PRESS RELEASE

Inventiva announces positive results from the Phase II, LEGEND, Proof-of-Concept study combining lanifibranor with empagliflozin in patients with MASH/NASH and T2D

- LEGEND achieved its primary efficacy endpoint by significantly lowering HbA1c level in both the lanifibranor arm and in the lanifibranor with empagliflozin arm compared to placebo.
- Statistical significance was also achieved on several markers of liver injury, markers of glucose and lipid metabolism, as well as hepatic steatosis.
- Patients treated with lanifibranor in combination with empagliflozin maintained a stable weight throughout the 24 weeks study, addressing the moderate, metabolically healthy, weight gain that has been observed in some patients treated with lanifibranor.
- Treatment with lanifibranor alone and in combination with empagliflozin decreased the ratio of visceral abdominal fat to subcutaneous fat, reflecting a shift from pro-inflammatory visceral fat towards metabolically healthy adipose tissue.
- The treatment with lanifibranor 800mg/once daily alone or in combination with empagliflozin for 24 weeks was well tolerated, with no safety concerns reported.
- Inventiva will host an investor webcast Tuesday, March 19th at 8am ET (details below).

Daix (France), Long Island City (New York, United States), March 18, 2024 – Inventiva (Euronext Paris and Nasdaq: IVA), a clinical-stage biopharmaceutical company focused on the development of oral small molecule therapies for the treatment of metabolic dysfunction-associated steatohepatitis (MASH), also known as non-alcoholic steatohepatitis (NASH), and other diseases with significant unmet medical needs, today announces positive results of its interim analysis of the Phase II, Proof-of-Concept clinical trial, LEGEND, evaluating lanifibranor in combination with empagliflozin in patients with MASH/NASH and poorly controlled Type 2 Diabetes (T2D).

The LEGEND trial has been designed as a multi-center, randomized, 24-week treatment, placebo-controlled Phase II Proof-of-Concept trial to assess the safety and efficacy of lanifibranor in combination with the SGLT2 inhibitor empagliflozin for the treatment of patients with non-cirrhotic MASH/NASH and T2D. The trial is double-blind for the placebo arm and lanifibranor (800mg daily) arm, and open-label for the combination of lanifibranor (800mg daily) and empagliflozin (10 mg daily) arm. The diagnosis of non-cirrhotic MASH/NASH was based on historic histology evaluation or a combination of non-invasive methods including diagnostic methods including imaging. As planned per protocol, the interim analysis was done once half of the 63 planned randomized patients with MASH completed the 24-week treatment period or prematurely discontinued from treatment.

The study achieved the primary efficacy endpoint with an absolute reduction in Hemoglobin A1c (HbA1c) of 1.14% and 1.59% in patients with MASH and T2D treated with lanifibranor (800mg daily) or in combination with empagliflozin (10mg daily) at week 24 compared to an increase of 0.26% observed in the placebo arm.

The study also demonstrated a statistically significant reduction in hepatic steatosis measured by MRI-PDFF[1], in patients treated with lanifibranor alone and in combination with empagliflozin, -47% and -38% respectively, compared to placebo (0%). 83% and 67% of patients treated with lanifibranor alone or in combination with empagliflozin respectively, showed a reduction greater or equal to 30% of their hepatic fat, compared to 0% in the placebo arm. In addition, the study demonstrated a statistically significant effect on several secondary and exploratory endpoints, including liver enzymes (alanine aminotransferase ("ALT") and aspartate aminotransferase ("AST")), insulin resistance (HOMA-IR), HDL, and adiponectin (see tables below). Markers of liver inflammation and fibrosis (corrected T1 relaxation time (cT1) assessed by LiverMultiScan®) were assessed for the first time with lanifibranor and showed a significant effect with lanifibranor alone and in combination with empagliflozin.

The study also demonstrated that patients treated with lanifibranor in combination with empagliflozin maintained a stable weight throughout the 24 weeks study, addressing the moderate, metabolically healthy, weight gain that can be observed in some patients treated with lanifibranor alone. Furthermore, these results demonstrated a significant relative reduction in the VAT/SAT ratio (visceral and subcutaneous adipose tissue) in patients treated with lanifibranor alone or in combination with empagliflozin, -5% and -17% respectively, compared to an increase of 11% in patients under placebo. This result reflects a shift from pro-inflammatory visceral fat towards metabolically healthy adipose tissue.

The treatment with lanifibranor 800mg/daily alone and in combination with empagliflozin 10mg/daily for 24 weeks appears to be well tolerated, with no safety concerns reported.

Dr. Michael Cooreman, M.D., Chief Medical Officer of Inventiva: *"The results of the LEGEND study announced today further illustrate the potential of lanifibranor to address the broad spectrum of the disease biology of MASH and T2D. These data complement the already published dataset of lanifibranor demonstrating fibrosis improvement and MASH resolution but also its role as a potent insulin sensitizer. With roughly 50% of the U.S. population estimated to have either prediabetes or diabetes, and the well-established correlation between MASH and T2D, lanifibranor has a unique mechanism of action to potentially address the medical need of patients with both MASH and T2D. We wish to thank the patients who participated in the study and the investigators of LEGEND."*

Dr. Onno Holleboom, MD PhD, endocrinologist and associate professor at Amsterdam UMC, co-principal investigator of the LEGEND Phase II clinical trial: *"It is a big step seeing these positive results of LEGEND demonstrating the impact of lanifibranor on steatosis, inflammation and fibrosis while stabilizing weight with empagliflozin in patients with poorly controlled T2D and MASH. The study was designed as a proof of concept and these results are significant and strengthen confidence in the potential of lanifibranor to address the specific metabolic unbalance in patients with T2D while also addressing steatosis and fibrosis, a hepatic consequence of insulin resistance."*

Prof. Michelle Lai, M.D., Ph.D., Beth Israel Deaconess Medical Center and co-principal investigator of the LEGEND Phase II clinical trial, said: "*These LEGEND results provide valuable insights on the complementary mechanisms of action of an SGLT2 inhibitor and the panPPAR agonist, lanifibranor. MASH is a multifaceted disease that we believe will benefit from combination therapies in order to properly address the full cardiometabolic spectrum of the disease. These results of LEGEND suggest that lanifibranor in combination with empagliflozin could be an ideal combination for patients we care for in our clinic who suffer from T2D and MASH*."

[1] MRI-PDFF: Magnetic resonance imaging-derived proton density fat fraction

Given that the primary endpoint of LEGEND was met, and statistically significant results were achieved on several key additional markers, the Company has decided to stop the recruitment as defined per protocol. More details on these results are expected to be presented in upcoming scientific conferences and submitted for publication.

Summary HbA1C improvement at Week 24

	Full Analysis Set[a] (N=30)		
	Placebo (n=9)	**Lani 800mg (n=11)**	**Lani 800mg +Empa 10mg (n=10)**
HbA1c (%), LS Mean Absolute Change from Baseline to Week 24	0.26	-1.14*	-1.59**
	Completers[b] (N=24)		
	Placebo (n=5)	**Lani 800mg (n=11)**	**Lani 800mg +Empa 10mg (n=8)**
Responders with HbA1C level < 6.5% at Week 24 (%)	0	55	63
Responders with HbA1c absolute decrease ≥1% from baseline, at Week 24 (%)	0	64	88

[a] Two patients were not considered in the Full Analysis Set because we do not have post-treatment HbA1c values available
*p<0.01, **p<0.001, versus placebo (Mixed Model Repeated Measure [MMRM])
[b] Eight patients were not considered in the Completers set because of premature discontinuation before Week 24 or missing data due to prior intercurrent events (Rescue medication or significant diet modification affecting the primary endpoint).
LS=Least Square.

Summary of improvement in non-invasive measures of hepatic steatosis, inflammation and fibrosis markers, and liver injury, at Week 24

	Full Analysis Set		
Mean Change from Baseline to Week 24	**Placebo**	**Lani 800mg**	**Lani 800mg +Empa 10mg**
MRI-PDFF (%)[a]	0 (n=5)	-47* (n=12)	-38* (n=9)
cT1 (ms)[b]	15 (n=4)	-82 (n=12)	-85 (n=9)
ALT (%)[a]	2.5 (n=9)	-36.4** (n=12)	-51.3*** (n=10)
AST (%)[a]	17.1 (n=9)	-24.7** (n=12)	-34.6*** (n=10)

[a] LS Mean relative change from baseline to week 24, from an Analysis of Covariance model (ANCOVA) or Mixed Model Repeated Measure (MMRM)
[b] LS Mean absolute change from baseline to week 24, from an ANCOVA.
*p≤0.05, **p<0.01, ***p<0.001, versus placebo (ANCOVA or MMRM)
ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase, cT1: Corrected T1, LS=Least Square, MRI-PDFF: Magnetic resonance imaging-derived proton density fat fraction.

Summary of improvement in Cardiometabolic Markers and Weight, at Week 24

	Full Analysis Set		
Mean Change from Baseline to Week 24	**Placebo**	**Lani 800mg**	**Lani 800mg +Empa 10mg**
HDL-C (mmol/L)[a]	-0.01 (n=9)	0.17 (n=12)	0.22* (n=10)
Insulin (pmol/L)[a]	-58.3 (n=9)	-93.9 (n=11)	-155.1* (n=10)
HOMA-IR (%)[b]	-7 (n=9)	-51* (n=11)	-69** (n=10)
Adiponectin[c]	1.1 (n=9)	2.8* (n=11)	3.0* (n=10)
Body weight[d] (%)	-0.8 (n=5)	3.6 (n=12)	-0.4 (n=8)
VAT/SAT (%)[b]	11 (n=4)	-5 (n=8)	-17** (n=7)

[a] LS Mean absolute change from baseline to week 24
[b] LS Mean relative change from baseline to week 24
[c] LS Mean fold change from baseline to week 24
[d] Relative change from baseline to week 24
*p<0.05, **p<0.01, ***p<0.001, versus placebo (Mixed Model Repeated Measure [MMRM] or Analysis of Covariance (ANCOVA)).
HDL-C: High density lipoprotein cholesterol, HOMA: Homeostasic model assessment, LS=Least Square, SAT=Subcutaneous Adipose Tissue, VAT=Visceral Adipose Tissue.

Conference call

Inventiva will host a conference call and webcast with slide presentation on Tuesday, March 19, 2024 at 8:00 am ET (New York time) 1:00 pm CET (Paris time).
Introduced by Frederic Cren, Chairman, CEO and cofounder of Inventiva, this event will be as follow:

- **Presentation of LEGEND Results -** Michael Cooreman, M.D., CMO of Inventiva
- **Metabolic and hepatic benefits of lanifibranor -** Stephen Harrison, M.D., Pinnacle Clinical Research and principal investigator of the exploratory cohort of NATiV3, Phase III clinical trial
- **Vascular benefits of lanifibranor** - Sven Francque, M.D., University Hospital Antwerp, co-principal investigator of NATiV3, Phase III clinical trial
- **Opportunity for lanifibranor** - Frederic Cren, CEO and cofounder of Inventiva

The conference call and the slides of the presentation will be webcast live at: **https://edge.media-server.com/mmc/p/hyuvxf9a** and will also be available on Inventiva's website: Investor Presentations - Inventiva Pharma. In order to receive the conference access information necessary to participate to the conference call, it is required to register in advance using the following link: **https://register.vevent.com/register/BI334d62953abb41cea27de99dc5da974c** . 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 -wellbalanced- 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 panPPAR- agonist in clinical development for the treatment of MASH/NASH. Inventiva believes that lanifibranor's moderate and balanced panPPAR- binding profile contributes to the favorable tolerability profile that has been observed in clinical trials and preclinical studies to date. The FDA has granted Breakthrough Therapy and Fast Track designation to lanifibranor- for the treatment of MASH/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 MASH/NASH, 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 MASH/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 a 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

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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 enrollment for those trials, including the ongoing NATiV3 Phase III clinical trial with lanifibranor in MASH/NASH and the LEGEND Phase II, Proof-of-Concept combination trial with lanifibranor and empagliflozin in patients with MASH/*NASH and*

T2D, and the results and timing thereof and regulatory matters with respect thereto, , clinical trial data releases and publications, the information, insights and impacts that may be gathered from clinical trials, the potential therapeutic benefits including reduction in HbA1c, reduction in hepatic steatosis, the effect on liver enzymes (ALT and AST), insulin resistance (HOMA-IR), HDL, adiponectin, liver inflammation and fibrosis, and reduction in the VAT/SAT ratio, of lanifibranor alone and in combination with empagliflozin in patients with MASH/NASH and T2D, of Inventiva's product candidates, including lanifibranor alone and in combination with empagliflozin, the effect of lanifibranor alone and in combination with empagliflozin on the weight of the patients receiving treatment, the tolerability and safety profile of lanifibranor observed during trials, the potential of lanifibranor to address the specific metabolic unbalance in patients with T2D while also addressing steatosis and fibrosis, a hepatic consequence of insulin resistance, the estimated market size and patient population, potential regulatory submissions, approvals and commercialization, Inventiva's pipeline and preclinical and clinical development plans, the potential development of and regulatory pathway for odiparcil, and future activities, expectations, plans, growth and prospects of Inventiva and its partners. Certain of these statements, forecasts and estimates can be recognized by the use of words such as, without limitation, "believes", "anticipates", "expects", "intends", "plans", "seeks", "estimates", "may", "will", "would", "could", "might", "should", "designed", "hopefully", "target", "potential", "opportunity", "possible", "aim", and "continue" and similar expressions. Such statements are not historical facts but rather are statements of future expectations and other forward-looking statements that are based on management's beliefs. These statements reflect such views and assumptions prevailing as of the date of the statements and involve known and unknown risks and uncertainties that could cause future results, performance, or future events to differ materially from those expressed or implied in such statements. Actual events are difficult to predict and may depend upon factors that are beyond Inventiva's control. There can be no guarantees with respect to pipeline product candidates that the clinical trial results will be available on their anticipated timeline, that future clinical trials will be initiated as anticipated, that product candidates will receive the necessary regulatory approvals, or that any of the anticipated milestones by Inventiva or its partners will be reached on their expected timeline, or at all. Future results may turn out to be materially different from the anticipated future results, performance or achievements expressed or implied by such statements, forecasts and estimates, due to a number of factors, including that Inventiva cannot provide assurance on the impacts of the pause on enrolment or the ultimate impact on the results or timing of the NATiV3 trial or regulatory matters with respect thereto, that Inventiva is a clinical-stage company with no approved products and no historical product revenues, Inventiva has incurred significant losses since inception, Inventiva has a limited operating history and has never generated any revenue from product sales, Inventiva will require additional capital to finance its operations, in the absence of which, Inventiva may be required to significantly curtail, delay or discontinue one or more of its research or development programs or be unable to expand its operations or otherwise capitalize on its business opportunities and may be unable to continue as a going concern, Inventiva's future success is dependent on the successful clinical development, regulatory approval and subsequent commercialization of current and any future product candidates, preclinical studies or earlier clinical trials are not necessarily predictive of future results and the results of Inventiva's and its partners' clinical trials may not support Inventiva's and its partners' product candidate claims, Inventiva's expectations with respect to its clinical trials may prove to be wrong and regulatory authorities may require holds and/or amendments to Inventiva's clinical trials, Inventiva's expectations with respect to the clinical development plan for lanifibranor for the treatment of MASH/*NASH may not be realized and may not support the approval of a New Drug Application, Inventiva and its partners may encounter substantial delays beyond expectations in their clinical trials or fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities, the ability of Inventiva and its partners to recruit and retain patients in clinical studies, enrollment and retention of patients in clinical trials is an expensive and time-consuming process and could be made more difficult or rendered impossible by multiple factors outside Inventiva's and its partners' control, Inventiva's product candidates may cause adverse drug reactions or have other properties that could delay or prevent their regulatory approval, or limit their commercial potential, Inventiva faces substantial competition and Inventiva's and its partners' business, and preclinical studies and clinical development programs and timelines, its financial condition and results of operations could be materially and adversely affected by geopolitical events, such as the conflict between Russia and Ukraine and related sanctions, impacts and potential impacts on the initiation, enrollment and completion of Inventiva's and its partners' clinical trials on anticipated timelines and the state of war between Israel and Hamas and the related risk of a larger conflict, health epidemics, and macroeconomic*

conditions, including global inflation, rising interest rates, uncertain financial markets and disruptions in banking systems. Given these risks and uncertainties, no representations are made as to the accuracy or fairness of such forward-looking statements, forecasts, and estimates. Furthermore, forward-looking statements, forecasts and estimates only speak as of the date of this 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 as amended on August 31, 2023, the Annual Report on Form 20-F for the year ended December 31, 2022 filed with the Securities and Exchange Commission (the "SEC") on March 30, 2023, and the Half-Year Report for the six months ended June 30, 2023 on Form 6-K filed with the SEC on October 3, 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.