inventiva

J.P.Morgan

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JANUARY 10-13, 2022
Westin St. Francis Hotel San Francisco, California

Developing innovative therapies in NASH and MPS

Corporate Presentation

January 2022

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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.

Key take-aways

Potential First-in Class & Best-in-Class NASH Drug

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

Positive Phase IIb topline data with statistical significance on NASH resolution and one stage fibrosis reduction

Mechanism of action addressing all key features of NASH

Breakthrough Therapy Designation granted by FDA

Pivotal Phase III initiated in Q3 2021

A Phase IIb Clinical Stage Collaboration with AbbVie

Cedirogant/ABBV-157 Small molecule RORγT Inverse Agonist

Potential to more effectively inhibit IL-17 production than antagonist approaches

Promising activity in Phase I study in psoriasis patients

Phase IIb dose-ranging study initiated Q4 2021

Inventiva eligible to receive milestone payments and sales royalties

Strong R&D Capabilities and Cash Position

R&D capabilities including wholly-owned 'pharma scale' discovery facilities with a discovery engine focused on nuclear receptors, transcription factors and epigenetic targets

Clinical Ops team in place in Europe and the United States

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

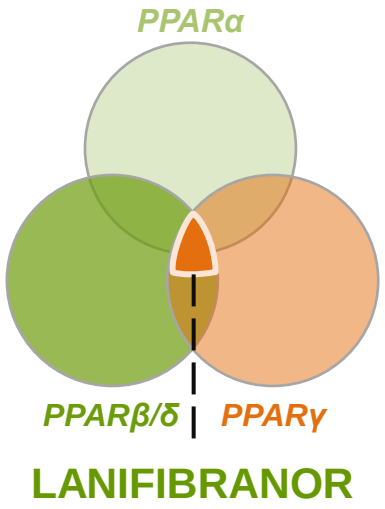
Cash position currently allowing a runway through Q1 2023

Lanifibranor in Nonalcoholic Steatohepatitis (NASH)

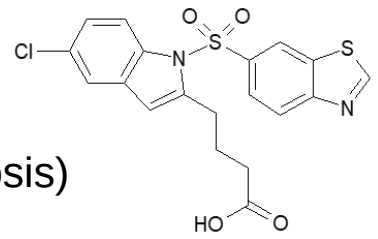
Lanifibranor: a pan-PPAR agonist in phase III development in NASH

LANIFIBRANOR

Moderate and balanced pan-PPAR agonist activity



- Small molecule that activates all three PPAR isoforms in humans
- Differentiated chemical structure: not a fibrate or a TZD
- Once daily oral administration
- **Positive Phase IIb trial** topline results in NASH
- **FAST Track** (including in NASH patients with compensated cirrhosis) **and Breakthrough Therapy** designations granted by FDA
- 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**



Favorable tolerability profile

- Phase I trials with more than **200** healthy volunteers and Phase IIa trial with **47** TD2M patients
- Approximately **250** patients treated for 24 or 48 weeks in Inventiva's completed Phase IIb clinical trials
- **Thorough QT/QTc study** demonstrates no impact of the drug on QT intervals
- FDA confirmation that the **non-clinical toxicology package is complete and acceptable for NDA filing**

Lanifibranor overall development plan in NASH

CLINICAL DEVELOPMENT

Phase I → **Phase IIa** → **Phase IIb (NATIVE)**

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*

Phase III in patients with NASH and F2-F3 fibrosis → **Registration**

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*

Phase II in NAFLD patients with T2D

Lani + empagliflozine Phase II in NASH patients with T2D

Phase III in NASH patients with compensated cirrhosis

Completed clinical trials

Ongoing clinical trials

Potential clinical trials

Lanifibranor overall development plan in NASH

CLINICAL DEVELOPMENT

Phase I → **Phase IIa** → **Phase IIb (NATIVE)**

- **Phase III in patients with NASH and F2-F3 fibrosis** — **H2 2024** Headline results
- **Phase II in NAFLD patients with T2D** — **H2 2022** Headline results
- **Lani + empagliflozine Phase II in NASH patients with T2D** — **H2 2023** Headline results

- Completed clinical trials
- Ongoing clinical trials
- Potential clinical trials

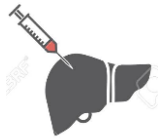
The Phase IIb NATIVE trial studied 800 mg and 1200 mg once-daily lanifibranor across 247 patients

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

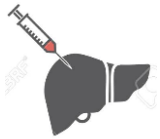
Screening
▶ **Liver biopsy**

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 (T2D)

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

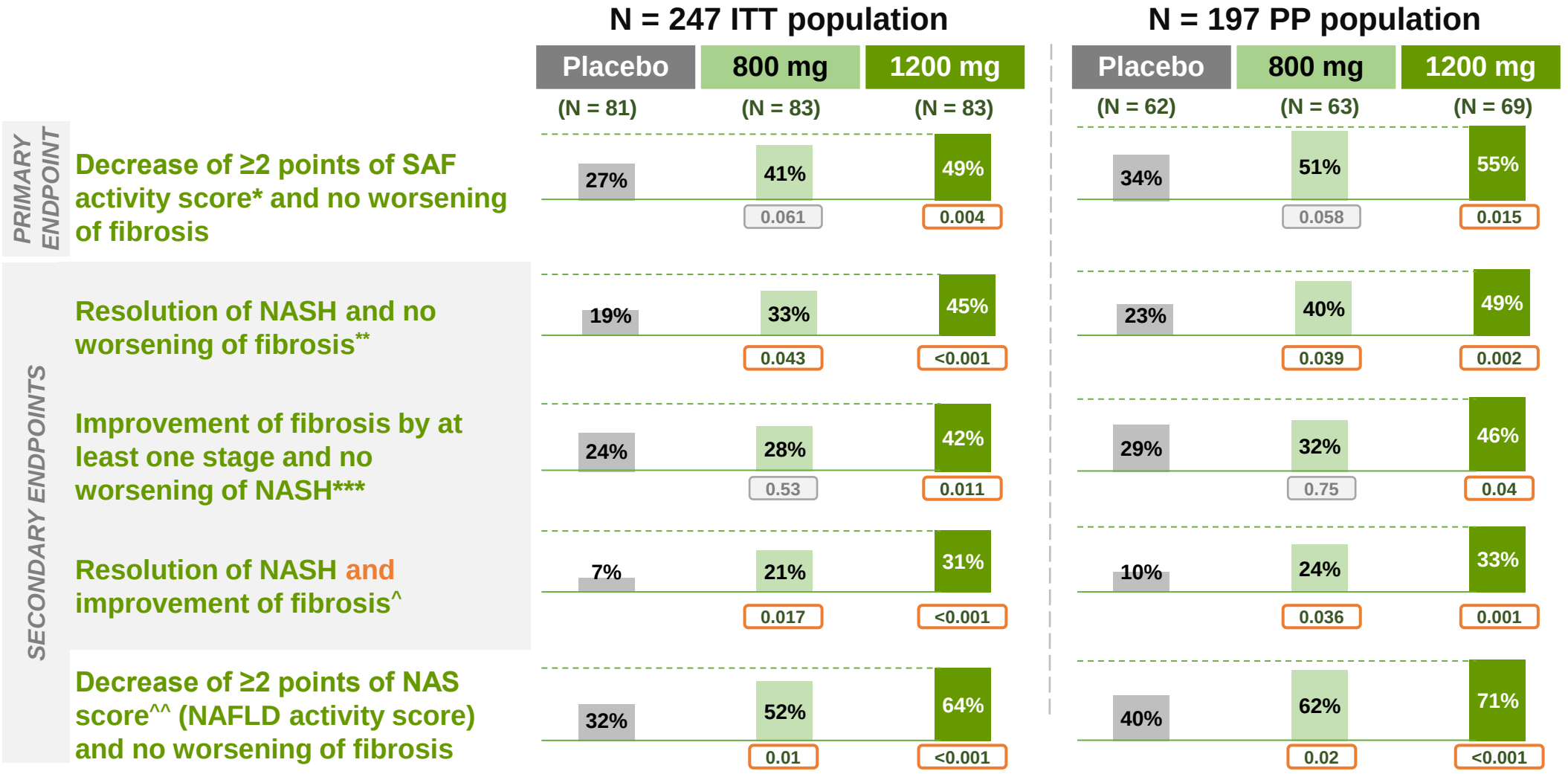
More information on: http://www.native-trial.com/ ; (1) https://www.nejm.org/doi/full/10.1056/NEJMoa2036205

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.*

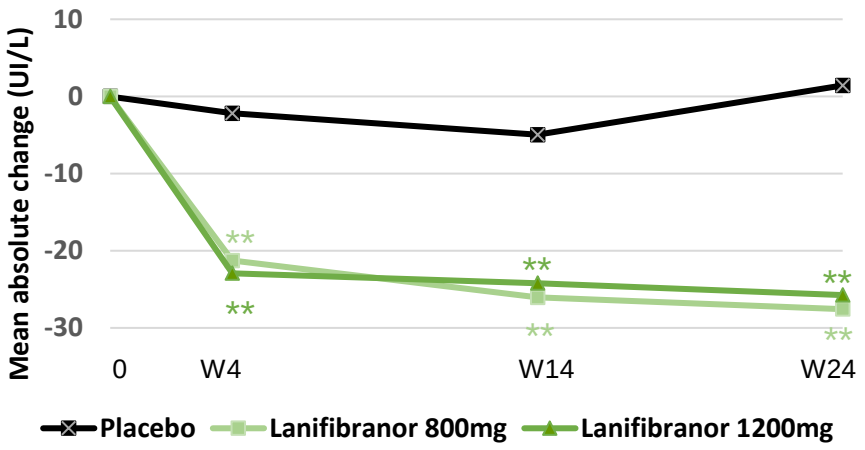
A statistically significant decrease in liver enzymes was observed

PHASE IIb | EFFICACY | OTHER

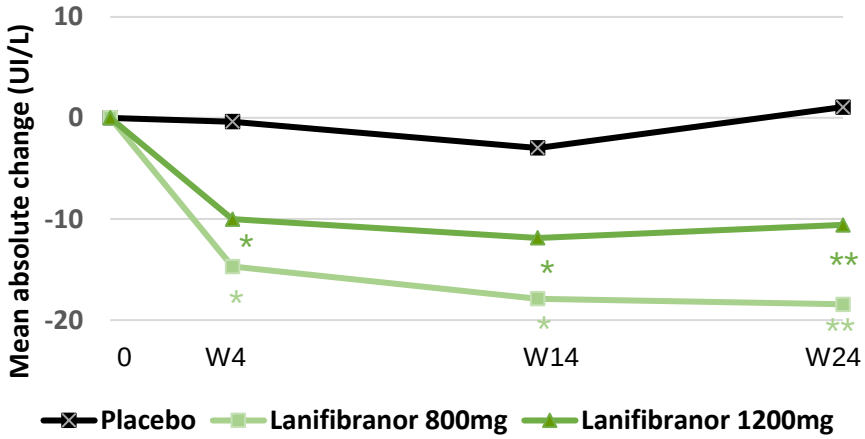
SECONDARY ENDPOINTS

Other secondary endpoints in ITT (N = 247)

Absolute change from baseline in ALT

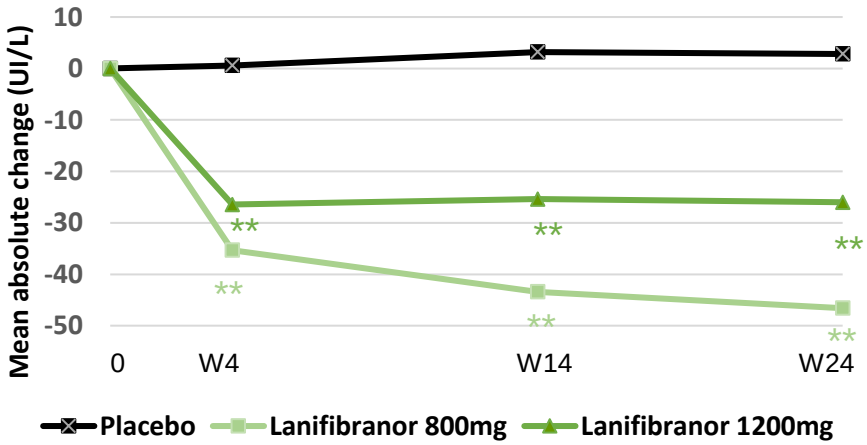


Absolute change from baseline in AST



* 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

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

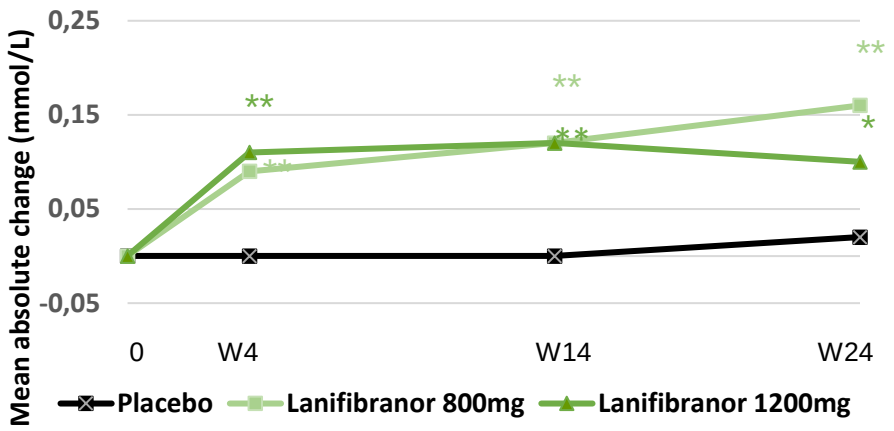
PHASE IIb | EFFICACY | OTHER

Other secondary endpoints in ITT (N = 247)

* p<0.01 **p<0.001

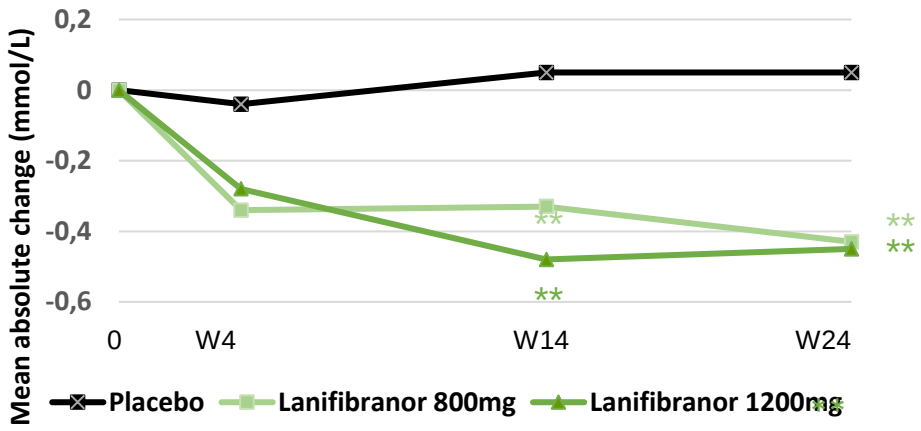
SECONDARY ENDPOINTS

Absolute change from baseline in HDL-C



Statistically significant change in HDL-cholesterol

Absolute change from baseline in triglycerides



Statistically significant change in triglycerides

- No change in LDL-cholesterol

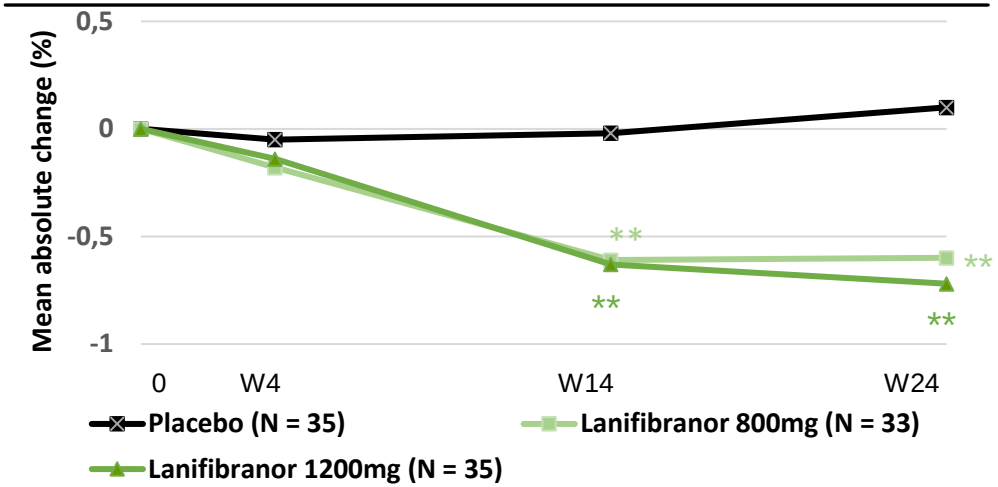
In patients with NASH and T2D, statistically significant reductions of fasting glucose and insulin, HbA1c were observed

PHASE IIb | EFFICACY | OTHER

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

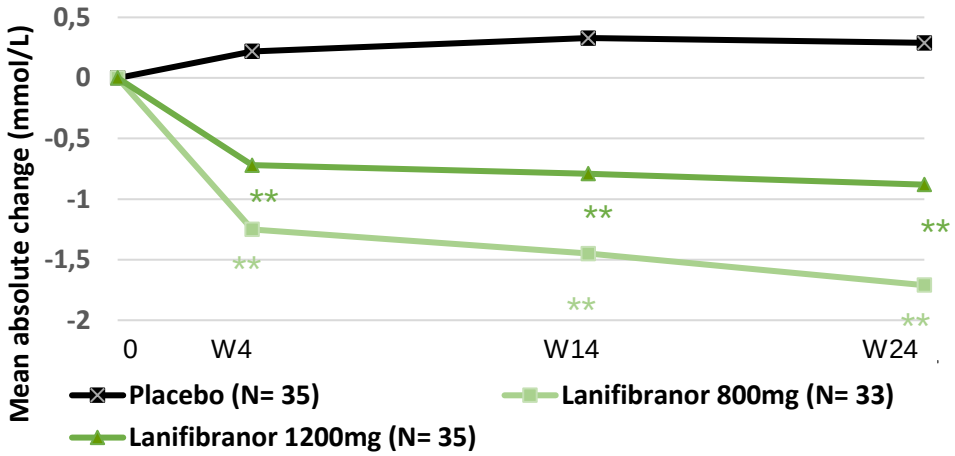
SECONDARY ENDPOINTS

Absolute change from baseline in HbA1c

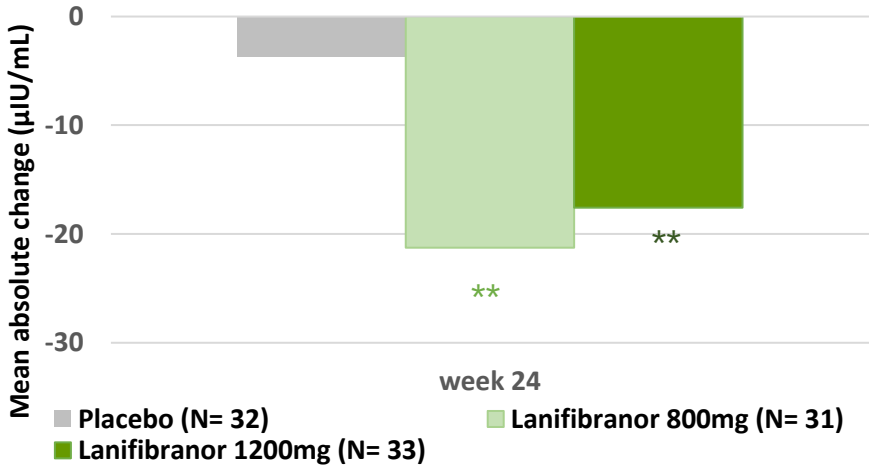


**p<0.001

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 NASH patients

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**

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

- Lanifibranor **effect on histology endpoints is higher in the F2-F3 patients**
- Lanifibranor **has beneficial effects on cardiovascular risk** biomarkers
- Preclinical data showing the **combination of lanifibranor and firsocostat**, an ACC inhibitor from Gilead, reached greater efficacy than monotherapy

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**.
- Lanifibranor showed **reduction in LSEC(2) capillarization**
- **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%)

The NEW ENGLAND JOURNAL of MEDICINE

October 21, 2021

RESEARCH SUMMARY

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

Francque SM et al. DOI: 10.1056/NEJMoa2036205

CLINICAL PROBLEM

Management options for nonalcoholic steatohepatitis (NASH) are limited. Peroxisome proliferator–activated receptors (PPARs) are key for regulating metabolism, inflammation, and fibrogenesis. In preclinical studies, the pan-PPAR agonist lanifibranor showed promise against markers of disease activity in NASH, but its efficacy remains unknown.

CLINICAL TRIAL

Design: A phase 2b, double-blind, randomized, placebo-controlled trial evaluated the efficacy and safety of lanifibranor in patients with noncirrhotic NASH with severe disease activity.

Intervention: 247 adults with biopsy-confirmed, noncirrhotic, highly active NASH were randomly assigned to receive oral lanifibranor (800 mg or 1200 mg) or placebo once daily for 24 weeks. At baseline, all participants had a score of 3 or higher on the SAF-A (the activity part of the Steatosis, Activity, Fibrosis [SAF] scoring system that incorporates ballooning and inflammation; SAF-A scores range from 0 to 4, with higher scores indicating more-severe disease activity). The primary end point was a decrease of at least 2 points in the SAF-A score and no worsening of fibrosis by week 24.

RESULTS

Efficacy: The 1200-mg dose of lanifibranor — but not the 800-mg dose — was superior to placebo with respect to the primary end point.

Safety: The percentage of patients with severe adverse events during the treatment period was identical in the three trial groups. Gastrointestinal adverse events, peripheral edema, anemia, and weight gain were more common with lanifibranor.

LIMITATIONS AND REMAINING QUESTIONS

- Most patients in the study were White; whether the findings apply to other races or ethnic groups is unknown.
- A phase 3 trial with longer follow-up and more extensive efficacy and safety assessments is needed.

Links: Full Article | NEJM Quick Take | Editorial

Decrease of ≥2 Points in SAF-A Score and No Worsening of Fibrosis

	Lanifibranor	Placebo	Risk Ratio (95%CI)	P Value
Lanifibranor, 800 mg	48%	33%	1.45 (1.00–2.10)	P=0.07
Lanifibranor, 1200 mg	55%	33%	1.69 (1.22–2.34)	P=0.007

Adverse Events

	Lanifibranor 1200 mg	Lanifibranor 800 mg	Placebo
	number (percent)		
Severe adverse events	3 (4)	3 (4)	3 (4)
Most frequent adverse events			
Diarrhea	10 (12)	8 (10)	1 (1)
Nausea	7 (8)	8 (10)	3 (4)
Weight gain	7 (8)	8 (10)	0
Peripheral edema	7 (8)	5 (6)	2 (2)

CONCLUSIONS

The pan-PPAR agonist lanifibranor, at a dose of 1200 mg daily, improved histologic outcomes in patients with noncirrhotic, highly active NASH.

https://www.nejm.org/doi/full/10.1056/NEJMoa2036205

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

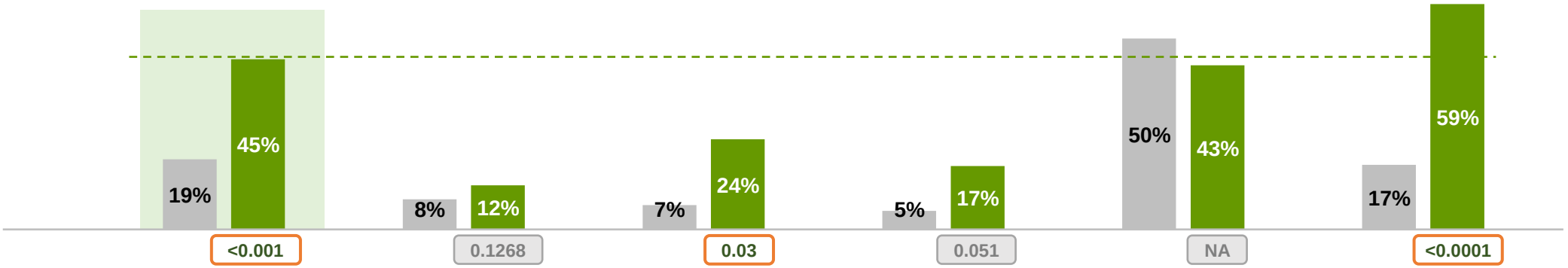
EFFICACY — Active | Placebo | xx Statistically significant | xx Non-statistically significant

Only drug achieving statistical significance on both endpoints

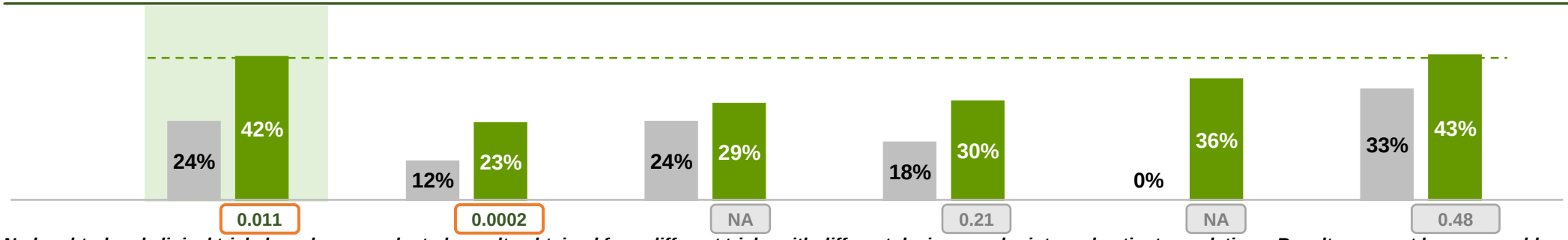
Injectables

	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



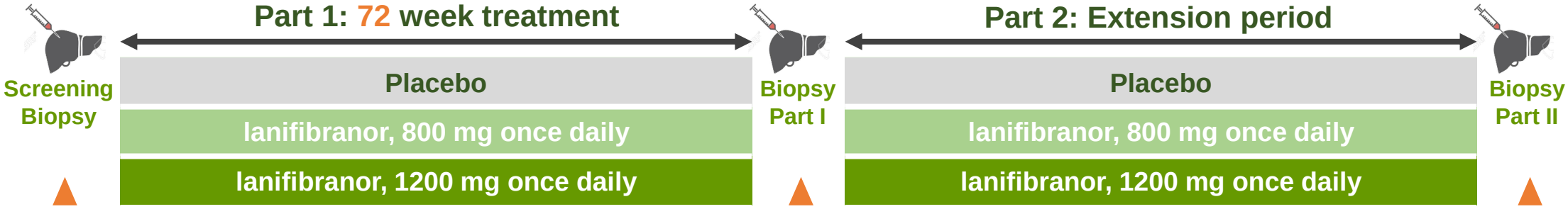
No head-to-head clinical trials have been conducted; results obtained from different trials, with different designs, endpoints and patient populations. Results may not be comparable.
**** Efruxifermin 70mg results only. Placebo N = 2. No information available regarding statistical significance of trial 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

The F2-F3 Phase III NATIV3 inclusion criteria and patient profile are in line with the NATIVE Phase IIb trial and is conduced across two parts

PHASE III OVERVIEW

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



PRINCIPAL INVESTIGATORS: Pr. Sven Francque and Pr. Arun Sanyal

MAIN INCLUSION CRITERIA aligned to Phase IIb trial:

- 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 patients from the U.S.

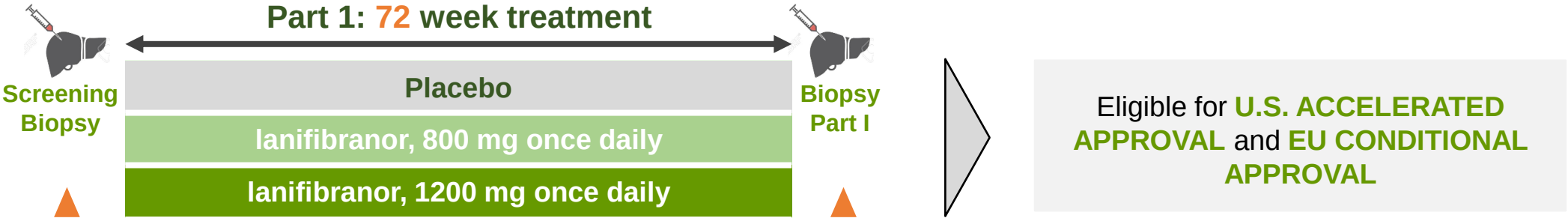
STATISTICAL POWERING: 90% considered for sample size calculations

CENTRAL BIOPSY review done by two pathologists for the first biopsy and three for the second one

Part 1 of the Phase III NATIV3 will enable U.S. accelerated approval and EU conditional approval based on a 72-week histology analysis

PHASE III OVERVIEW

Part 1 F2-F3 Phase III



PRIMARY ENDPOINT at week 72 on 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
- Improvement of fibrosis and no worsening of NASH

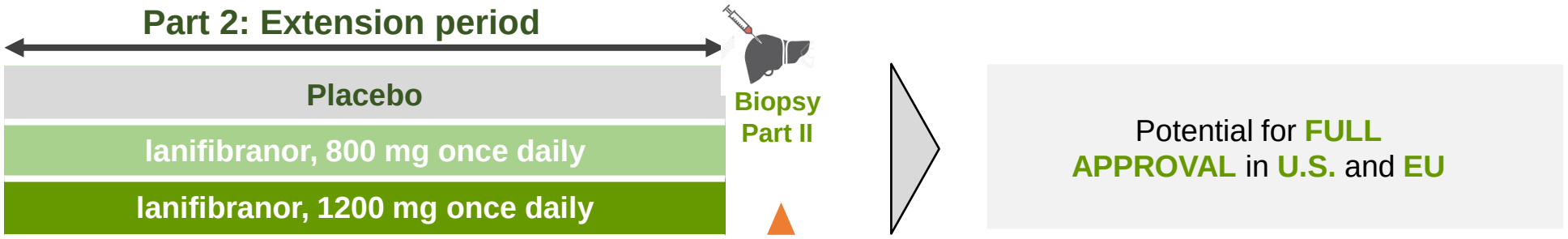
OTHER SECONDARY ENDPOINTS AND HIGH-LEVEL KEY EXPLORATORY ENDPOINTS *(non-exhaustive)*

- Glycaemic parameters at week 12 and week 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 (including major adverse cardiovascular events 'MACE'; non-fatal myocardial infarction, non-fatal stroke, cardiovascular death, hospitalisation for unstable angina)
- Quality of life (NASH-CLDQ) and PRO (PROMIS)

Part 2 of the Phase III NATIV3 extension study will allow for a broader "full approval" for lanifibranor in F2-3

PHASE III OVERVIEW

Part 2 F2-F3 Phase III



KEY ENDPOINTS IN PART 2 *(non-exhaustive)*

- Based on time to first clinical event on c.2,000 patients
  - histological progression to cirrhosis
  - all cause mortality
  - hepatic decompensation events
    - hepatic encephalopathy
    - variceal bleeding
    - new onset ascites requiring treatment
    - spontaneous bacterial peritonitis
  - MELD score ≥15
  - liver transplant

TRIAL END DATE

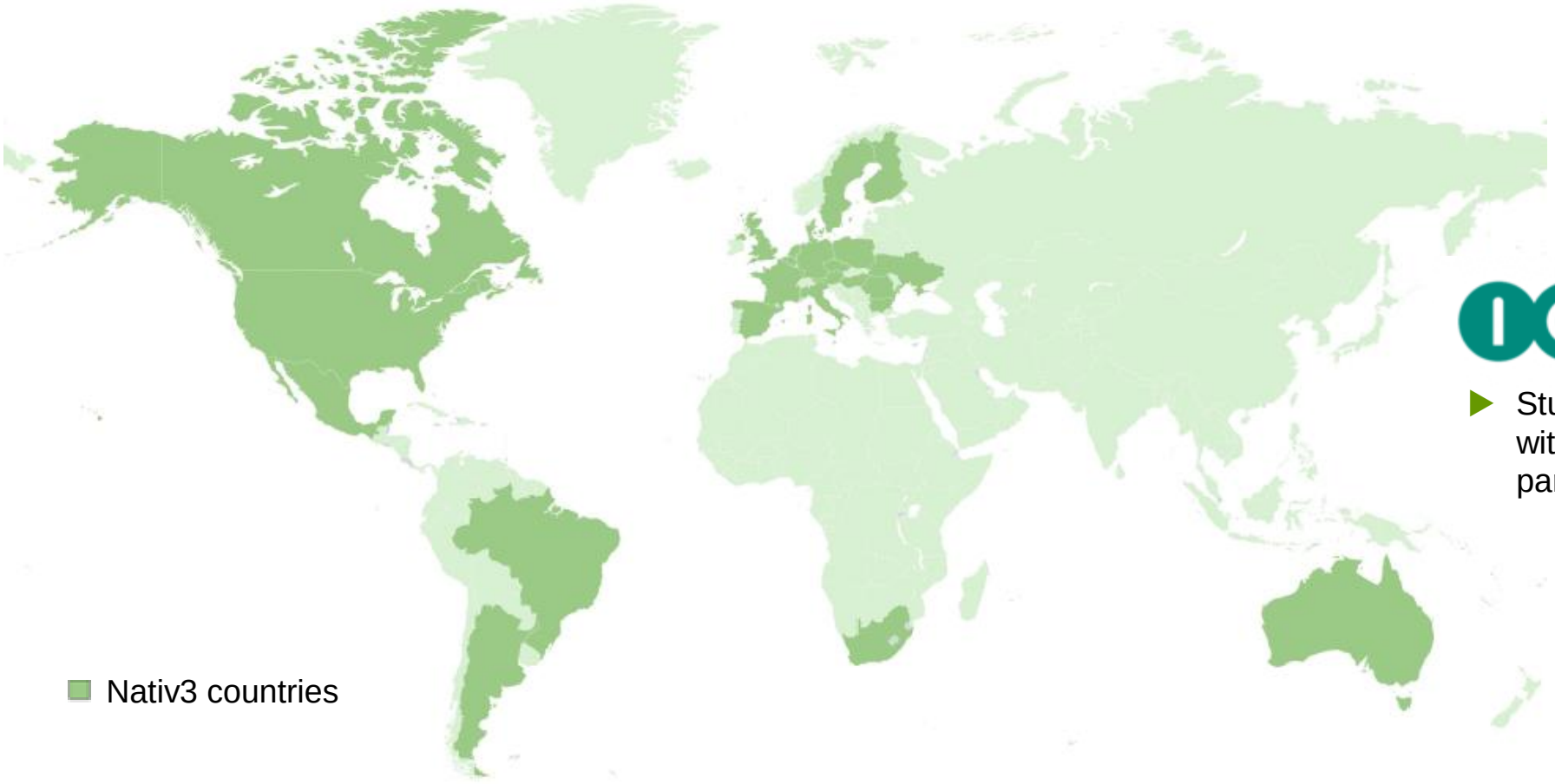
- Defined by first occurrence of following events (whichever comes first):
  - pre-defined number of clinical events registered

TIMING OF FINAL BIOPSY

- On per-patient basis, defined by:
  - suspicion of progression to cirrhosis (based on non-invasive testing), or
  - trial has ended

The Phase III patients will be randomised across more than 330 sites worldwide

PHASE III | DESIGN | SITE SELECTION



Nativ3 countries

- Study conducted with our global partner ICON

25 countries worldwide expected to participate

Lanifibranor clnical trial in patients with NAFLD and T2D

PHASE II **NAFLD T2D TRIAL**

Objective: Establish safety, efficacy and mechanism of action of lanifibranor in patients with T2D 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 H2 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

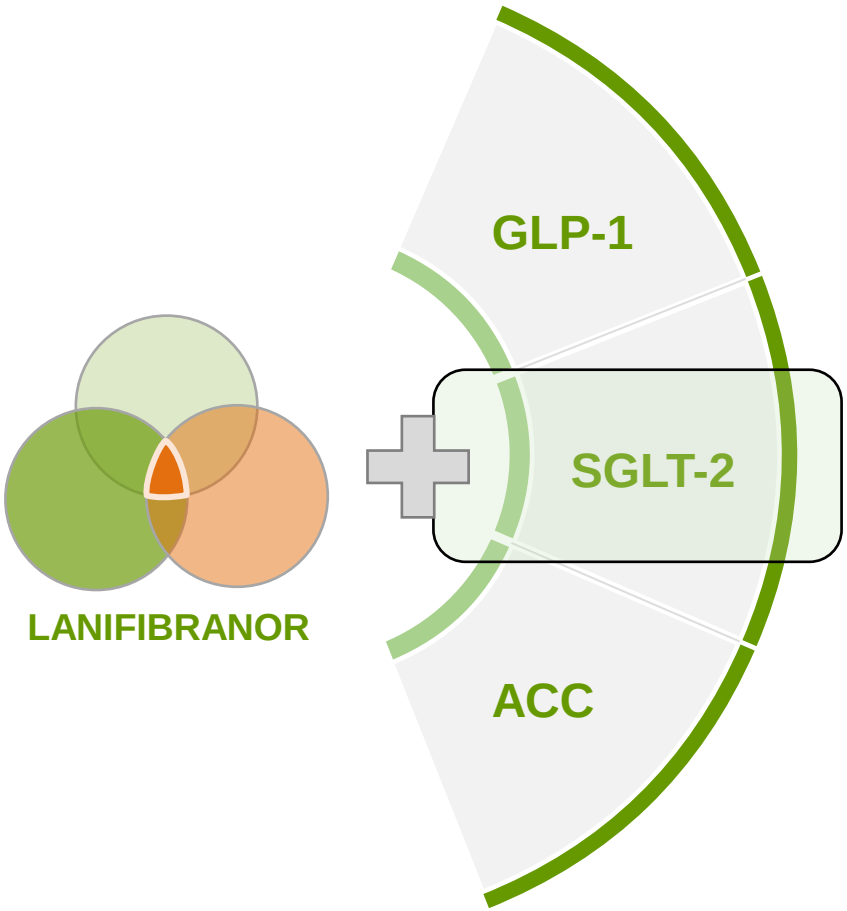
Lanifibranor, 800 mg once daily, 17 patients

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

Combination of SGLT2 with pioglitazone has shown additional metabolic health benefits and favorable weight management

Lanifibranor and SGLT2 rationale



- **Four randomized trials**
  - Pioglitazone alone vs pioglitazone + sGLT2i
  - N = 1411 T2D patients
    - Centers were in US, Canada, South America, China, Japan, India, Europe
    - Patients were on a stable dose of pioglitazone (monotherapy or with metformin)
  - Duration 24-72 weeks
- **Efficts of combination vs monotherapy with pioglitazone**
  - Efficacy:
    - Larger decrease of HbA1c; more patients reaching HbA1C < 7%
    - Larger reduction of fasting blood glucose level
    - Weight reduction
    - Blood pressure reduction
  - Safety
    - No difference in death, heart failure, hypoglycemia, urinary tract infection
    - More frequent genital infections

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

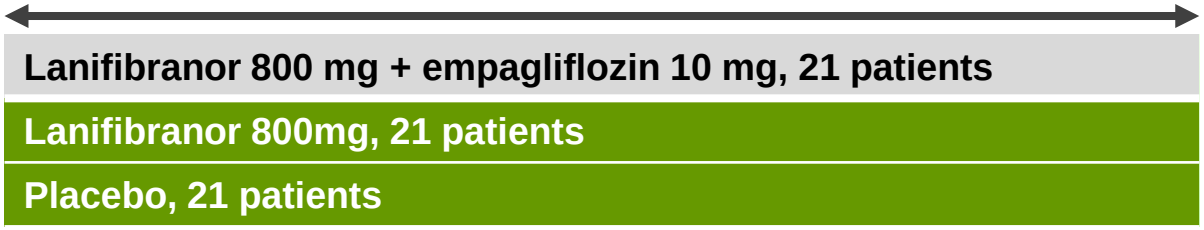
- MRI-based imaging to collect non-invasive data on hepatic fat, inflammation and fibrosis
- Glycaemic/lipid parameters, inflammatory markers
- Changes in body fat composition

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



Cedirogant

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

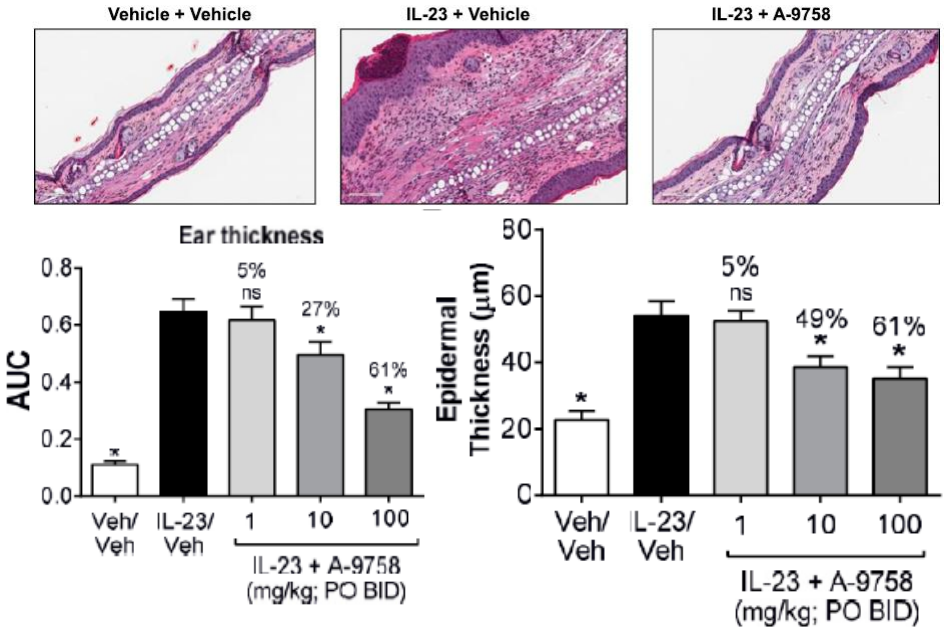
abbvie

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

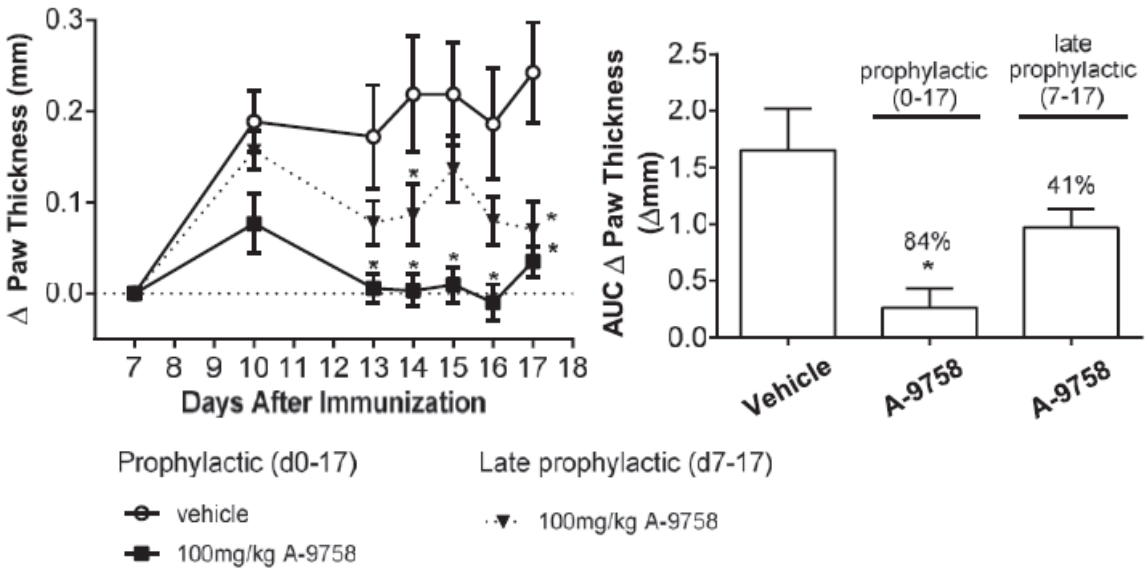
A-9758(1) attenuates IL-23 mediated skin inflammation

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 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

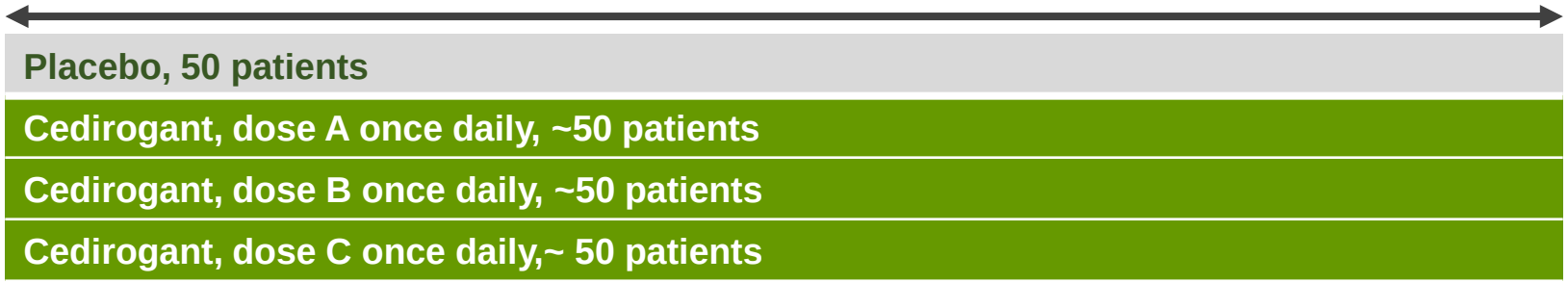
- Percentage of participants achieving >=75% reduction from baseline in Psoriasis Area Severity Index(1) (PASI) score (PASI 75)

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

Upcoming milestones

Anticipated key milestones

Lanifibranor

H1 2022
- Activation of first clinical sites for the phase II trial combining lanifibranor with SGLT2i empaglifloxin

H2 2022
- **Headline results of Phase II in patients with NAFLD and T2D**
- Last Patient First Visit of the phase III trial in NASH (Part I)

H2 2023
- **Headline results of Phase II of lanifibranor in combination with SGLT2i empagliflozine in patients with NASH and T2D**

H2 2024
- **Headline results of the phase III trial in patients with NASH (Part I)**

Cedirogant

abbvie

H2 2021
- Launch of phase IIB trial in psoriasis and milestone payment from AbbVie

H1 2023
- **Study completion of phase IIB trial in psoriasis**

Odiparcil

2022
- Strategy update on odiparcil development

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