Inventiva announces positive topline results from the investigator-initiated Phase II clinical trial evaluating lanifibranor in patients with T2D and NAFLD

- Lanifibranor 800mg achieved the primary efficacy endpoint demonstrating a 44% reduction of hepatic fat measured by proton magnetic resonance spectroscopy (^{1}H-MRS) following 24 weeks of treatment in patients with nonalcoholic fatty liver disease (NAFLD).

- A significantly higher proportion of patients achieved a greater than 30% liver triglyceride reduction as well as NAFLD resolution with lanifibranor compared to placebo.

- Lanifibranor treatment significantly improved both hepatic and peripheral insulin sensitivity (i.e. fasting plasma insulin, fasting hepatic glucose production, hepatic insulin resistance index, insulin-stimulated muscle glucose disposal), which translated into better glycemic control (i.e. HbA1c).

- The study met multiple secondary metabolic endpoints confirming the cardiometabolic benefit of lanifibranor in patients with NAFLD, and ability to improve adipose tissue function (i.e. significant increase in plasma adiponectin and reverse NAFLD).

- The study confirmed the favorable safety and tolerability profile of lanifibranor.

- Inventiva and Dr. Cusi will host an investors webcast Wednesday, June 14th at 8am EST (details below).

Daix (France), Long Island City (New York, United States), June 13, 2022 –Inventiva (Euronext Paris and Nasdaq: IVA), a clinical-stage biopharmaceutical company focused on the development of oral small molecule therapies for the treatment of non-alcoholic steatohepatitis (NASH), mucopolysaccharidoses (MPS) and other diseases with significant unmet medical needs, today announced positive topline results of the clinical study conducted by Dr. Kenneth Cusi from the University of Florida, evaluating lanifibranor in patients with NAFLD and type 2 diabetes mellitus (T2D).

The Phase II clinical trial randomized 38 patients into two arms, with patients receiving placebo or treatment with lanifibranor at 800mg/day for 24 weeks. The study achieved the primary efficacy endpoint with a 44% reduction of Intra Hepatic Triglycerides (IHTG) measured using proton magnetic resonance spectroscopy (^{1}H-MRS) in patients with NAFLD and T2D treated with lanifibranor (800mg/daily) for 24 weeks compared to 12% in the

placebo arm. This result is consistent with the Phase IIb NATIVE trial findings, in which lanifibranor demonstrated a statistically significant effect on steatosis reduction as measured by CAP/Fibroscan.[1]

The study demonstrated a statistically significant higher proportion of patients achieving a greater than 30% liver triglyceride reduction (65% vs. 22%, p =0.008) as well as NAFLD resolution (25% vs. 0%, p = 0.048) defined as IHTG ≤ 5.5% at week 24, with lanifibranor compared to placebo.

In addition, the study demonstrated a significant effect on a series of secondary endpoints including (see tables below), glycemic control (reduction in hemoglobin A1c), atherogenic dyslipidemia (i.e., increase in HDL-C), hepatic insulin action (i.e., fasting hepatic glucose production, hepatic insulin resistance index), insulin-stimulated muscle glucose disposal (i.e., in gold-standard euglycemic insulin clamp studies during high-dose insulin stimulation) and amelioration of the adipose tissue dysfunction with a robust increase in plasma adiponectin. The treatment with lanifibranor 800mg/once daily for 24 weeks was well tolerated, with no safety concerns reported.

Additional secondary endpoints including a series of markers of cardiometabolic health are anticipated to be presented by Dr. Cusi in upcoming scientific conferences and publications.

Dr. Michael Cooreman, M.D., Chief Medical Officer of Inventiva: *"The results published today, by showing that lanifibranor reduces intrahepatic triglycerides and contributes to resolve NAFLD in patients with T2D further bolster our robust dataset from our Phase IIb NATIVE study on the efficacy of lanifibranor across the disease spectrum of NAFLD, i.e. histological benefits on NASH resolution and fibrosis improvement as well as an improvement of a broad panel of markers of cardiometabolic health. In addition, we are pleased to see that this study confirms the safety and tolerability of lanifibranor. We want to thank Dr. Cusi for successfully leading this study and for his innovative thinking in designing a clinical trial with these state-of-the-art NITs."*

Dr. Kenneth Cusi, M.D., F.A.C.P., F.A.C.E., Professor of Medicine at the Division of Endocrinology, Diabetes and Metabolism in the Department of Medicine, University of Florida and Principal Investigator of the study, stated: *"This is an important study for a drug that has already shown promising results in patients with NASH. Lanifibranor is an insulin-sensitizer with demonstrated effects to reverse steatohepatitis and fibrosis. The positive results of our study on hepatic fat and liver and muscle insulin sensitivity, as well as fat metabolism, within just 24 weeks of treatment confirm the robustness of the mechanism of action of lanifibranor in key tissues, and its potential to manage patients with T2D but also patients with pre-diabetes and obesity. This study brings new and critical results for our patients with T2DM and NASH, which constitute a large proportion of the whole NASH patient population and for whom there are still no approved drugs available. I look forward to publishing more detailed analyses from this exciting study."*

Summary of Week 24 changes in Liver Fat

	Full Analysis Set (N=38)		
	Placebo (n=18)	**Lani 800mg (n=20)**	**p value**
Change in liver fat (intrahepatic TGs) (%)[a]	-12%	-44%	0.002 (S)
Proportion of patients with >30% liver fat reduction % [b]	22%	65%	0.008 (S)
NAFLD resolution (defined as IHTG ≤ 5.5% at Week 24) [c]	0%	25%	0.048 (S)

[a] P-value from an Analysis of Covariance. Missing data at Week 24 were imputed by baseline data.

[1] Lanifibranor treatment improves hepatic steatosis in patients with NASH, evaluated by histological grading and Controlled Attenuation Parameter (CAP); Cooreman MP, Abedelmalek MP, Baudin, Huot-Marchand, Dzen, Fournier, Junien, Broqua, Francque; https://inventivapharma.com/wp-content/uploads/2021/11/LANIFIBRANOR-TREATMENT-IMPROVES-HEPATIC...pdf

[b] Missing data at Week 24 were imputed as non-achieving reduction of 30% liver fat reduction.
[c] Missing data at Week 24 were imputed as non-responders.

Summary of Week 24 changes in glycemic control, insulin sensitivity and cardiometabolic biomarkers

	Completers (N=28)	
	Placebo (n=14)	**Lani 800mg (n=14)**
Glycemic control		
Absolute change in HbA1c, %	-0.2%	-0.9***
Absolute change in Fasting plasma insulin, µU/ml	-1.0	-6.7*
Insulin sensitivity		
Absolute change in Hepatic Insulin Resistance index	-9.5	-30.1*
Absolute change in basal Endogenous glucose production (mg/kgLBM/min)	0.1	-0.5***
Absolute change in muscle insulin-stimulated glucose disposal (mg/kg LBM/min)	-0.2	+2.2**
Cardiometabolic biomarkers		
Absolute change in HDL-C, mg/dl	-0.3	6.3*
Absolute change in Adiponectin, µg/mL	-0.2	7.5***

*p≤0.05,**p≤0.01, ***p≤ 0.001 versus placebo

Conference call

Inventiva will host a conference call and webcast with slide presentation on Wednesday, June 14, 2023 at 8:00 am ET (New York time) 2:00 pm CET (Paris time). The conference call and the slides of the presentation will be webcast live at: https://edge.media-server.com/mmc/p/8y8icxm8 and will also be available on Inventiva's website: Investor Presentations - Inventiva Pharma.
In order to receive the conference access information necessary to join the conference call, it is required to register in advance using the following link:https://register.vevent.com/register/BI22f830c9addc4b7eaf2698bf8c72e1fe. Participants will need to use the conference access information provided in the e-mail received at the point of registering (dial-in number and access code).

About lanifibranor

Lanifibranor, Inventiva's lead product candidate, is an orally-available small molecule that acts to induce anti-fibrotic, anti-inflammatory and beneficial vascular and metabolic changes in the body by activating all three peroxisome proliferator-activated receptor (PPAR) isoforms, which are well-characterized nuclear receptor proteins that regulate gene expression. Lanifibranor is a PPAR agonist that is designed to target all three PPAR isoforms in a moderately potent manner, with a well-balanced activation of PPARα and PPARδ, and a partial activation of PPARγ. While there are other PPAR agonists that target only one or two PPAR isoforms for activation, lanifibranor is the only pan-PPAR agonist in clinical development for the treatment of NASH. Inventiva believes that lanifibranor's moderate and balanced pan-PPAR binding profile contributes to the favorable tolerability profile that has been observed in clinical trials and pre-clinical studies to date. The FDA has granted Breakthrough Therapy and Fast Track designation to lanifibranor for the treatment of NASH.

About Inventiva

Inventiva is a clinical-stage biopharmaceutical company focused on the research and development of oral small molecule therapies for the treatment of patients with NASH, mucopolysaccharidoses ("MPS") and other diseases with significant unmet medical need. The Company benefits from a strong expertise and experience in the domain of compounds targeting nuclear receptors, transcription factors and epigenetic modulation. Inventiva is currently advancing one clinical candidate, has a pipeline of two preclinical programs and continues to explore other development opportunities to add to its pipeline.

Inventiva's lead product candidate, lanifibranor, is currently in a pivotal Phase III clinical trial, NATiV3, for the treatment of adult patients with NASH, a common and progressive chronic liver disease for which there are currently no approved therapies.

Inventiva's pipeline also includes odiparcil, a drug candidate for the treatment of adult MPS VI patients. As part of Inventiva's decision to focus clinical efforts on the development of lanifibranor, it suspended its clinical efforts relating to odiparcil and is reviewing available options with respect to its potential further development. Inventiva is also in the process of selecting an oncology development candidate for its Hippo signaling pathway program.

The Company has a scientific team of approximately 90 people with deep expertise in the fields of biology, medicinal and computational chemistry, pharmacokinetics and pharmacology, and clinical development. It owns an extensive library of approximately 240,000 pharmacologically relevant molecules, approximately 60% of which are proprietary, as well as a wholly-owned research and development facility.

Inventiva is a public company listed on compartment B of the regulated market of Euronext Paris (ticker: IVA, ISIN: FR0013233012) and on the Nasdaq Global Market in the United States (ticker: IVA). www.inventivapharma.com

Contacts

Inventiva
Pascaline Clerc
VP of Global External Affairs
media@inventivapharma.com
+1 240 620 9175

Brunswick Group
Tristan Roquet Montegon /
Aude Lepreux /
Matthieu Benoist
Media relations
inventiva@brunswickgroup.com
+33 1 53 96 83 83

Westwicke, an ICR Company
Patricia L. Bank
Investor relations
patti.bank@westwicke.com
+1 415 513-1284

Important Notice

This press release contains "forward-looking statements" within the meaning of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. All statements, other than statements of historical facts, included in this press release are forward-looking statements. These statements include, but are not limited to, forecasts and estimates with respect to Inventiva's pre-clinical programs and clinical trials, including design, duration, timing, recruitment costs, screening and enrolment for those trials, including the ongoing NATiV3 Phase III clinical trial with lanifibranor in NASH and the LEGEND Phase IIa combination trial with lanifibranor and empagliflozin in patients with NASH and type 2 diabetes, potential development of and regulatory pathway for odiparcil, clinical trial data releases and publications, the information, insights and impacts that may be gathered from clinical trials, the potential therapeutic benefits, including reduction of IHTG, reduction of steatosis, improvement of hepatic and peripheral insulin sensitivity and improvement of a panel of markers of cardiometabolic health, reduction in fasting plasma glucose, atherogenic dyslipidemia, hepatic insulin action, insulin-stimulated muscle glucose disposal, reversal of adipose tissue dysfunction with a robust increase in plasma adiponectin, and reversal of steatohepatitis and fibrosis, of Inventiva's product candidates, including lanifibranor, the publication by Dr. Cusi of additional secondary endpoints, including a series of markers of cardiometabolic health and more detailed analyses, potential regulatory submissions and approvals, and Inventiva's pipeline and preclinical and clinical development plans,

future activities, expectations, plans, growth and prospects. Certain of these statements, forecasts and estimates can be recognized by the use of words such as, without limitation, "believes", "anticipates", "expects", "intends", "plans", "seeks", "estimates", "may", "will", "would", "could", "might", "should", "designed", "hopefully", "target", "aim", and "continue" and similar expressions. Such statements are not historical facts but rather are statements of future expectations and other forward-looking statements that are based on management's beliefs. These statements reflect such views and assumptions prevailing as of the date of the statements and involve known and unknown risks and uncertainties that could cause future results, performance or future events to differ materially from those expressed or implied in such statements. Actual events are difficult to predict and may depend upon factors that are beyond Inventiva's control. There can be no guarantees with respect to pipeline product candidates that the clinical trial results will be available on their anticipated timeline, that future clinical trials will be initiated as anticipated, that product candidates will receive the necessary regulatory approvals, or that any of the anticipated milestones by Inventiva or its partners will be reached on their expected timeline, or at all. Actual results may turn out to be materially different from the anticipated future results, performance or achievements expressed or implied by such statements, forecasts and estimates, due to a number of factors, including that Inventiva is a clinical-stage company with no approved products and no historical product revenues, Inventiva has incurred significant losses since inception, Inventiva has a limited operating history and has never generated any revenue from product sales, Inventiva will require additional capital to finance its operations, in the absence of which, Inventiva may be required to significantly curtail, delay or discontinue one or more of its research or development programs or be unable to expand its operations or otherwise capitalize on its business opportunities and may be unable to continue as a going concern, Inventiva's future success is dependent on the successful clinical development, regulatory approval and subsequent commercialization of current and any future product candidates, preclinical studies or earlier clinical trials are not necessarily predictive of future results and the results of Inventiva's clinical trials may not support Inventiva's product candidate claims, Inventiva's expectations with respect to the changes to the clinical development plan for lanifibranor for the treatment of NASH may not be realized and may not support the approval of a New Drug Application, Inventiva may encounter substantial delays in its clinical trials or Inventiva may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities, the ability of Inventiva to recruit and retain patients in clinical studies, enrolment and retention of patients in clinical trials is an expensive and time-consuming process and could be made more difficult or rendered impossible by multiple factors outside Inventiva's control, Inventiva's product candidates may cause adverse drug reactions or have other properties that could delay or prevent their regulatory approval, or limit their commercial potential, Inventiva faces substantial competition and Inventiva's business, and preclinical studies and clinical development programs and timelines, its financial condition and results of operations could be materially and adversely affected by geopolitical events, such as the conflict between Russia and Ukraine, related sanctions and related impacts and potential impacts on the initiation, enrolment and completion of Inventiva's clinical trials on anticipated timelines, health epidemics, and macroeconomic conditions, including global inflation, uncertain financial markets and disruptions in banking systems. Given these risks and uncertainties, no representations are made as to the accuracy or fairness of such forward-looking statements, forecasts and estimates. Furthermore, forward-looking statements, forecasts and estimates only speak as of the date of this press release. Readers are cautioned not to place undue reliance on any of these forward-looking statements.

Please refer to the Universal Registration Document for the year ended December 31, 2022 filed with the Autorité des Marchés Financiers on March 30, 2023, and the Annual Report on Form 20-F for the year ended December 31, 2022 filed with the Securities and Exchange Commission on March 30, 2023 for other risks and uncertainties affecting Inventiva, including those described from time to time under the caption "Risk Factors". Other risks and uncertainties of which Inventiva is not currently aware may also affect its forward-looking statements and may cause actual results and the timing of events to differ materially from those anticipated.

All information in this press release is as of the date of the release. Except as required by law, Inventiva has no intention and is under no obligation to update or review the forward-looking statements referred to above. Consequently, Inventiva accepts no liability for any consequences arising from the use of any of the above statements.