1 2022

Primary endpoint

- Change in IHTG quantified by H-MRS(3) from baseline to week 24

Key secondary endpoints

- Proportion of responders (patients with a IHTG decrease ≥ 30%)
- NAFLD resolution (patients with IHTG ≤ 5%)
- Change in hepatic fibrosis (MRE(4), fibroscan, biomarkers)
- Change in metabolic outcomes (insulin sensitivity, DNL(3), glycemic control/HbA1c, lipids)
- Safety

34 patients; 24 week treatment

Double blind randomized placebo controlled

Healthy non-obese control group, 10 subjects

Placebo, 17 patients

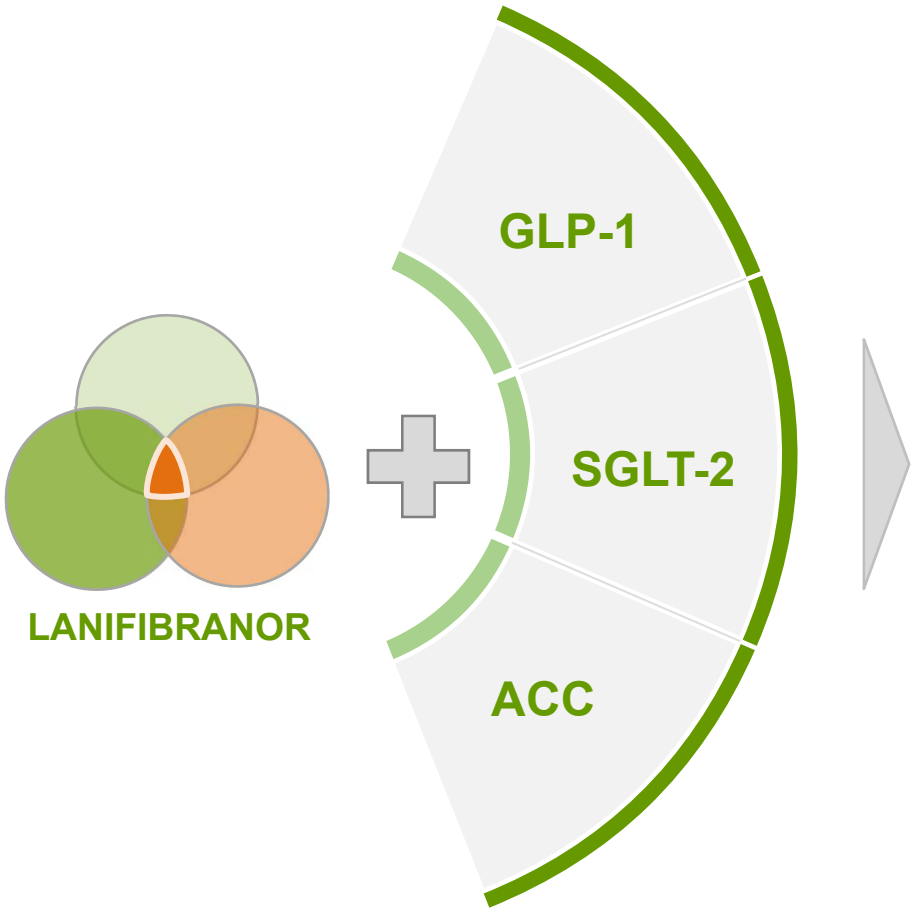
Lanifibranor, 800 mg once daily, 17 patients

Trial could provide additional supporting clinical data regarding lanifibranor's potential for the treatment of NASH

(1) Intrahepatic triglycerides (2) De-novo lipogenesis (3) Proton Magnetic Resonance Spectroscopy (4) Magnetic resonance elastography

Lanifibranor can be used in association with other therapies to further strengthen its value proposition

Examples and potential benefits of combination therapies



- **Potential complementary effects** on the multistep disease biology of NASH (disturbances of lipid and carbohydrate metabolism, insulin resistance, inflammation, fibrosis)
- Eventually **potentiate therapeutic efficacy** on histological endpoints: NASH resolution and fibrosis
- Ideally could manage metabolically ‘healthy’ **weight increase** in association with lanifibranor

Adding a SGLT2i to lanifibranor could prove to be a promising therapeutic approach

PHASE II SGLT2 combination study

Lanifibranor and SGLT2 rationale

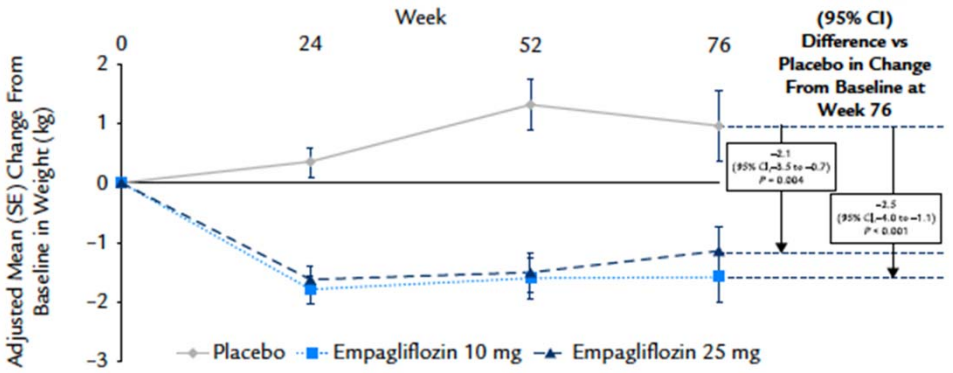
- Complementary MOA: inhibition of renal reabsorption of glucose, diuretic effect, stimulation of erythropoiesis
- Proven clinical benefits: improvements of glycaemia and lipid related metabolic markers
- Weight loss
- Oral therapy
- Four randomized trials of patients on pioglitazone vs pio. + SGLT2i (N=1411 T2DM patients; 24-72 weeks trials)
  - Efficacy:
    - Larger reduction of HbA1c and fasting blood glucose level
    - More patients reaching HbA1C < 7%
    - Weight and blood pressure reduction
  - Safety : no difference in death, heart failure, hypoglycemia, urinary tract infection. More frequent genital infections

Empagliflozin choice(2)

- Four SGLT2i products are approved in the US and EU as an adjunct to diet and exercise to improve glycemic control
  - Lilly/BI: empagliflozin/Jardiance® 2.8b$ sales in 2020
  - AstraZeneca: dapaglifozin/Farxiga® 1,9b$ sales in 2020
  - J&J: canagliflozin/Invokana® 795M$ sales in 2020
  - Merck: ertugliflozin/Steglatro®
- These four medicines having comparable efficacy and safety profiles, the choice was made to use the most successful and available product

Empagliflozin as add-on therapy to pioglitazone in patients with TD2M(1)

- 498 patients treated with pioglitazone randomized to empagliflozin 10 mg, 25 mg or placebo once daily for 24 weeks in the EMPA-REG PIO™ study, 305 (61.2%) were treated in a double-blind extension trial for ≥52 weeks (total duration ≥76 weeks)
- Compared with placebo, adjusted mean (95% CI) changes from baseline in HbA1c level at week 76 were -0.59% (P < 0.001) and -0.69% (P < 0.001) empagliflozin 10 mg and 25 mg, respectively
- Compared with placebo, adjusted mean (95% CI) changes from baseline in weight at week 76 were -2.0 kg (P < 0.001) and -1.7 kg (P < 0.001) for empagliflozin 10 mg and 25 mg, respectively



Source: (1) Empagliflozin as Add-on Therapy to Pioglitazone With or Without Metformin in Patients With Type 2 Diabetes Mellitus, Kovacks et al, Clin Ther. 2015;37:1773–1788; (2) company reports

LEGEND Study Design

PHASE II | **Lani + SGLT2i**

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

LEGEND Study

Principal investigator

- Prof. M. Lai, gastroenterologist-hepatologist, associate professor of medicine; Beth Israel Deaconess Medical Center (USA)
- Prof. O. Holleboom, academic medical specialist (diabetes and metabolism) at the Amsterdam University Medical Center (NL)

Status

- **First site activated:** H1 2022
- **Headline results**: H2 2023

Inclusion criteria

- Adult patients with diabetes and NASH

Primary outcome measures

- HbA1c change

Secondary outcome measures

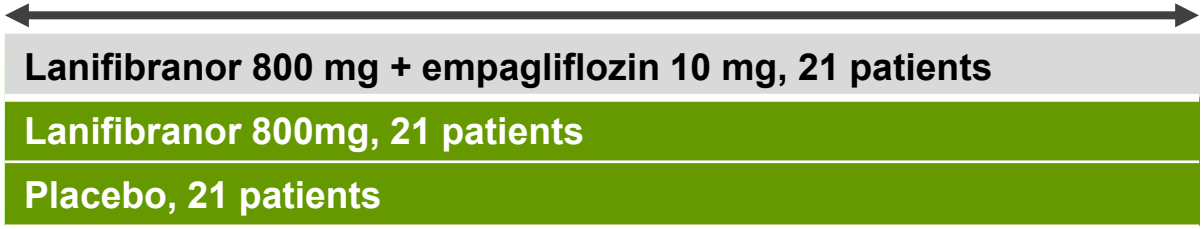
- MRI-based imaging to collect non-invasive data on hepatic fat, inflammation and fibrosis
- Glycaemic/lipid parameters, inflammatory markers
- Changes in body fat composition

Other outcome measures (safety/exploratory)

- AEs, body weight, PK, IHTG, cT1, biomarkers

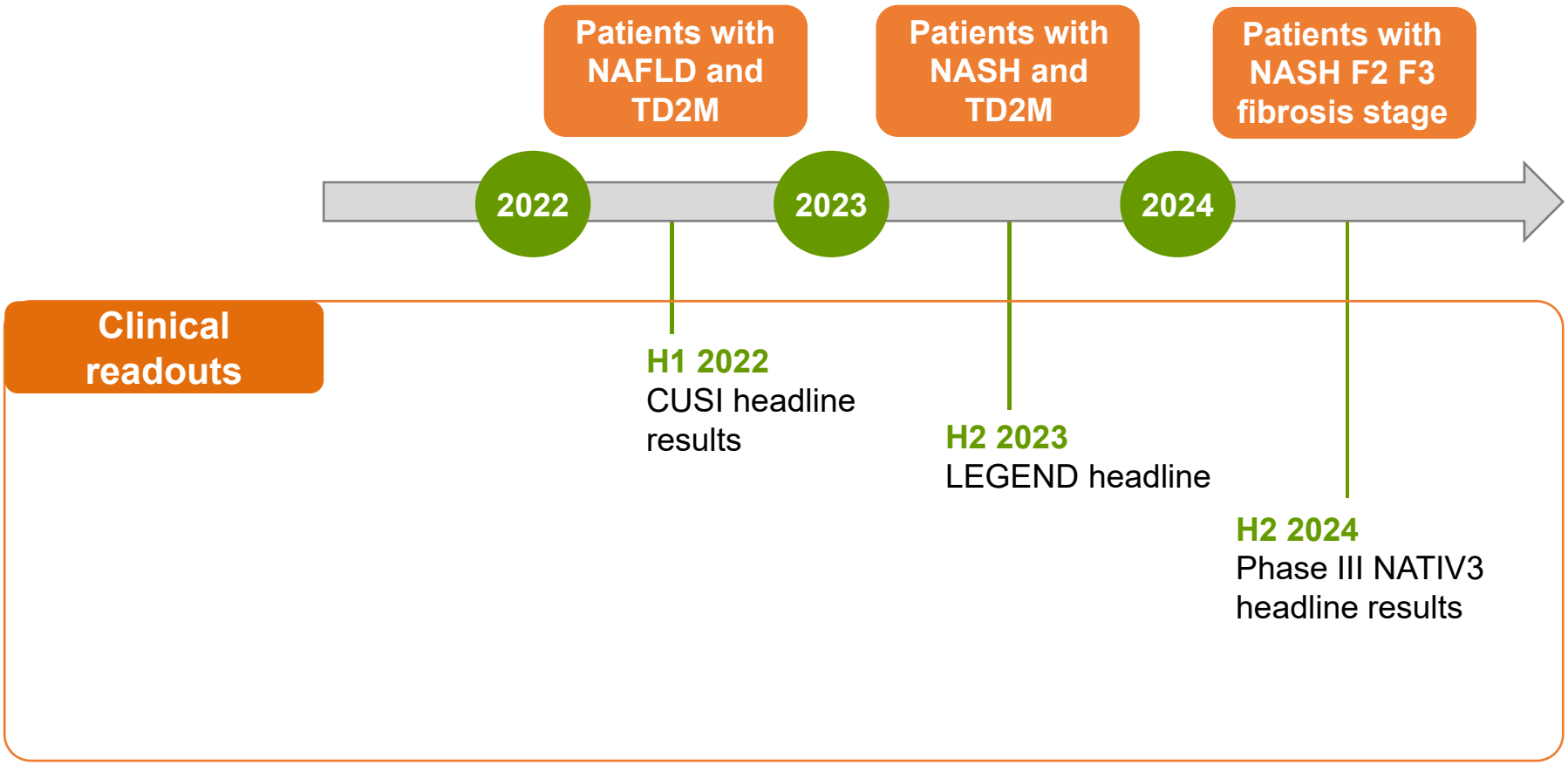
63 patients / 24 week treatment

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



With LEGEND study, Inventiva will have a clinical readout every year up to the phase 3 data

CLINICAL **READOUTS**



Odiparcil – MPS

Mucopolysaccharidoses (MPS) are devastating diseases with high unmet medical needs

MPS is a group of inherited lysosomal storage disorders

- Lysosomes function as the primary digestive units within cells: enzymes within lysosomes break down or digest particular nutrients, such as certain carbohydrates and fats
- The absence or malfunctioning of lysosomal enzymes are responsible for metabolic disorders caused by the abnormal degradation of glycosaminoglycans (GAGs) or mucopolysaccharides
- MPS symptoms first appear during early childhood and a patient's life expectancy depends on the severity of symptoms: without treatment, severely affected individuals may survive only a few years, those with milder forms of the disorder usually live into adulthood, although their life expectancy may be reduced
- The prevalence of all forms of MPS depends on the subtype: the incidence of MPS VI is estimated to be approximately 1 / 240,000 to 1 / 400,000 live births

MPS has devastating clinical consequences: example MPS I, II and VI

- The progressive accumulation of GAGs in the lysosomes causes progressive damage throughout the body, including the heart, eyes, bones, joints, respiratory system and central nervous system

Consequences	MPS I	MPS II	MPS VI
Intellectual development impairment	☑	☑	
Coarse facies, short stature	☑	☑	☑
Dysostosis multiplex	☑	☑	☑
Joint stiffness	☑	☑	☑
Spinal cord compression	☑	☑	☑
Organomegaly	☑	☑	☑
Poor vision (corneal clouding)	☑	☑(1)	☑
Hearing loss	☑	☑	☑
Cardiac/respiratory disease	☑	☑	☑

(1) Retinal degeneration with no corneal clouding

Source: (1) Source: Rheumatology 2011 Therapy for mucopolysaccharodises; Vassili Valayannopoulos and Frits A. Wijburg

Despite enzyme replacement therapies (ERT) being commercially successful, many unmet medical needs remain

Enzyme replacement therapies are standard of care in MPS

- Recombinant human enzymes, **requiring a once a week intravenous infusion over 4 hours**
- **Limited penetration into protected or poorly vascularized tissues** such as cornea or cartilage, where MPS symptoms often manifest

Product	Company	MPS	Est. yearly cost	2019 sales
Aldurazyme (laronidase)	genzyme	MPS I	$ 217K	€ 224M
elaprase (idursulfase)	Takeda	MPS II	$ 522K	$ 640M
Vimizim (elosulfase alfa)	BIOMARIN	MPS IVA	$ 578K	$ 544M
Naglazyme (galsulfase - rch)	BIOMARIN	MPS VI	$ 476K	$ 374M
Mepsevii (vestronidase alfa-vjbk) injection, for intravenous use	ultragenyx pharmaceutical	MPS VII	$ 550K	$ 12.6M

Source: Sales - Full year 2019 press-release; WAC without discounts for a 25-kg patient - BioCentury "Making of MEPSEVII" Dec 11, 2017

ERT is expensive and usually requires outpatient administration. Significant unmet need remains in addressing symptoms in organs where ERT fails to penetrate

Source: H. Noh, J. I. Lee; Current and potential therapeutic strategies for mucopolysaccharidoses; Journal of Clinical Pharmacy

Odiparcil: an orally available small molecule GAG reduction therapy designed to treat several forms of MPS

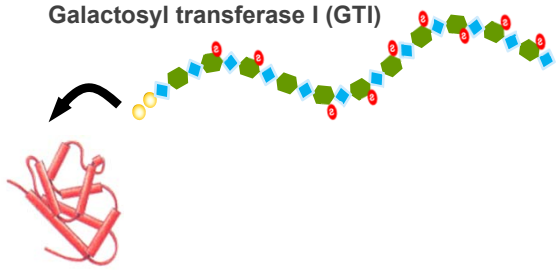
- **Acts to decrease lysosomal accumulation** of GAGs by promoting formation of soluble DS / CS which can be excreted in the urine
- **Oral administration** and **distribution** in tissues that are poorly penetrated by enzyme replacement therapy (ERT)
- Potential to be prescribed in **combination with ERT and as monotherapy**
- Odiparcil-mediated reduction of intracellular GAG accumulation **demonstrated in *in vitro* and *in vivo* models**
- **Positive Phase IIa trial results in MPS VI adult patients** with favorable tolerability profile
- **Low toxicity observed** *in vivo and* **favorable tolerability** profile **in multiple Phase I and Phase II clinical trials** in unrelated indication(1) (administered to >1,800 subjects)
- Method of use patent granted in the United States and in Europe with **LOE(2) 2039, including 5-year extension**
- MPS VI **Orphan Drug Designation granted in the U.S. and in the EU** and **Rare Pediatric Disease Designation** in MPS VI granted in the U.S.
- **FAST Track** designation granted by FDA

(1) Trial conducted by GSK prior to Inventiva's founding (2) LOE: Loss of exclusivity

Differentiated mechanism of action potentially synergistic with ERT

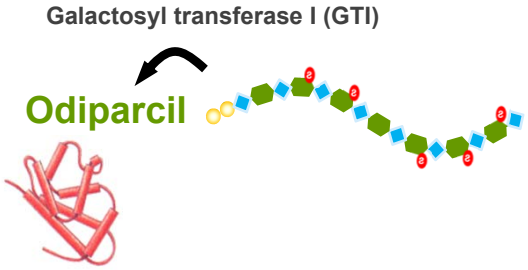
Odiparcil acts to divert endogenous protein-bound GAG synthesis to soluble odiparcil-bound chondroitin sulfate (CS) and dermatan sulfate (DS) synthesis

Synthesis of proteoglycans (HS, CS, DS)



GTI activity

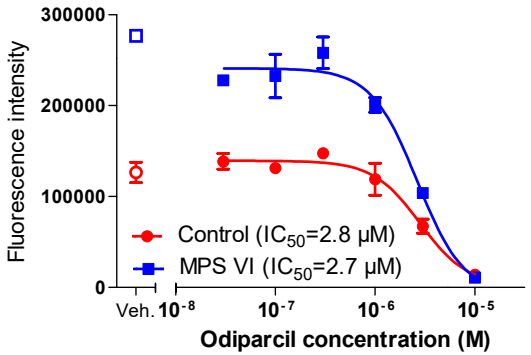
Substrate	Vm/Km
D-xylose	0.8
Odiparcil	1857

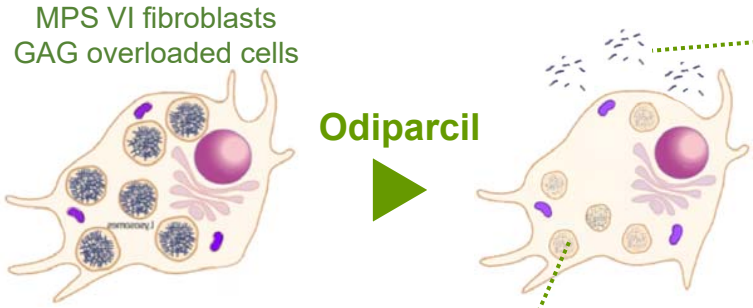


Synthesis of soluble DS and CS

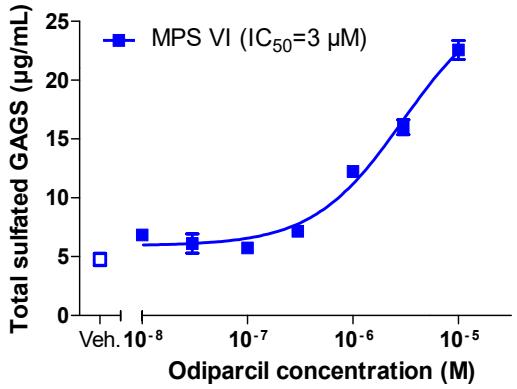
Odiparcil and intracellular GAG accumulation *in vitro* in MPS VI patient cells

Intracellular CS storage





Extracellular GAG



Odiparcil associated with reduced GAG accumulation in MPS VI patient cells

Source: H. Noh, J. I. Lee; Current and potential therapeutic strategies for mucopolysaccharidoses; Journal of Clinical Pharmacy, company data

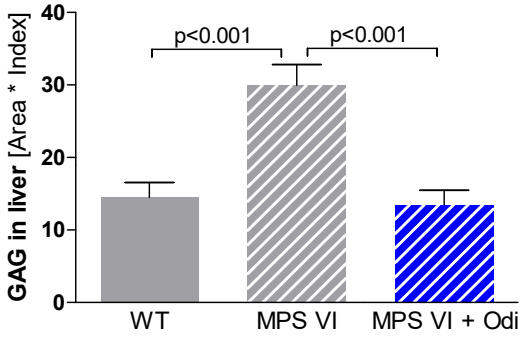
Odiparcil mechanism of action potentially relevant to MPS subtypes with excess DS and CS

MPS Type	Frequency	DS	CS	HS(1)	KS(2)
MPS I-H		✓		✓	
MPS I-S	1/100,000	✓			
MPS I-H/S		✓		✓	
MPS II Types A & B	1/100,000	✓		✓	
MPS IV Type A	1/40,000 to 1/200,000		✓		✓
MPS VI	1/240,000 to 1/400,000	✓	✓		
MPS VII	Very rare	✓	✓	✓	

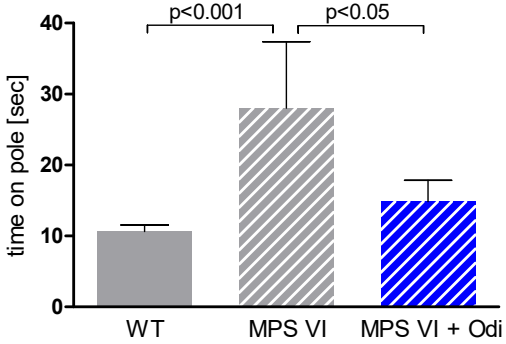
Source:Rheumatology 2011 Therapy for mucopolysaccharodises; Vassili Valayannopoulos and Frits A. Wijburg; (1) Heparan Sulfate; (2) Keratan Sulfate

Odiparcil GAG clearance mechanism of action observed in MPS VI mice

Odiparcil and GAG accumulation in livers tissues

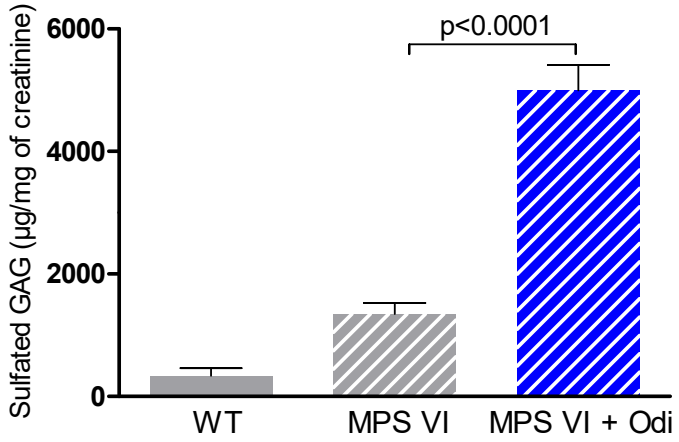


Odiparcil and animal mobility



Wild-type and MPS VI mice

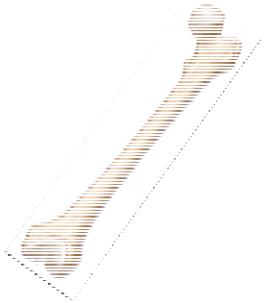
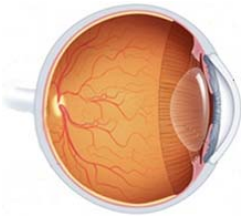
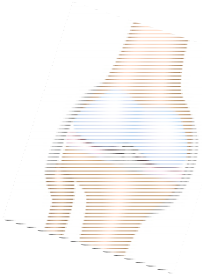
Soluble GAGs produced from odiparcil are excreted in urine



Source: Company data

Odiparcil penetrates tissues where ERT has limited efficacy

Odiparcil observed to be well distributed in tissues and organs poorly penetrated by recombinant enzymes

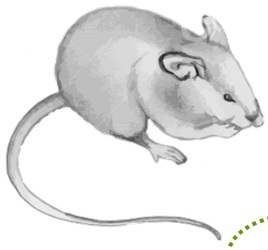
	Heart	Bone	Cornea	Cartilage
				
Odiparcil[1]	✓	✓	✓	✓
rhASB[2]	✓	Not tested	Not detected	Not detected

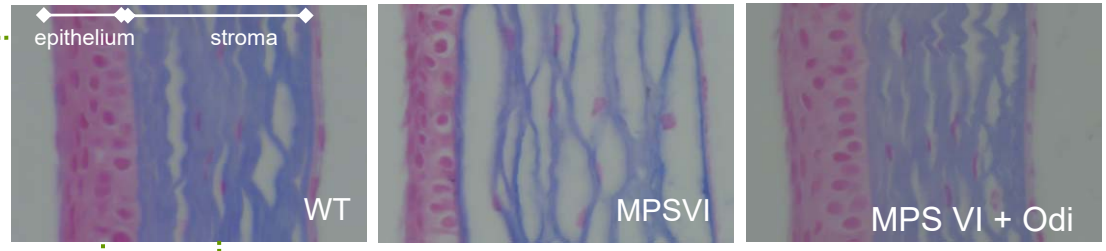
Meaningful concentrations of odiparcil observed in tissues that are poorly vascularized or protected by a barrier: bone, corneal tissue and cartilage

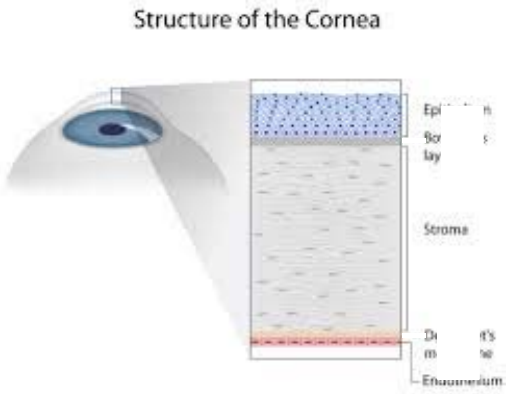
Source: (1) Odiparcil: tissue distribution following 25mg/kg oral administration , TID for 5 days; (2) Recombinant human ARB: Expressed as ratio of ARSB enzyme activity in the liver in MPS VI cats after repeat infusion (conditions: preliminary trial, Trial A and Trial B from Auclair et al. 2003)

Odiparcil reverses corneal impairment in MPS VI mice

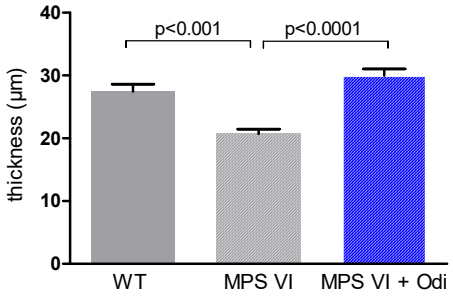
Odiparcil administration observed to affect corneal structure and corneal GAG storage





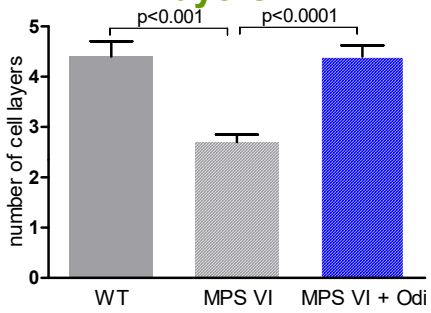


Odiparcil effect on corneal epithelium thickness



N=10 for all groups

Odiparcil effect on number of corneal epithelium cell layers



Odiparcil effect on GAG storage in corneal stroma

Blinded corneal stroma vacuolation scoring

WT	0.0
MPS VI	2.9
MPS VI + Odi	0.5

scale (0-3)

0. no detectable vacuolation, no GAG accumulation
1. some large vacuolation with some distended cells
2. extensive area of large vacuolation with GAG accumulation
3. extensive area of large vacuolation with GAG accumulation and separate collagen fibers

Source: Company data

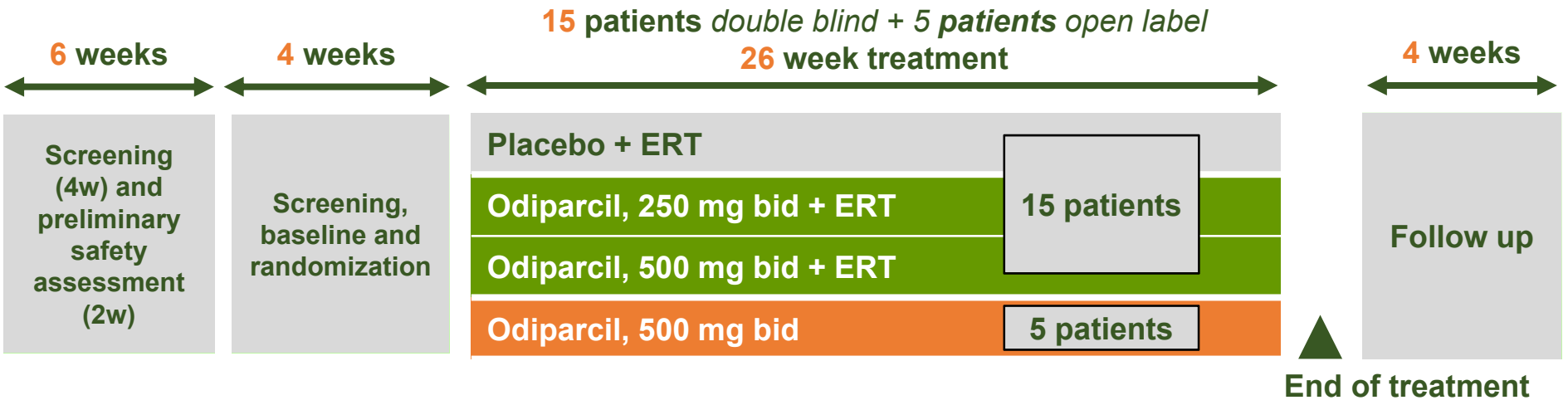
iMProveS Phase IIa trial of odiparcil in MPS VI

Phase IIa

- Safety and efficacy trial with evidence for dose selection and PK / PD response characterization
- **Clinicaltrials.gov identifier:** NCT03370653

Population

≥ 16yo



Endpoints

Safety

- Clinical and biological assessments (standard tests)

Pharmacokinetics

- Odiparcil plasma levels

Efficacy

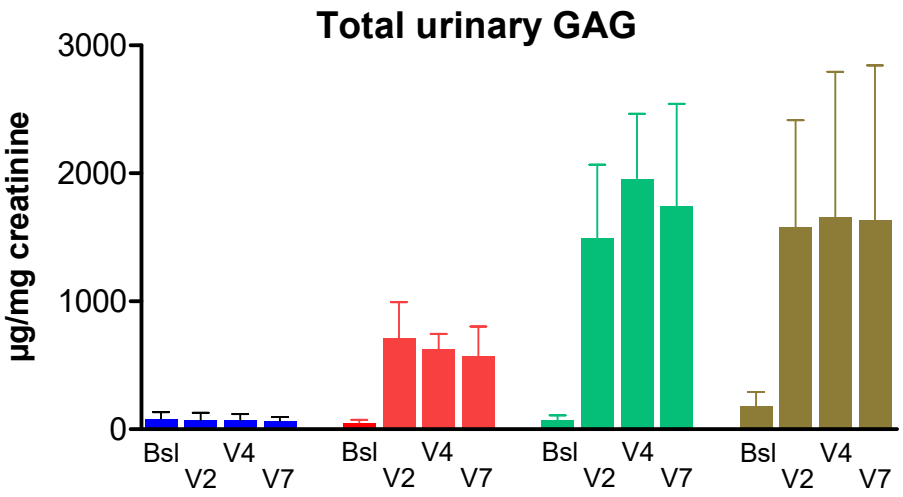
- Leukocyte, skin and urinary GAG content
- Activity and mobility tests (6 minute walk test, upper limb function, shoulder mobility range)
- Cardiac, vascular and respiratory functions
- Eye impairment, hearing capacity, pain assessment, quality of life questionnaires

Safety data

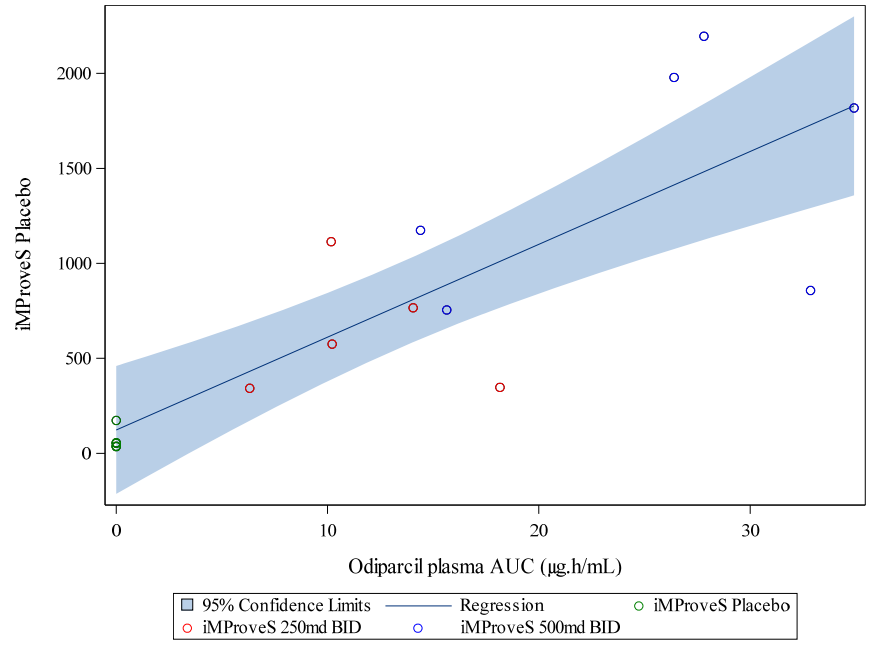
- The **clinical trial met its safety primary endpoint with a favourable tolerability profile consistent with that** observed in previous Phase I and Phase II clinical trials
- The majority of adverse events were **mild or moderate**
- One death occurred in the placebo group
- Three serious adverse events (SAEs) were assessed as treatment-related in patients in the odiparcil groups.
  - Two SAEs were biological findings qualified as laboratory false-positive
  - One SAE was a skin reaction, which is frequently observed in MPS patients treated with ERT
- Compared to previous Phase I and II clinical trials conducted with odiparcil in another indication, **no new safety conclusions were drawn**

Odiparcil pharmacodynamics: total GAG levels in urine and PK/PD correlation

A dose-dependent urinary GAGs clearance, used as an activity biomarker, was observed in the odiparcil treated patient population



- uGAG (total) increased after 4 week of odiparcil
- uGAG increase reaches a steady state after 4 weeks of treatment
- At 1000 mg/day the increase is comparable in ERT and non-ERT cohorts



- Urinary GAG (total) is correlated with odiparcil exposure in plasma

● ERT + placebo ● ERT + odiparcil 500mg ● ERT + odiparcil 1000mg ● Non-ERT, odiparcil 1000mg

- The PK profile in MPS VI patients treated with odiparcil is not observed to be impacted by ERT and is consistent with profiles previously observed in other Phase I and Phase II trials in another indication

Efficacy endpoints

iMProveS
IMPROVE MPS TREATMENT

Partially addressed by ERT

Endurance and mobility
- 6-minute walk test (6MWT)
- 9 hole peg test (9HPT)
- Range of motion of left and right shoulders (S-ROM)

Respiratory function
- Forced vital capacity (FVC)
- Forced expiratory volume in 1 second (FEV1)

- Number of evaluable patients at Visit 7 (26w) N=13
- Efficacy parameters assessed at baseline and end-of-treatment (EOT)
- Two efficacy analyses
  - Statistical approach
  - Interpretation of blinded individual results by experts

Not addressed by ERT (hard-to-reach tissues)

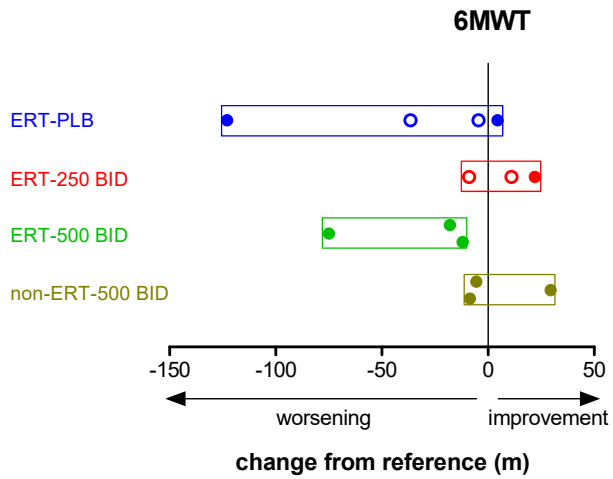
Cardiac and vascular system
- ECG, Echocardiogram
- Carotid intima media thickness (CIMT)

Ophthalmology
- Visual acuity
- Corneal clouding
  - Subjective evaluation (slit lamp)
  - Quantitative measurement (iris camera: corneal opacity measure (COM))

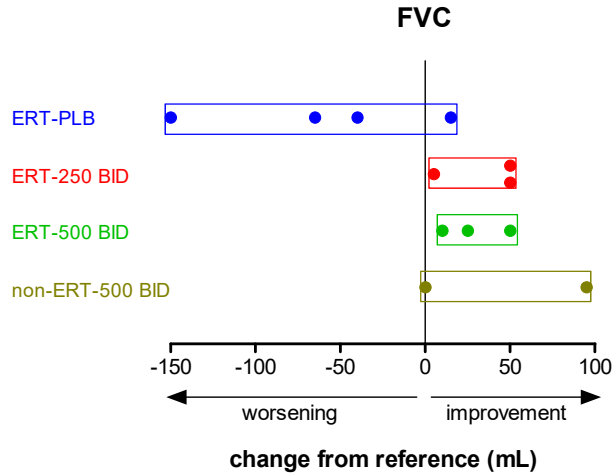
Pain assessment
- Brief Pain Inventory (BPI) questionnaire
  - 'Intensity' dimension
  - 'Interferences' dimension

Audiology
- Pure tone audiometry (PTA)

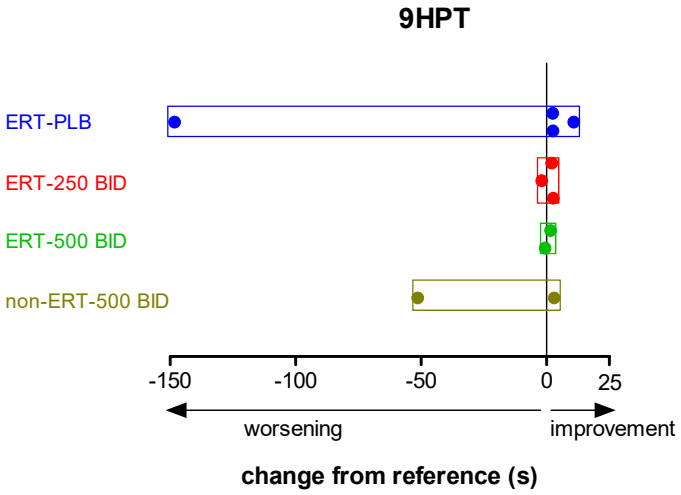
Efficacy data: trends of improvement on 6MWT and FVC

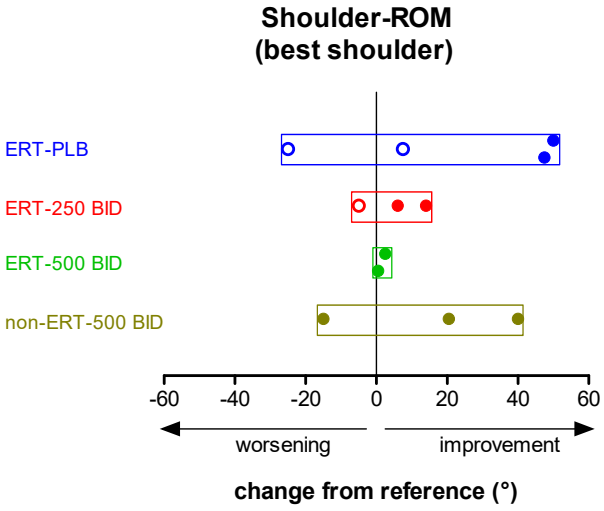


Trends of improvement in ERT-250 BID and non-ERT-500 BID compared to ERT-placebo



Improvement in all odiparcil treated groups compared to ERT-placebo





No significant differences between groups observed

Efficacy data: several patients treated by ERT and odiparcil show improvements in one or several parameters

Treatment (N=10)	Respiratory (FVC)	Ophthalmology (COM left eye, right eye)	Cardiology
Placebo + ERT (N=4)	**0**	**1** (slightly improved) Patient A(1): +4, +11 -	**1** (slightly improved) - Patient B: ↓ 30% LVMI
Odiparcil + ERT (N=6)	**3** (slightly improved) **250mg bid** Patient C: + 5% - **500mg bid** Patient E: + 4% Patient F: +9% -	**2** (improved) **250mg bid** - Patient D: +11, +14 **500mg bid** - Patient F: +13(2) -	**4** (3 slightly improved + 1 improved) **250mg bid** Patient C: ↓ 17% LVMI Patient D: no longer mitral regurgitation **500mg bid** - Patient F: ↓ severity mitral regurgitation Patient G(1): ↓ 14.5% LVMI, ↓ severity aortic regurgitation

(1) Patient presenting a CIMT reduction in both carotids
(2) Corneal transplant of the other eye
LVMI: left ventricular mass index (echocardiogram); CIMT: carotida intima media thickness

Efficacy data: signals of activity were also detected in patients only treated with odiparcil

iMProveS
IMPROVE MPS TREATMENT

Odiparcil 500mg Bid (N=3)	Respiratory (FVC)	Ophthalmology	Cardiology	Range of Motion	Other
Patient H	Improved FVC by +18%	NA	Stable	Improved range of motion on both shoulders (+17.8%/+21.0%)	Pain improved
Patient I	Stable	Stable	Slightly Worsened	Improved range of motion on both shoulders (+8.1%/+8.5%)	Pain improved
Patient J • Severe patient hospitalized • Poor compliance	NA	Stable	Worsening	Worsening	Pain improved

Odiparcil: anticipated clinical development path for approval in MPS VI

Completed

Phase IIa (6-m treatment)
MPS VI adults (16y+)
- Add on to ERT, n=15
- Not receiving ERT, n=5

iMProveS IMPROVE MPS TREATMENT

- Safety
- PK, PD (uGAG) and BM (leukoGAG, skinGAG)
- Exploratory assessment of efficacy

Open-label (iMProveS Extension)
Completers of iMProveS trial
- Add on to ERT, n=10
- Not receiving ERT, n=3

iMProveS IMPROVE MPS TREATMENT extension

- Safety
- Efficacy

Phase Ib/II (12-m treatment)
MPS VI children (5y to 15y)
- Add on to ERT, n=24

Safe-KIDDS

- Safety
- PK / PD
- Efficacy

Phase III
MPS VI patients (5y to adult)
Monotherapy and add on to ERT

Cedirogant

Cedirogant: a clinical stage RORγ inverse agonist co-discovered by Inventiva with potential in several auto-immune diseases (I)

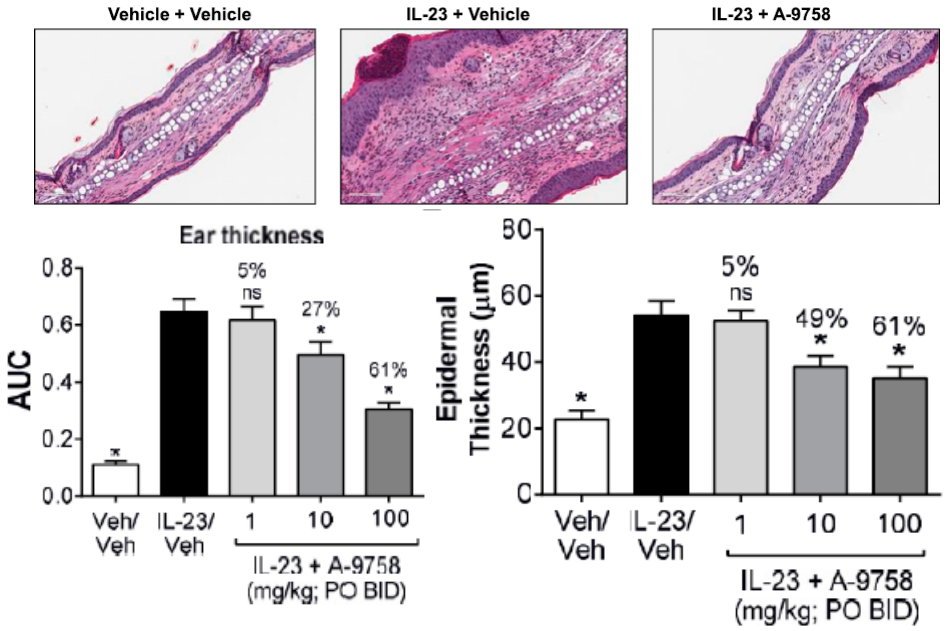
abbvie

RORγ is believed to be a master regulator of Th17 differentiation and IL-17 expression, an approach validated by several successful biologics

- Pharmacological inhibition of RORγ by small molecules has been observed **to suppress Th17 production, block cutaneous inflammation in animal models of psoriasis and inhibit TH17 signature gene expression** by cells isolated from psoriatic patient samples
- RORγ is therefore a **validated drug target** for the treatment of psoriasis and potentially other cutaneous inflammatory disorders

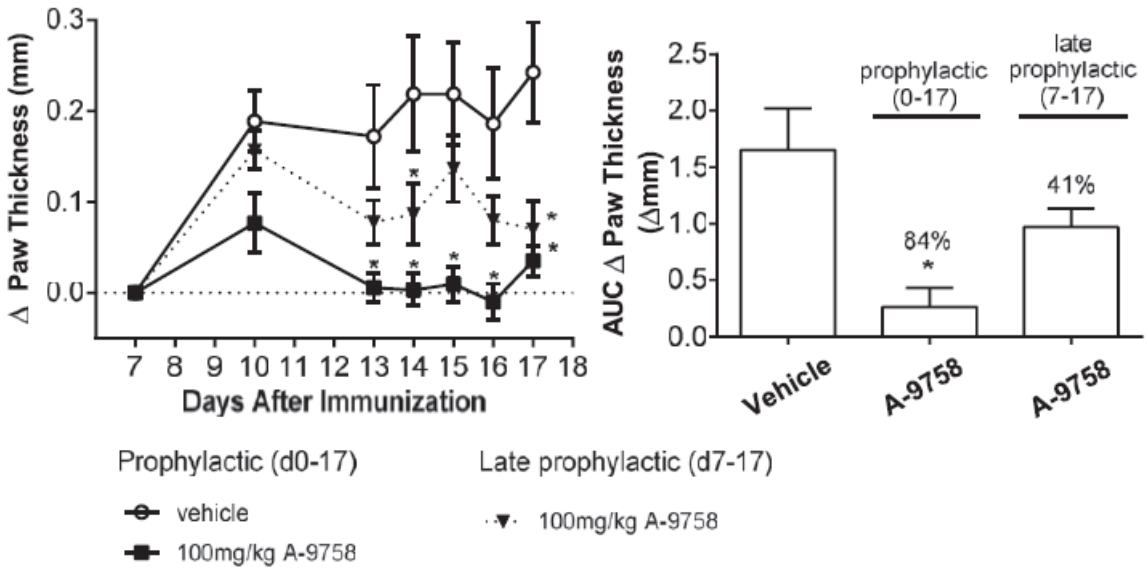
A-9758(1) attenuates IL-23 mediated skin inflammation

Effect of RORγ inhibition on IL-23 mediated psoriasiform dermatitis



A-9758(1) blocks GPI-mediated arthritis

Effect of RORγ inhibition on paw swelling both on prophylactic and late prophylactic treatment



(1) A-9758 is first generation compound developed within the collaboration with AbbVie previously to identifying cedirogant

Source: Inhibition of interleukin-32 mediated inflammation with a novel small molecule inverse agonosit RORγt; The Journal of Pharmacology and Experimental Therapeutics 371:208-218, October 2019

Cedirogant: a clinical stage RORγ inverse agonist co-discovered by Inventiva with potential in several auto-immune diseases (II)

Cedirogant (ABBV-157) is targeting indications where competitors have reached block-buster status

- Cedirogant Target Product Profile: **Humira in a pill + better safety**
- Inventiva to receive development, regulatory, commercial milestones and **tiered royalties from the mid-single to low-double digits**
- **Composition of matter patent** filed in June 2016 and approved in October 2018

Brand	Company	Target	Posology	2020 sales(1)
Humira	AbbVie	Anti-TNFα	Injectable	$19,8b
Stelara	Janssen	IL-12/23	Injectable	$7,7b
Cosentyx	Novartis	IL-17A	Injectable	$3,9b
Otezla	Celgene	TNFα	Oral	$2,2b
Taltz	Eli Lilly	IL-17A	Injectable	$1,8b
Skyrizi	BI / AbbVie	IL-23	Injectable	$1,6b

Cedirogant (ABBV-157) is currently being developed in moderate to severe psoriasis, a common skin condition that affects 2-4% of the population in Western countries

- **Single ascending dose and multiple ascending dose** trials in healthy volunteers **completed** with no safety signals
- **Phase Ib in patients with chronic plaque psoriasis completed: clinical proof of efficacy achieved**
- Following Phase Ib results, AbbVie has communicated its **plans to initiate a Phase IIb in H2 2021**

"In our Phase Ib study, 157 showed promising activity as an oral psoriasis agent and we plan to move the asset forward to a larger Phase IIb dose-ranging study in the second half of this year … with respect to oral psoriasis agents, we would want to come in from an efficacy perspective with something that clearly exceeded the threshold that existed in the past with Otezla ... we'd be looking for that Humira-like efficacy or greater as something that we would like to use to enter the space within oral, obviously, coupled with a strong safety profile."

Dr. Michael Severino AbbVie Vice Chairman and President(2)

Next milestone expected for phase IIb initiation which is planned for November 2021

(1) Company Q1 2021 and full year 2020 press releases; (2) ABBV-157 is Cedirogant Abbvie code; AbbVie Q1 2021 earnings call April 30 2021 9 AM ET; Transcript from FactSet;

Cedirogant Phase IIb in in adults with moderate to severe psoriasis

A Phase IIb, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study to Evaluate the Safety and Efficacy of Cedirogant (ABBV-157) in Adult Subjects With Moderate to Severe Psoriasis

Status

- Sponsor: **AbbVie**
- ClinicalTrials.gov Identifier: NCT05044234
- Approx. 200 adult participants with moderate to severe plaque psoriasis will be enrolled at approx. 45 sites
- Estimated study start date: **November, 2021**
- Estimated study completion date: **March, 2023**

Inclusion criteria

- Participants with stable moderate to severe plaque psoriasis of at least 6 months duration and who are candidates for systemic therapy or phototherapy

Primary outcome measures

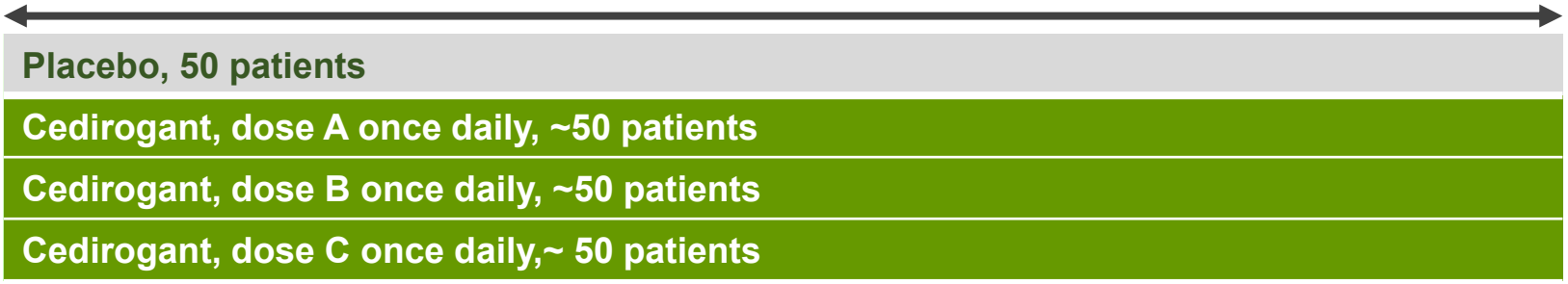
- Percentage of participants achieving >=75% reduction from baseline in Psoriasis Area Severity Index(1) (PASI) score (PASI 75)

Secondary outcome measures

- Percentage of participants achieving a Static Physician Global Assessment(2) (sPGA) score of clear or almost clear
- Percentage of participants achieving >=50% / >=90% / 100% reduction from baseline in PASI Score (PASI 50; PASI 90; PASI 100)
- Percentage of participants achieving Psoriasis Symptoms Scale(3) (PSS) total score of 0 for participants with PSS >0 at baseline
- Percentage of participants achieving an Itch Numerical Rating Scale(4) (NRS) >=4 point improvement from baseline for participants with Itch NRS >=4 at baseline

200 patients / 16 week treatment / ~45 sites

Double blind randomized placebo controlled



(1) The PASI is a tool that provides a numeric scoring for participants' overall psoriasis disease state, ranging from 0 to 72, with a higher score indicating more severe disease; (2) The sPGA is a 5-point score ranging from 0 to 4, based on the physician's assessment of the average thickness, erythema, and scaling of all psoriatic lesions. A lower score indicates less body coverage, with 0 being clear and 1 being almost clear; (3) The PSS is a 4-item patient-reported outcome instrument that assesses the severity of psoriasis symptoms in patients with moderate to severe psoriasis. Current symptom severity is assessed using a 5-point Likert-type scale ranging from 0 (none) to 4 (very severe); (4) The Itch NRS is an 11-point scale that participants complete daily to describe the intensity of their itch using a 24-hour recall period. Scores vary between 0, representing "no itching" and 10, representing "worst itch imaginable

Source: clinicaltrials.gov

Competitive landscape

Product name	Company	Development Phase
Cedirogant	abbvie	**Phase 2**
Bevurogant	Boehringer Ingelheim	Phase 2
AUR-101	AURIGENE Accelerating Discovery	Phase 2
JTE-761	JTI Japan Tobacco International	Phase 1
IMU-935	Immunic Therapeutics	Phase 1

Selected RORγ programs stopped

Pfizer · Allergan · Takeda · SANOFI · gsk · Genentech A Member of the Roche Group

Source: Companies web sites; clinicaltrials.gov

YAP-TEAD and TGF-β programs

YAP-TEAD and TGF-β programs

YAP-TEAD program

- Hippo signalling pathway is potentially implicated in the **process of cell differentiation and proliferation**, tissue growth and organ size
- Inventiva compounds observed to **disrupt interaction between YAP and TEAD** along the pathway
- Potentially **relevant in multiple cancer indications** including malignant mesothelioma, lung cancer and triple negative breast cancer
- *In vitro* evidence for **synergies with standard of care** and suppression of tumor resistance
- ***In vivo* tumor repression observed** in pre-clinical models (alone and in combination with standard of care)
- Proprietary chemistry
- Lead and back-up compounds available
- Pre-clinical candidate screening and **clinical candidate selection** ongoing
- **Pre-clinical development start planned in 2022**

TGF-β program

- TGF-b is a cytokine that is a key driver of fibrosis and acts by activating fibroblasts into myofibroblasts, driving the production of fibrotic tissues
- Target validated
- **Program progressing into lead generation**

Recent and upcoming catalysts

Recent and anticipated key milestones

Lanifibranor

- ☑ Positive topline results of NATIVE Phase IIb trial in NASH
- ☑ Breakthrough Therapy Designation granted by FDA
- ☑ NATIVE Phase IIb meeting with FDA and EMA Scientific Advice
- ☑ Activation of first clinical sites and start of patient screening in phase III trial in NASH **– H2 2021**
- ▶ Activation of first clinical sites for LEGEND trial combining lanifibranor with SGLT2i empaglifloxin **– H1 2022**
- ▶ Results of Phase II trial in T2DM patients with NAFLD **– H1 2022**
- ▶ Last Patient First Visit of the phase III trial in NASH **– H2 2022**
- ▶ Results of LEGEND trial combining lanifibranor with SGLT2i empaglifloxin **– H2 2023**

Odiparcil

- ▶ Strategy update on odiparcil development **– 2022**

Cedirogant abbvie

- ☑ Clinical POC trial (Phase IB) in psoriasis
- ▶ Launch of phase IIB trial in psoriasis and milestone from AbbVie **– H2 2021**
- ▶ Study completion of phase IIB trial in psoriasis **– H1 2023**

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