

## Inventiva will present data from the final analysis of the Phase 2 study evaluating the combination of lanifibranor with empagliflozin in patients with MASH and T2D at the AASLD The Liver Meeting® late-breaker session

- ▶ Data will be presented on Monday, November 18<sup>th</sup> as a late breaker poster at the American Association for the Study of Liver Diseases (AASLD) The Liver Meeting® 2024 in San Diego.
- ▶ 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.
- ▶ 50% percent of patients saw their HbA1c levels below 6.5% at week 24 following treatment with lanifibranor alone or in combination with empagliflozin.
- ▶ 58% of patients on lanifibranor alone and 80% of those on the combination therapy had a decrease of at least 1% in HbA1c at week 24, compared to 0% in the placebo group.
- ▶ Liver function tests, markers of liver fibrosis and markers of cardiometabolic health including HOMA-IR, hsCRP, ferritin, lipid profile and adiponectin levels were also improved with lanifibranor alone or in combination with empagliflozin.
- ▶ The weight gain observed in a proportion of patients under lanifibranor was not observed in patients treated with the combination of lanifibranor with empagliflozin.

**Daix (France), Long Island City (New York, United States), November 15, 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 announced the presentation of the final analysis of LEGEND, Phase 2 proof-of-concept clinical trial, evaluating lanifibranor in combination with empagliflozin in patients with MASH and Type 2 Diabetes (T2D). The data will be presented Monday November 18, 2024, as a late breaker poster at the American Association for the Study of Liver Diseases (AASLD) The Liver Meeting®, taking place in San Diego California.

**Dr. Michael Cooreman, Chief Medical Officer of Inventiva, stated:** “We are pleased to present the results of our LEGEND study at The Liver Meeting. We believe that the results on the combination of lanifibranor with empagliflozin not only confirm the benefits of lanifibranor as a monotherapy for patients with MASH and type 2 diabetes but also support a treatment paradigm for combination therapy for this patient population.”

**Dr. Nezam (“Nid”) Afdhal, Chief of Gastroenterology, Beth Israel Deaconess Medical Center, Professor of Medicine, Harvard Medical School, said:** “It is frequently overlooked that MASH is a liver manifestation of insulin resistance. The exciting new data from the LEGEND study, which evaluates the combination of lanifibranor and empagliflozin, confirms that lanifibranor has the potential to target the underlying biology of the disease. Additionally, LEGEND should alleviate the concerns about weight gain, as this can be managed with sGLT2 inhibitors or other treatments like GLP-1 agonists, which are treatments of choice for T2D management.”

The Phase 2, LEGEND, included patients with MASH and T2D with a Hemoglobin A1c (HbA1c) between 7-10% at screening. The trial was double-blind for lanifibranor and placebo, but open-label for the combination of lanifibranor and empagliflozin.

The study met the primary efficacy endpoint of HbA1c improvement with both treatment groups and patients treated with lanifibranor-only and in combination with empagliflozin showed a significant reduction in their HbA1c levels, with 50% of patients reaching an HbA1c under 6.5% by week 24 ( $p < 0.001$ ). Additionally, 58% of patients on lanifibranor alone and 80% of those on the combination therapy had a decrease of at least 1% in HbA1c at week 24, compared to 0% in the placebo group.

In addition, patients treated with lanifibranor alone and in combination with empagliflozin showed significant improvement in hepatic steatosis, -49% and -41% respectively, measured by Magnetic resonance imaging-proton density fat fraction (MRI-PDFF), as well as the composite MASH activity and fibrosis measured with cT1, -86 and -75 ms respectively.

Furthermore, adiponectin levels increased by a mean of 3-fold in patients with T2D and MASH treated with lanifibranor ( $p = 0.009$ ) and lanifibranor in combination with empagliflozin ( $p = 0.004$ ) compared to no increase measured in patients under placebo.

Regarding weight, the lanifibranor-only group saw a small increase of 3.6%, while the weight remained stable in the group on lanifibranor and empagliflozin. Importantly, the ratio of visceral abdominal fat to subcutaneous fat decreased in both groups of patients treated with lanifibranor alone or in combination with empagliflozin (-5 and -18% respectively compared to +2% in the placebo group), reflecting a shift from pro-inflammatory visceral fat towards metabolically healthy adipose tissue

Liver function tests (ALT, AST, GGT) and markers of liver fibrosis (TIMP-1, P3NP, Pro-C3) improved with lanifibranor, whether used alone or in combination with empagliflozin. Other cardiometabolic health markers, such as insulin sensitivity (HOMA-IR), inflammation (hs-CRP), ferritin, glycemia, and lipid levels (HDL-C, triglycerides), also showed improvement in both treatment groups.

The details of the presentations are as follows:

<b>Abstract title</b>	Combination therapy of lanifibranor with empagliflozin: metabolic improvement in patients with Metabolic Dysfunction-Associated Steatohepatitis (MASH) and Type-2 Diabetes (T2D)
<b>Publication number</b>	5040
<b>Authors</b>	Michelle Lai, Onno Holleboom, Lucile Dzen, Philippe Huot-Marchand, Jean-Louis Junien, Pierre Broqua, Louis Griffel, Sanjay Patel, Michael P Cooreman.
<b>Date and time</b>	Monday, November 18 <sup>th</sup> 8:00AM-5:00PM PST

**Inventiva will exhibit from Saturday November 16, through Monday November 18<sup>th</sup> at booth #1445.**

## 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 3 clinical trial, NATiV3, for the treatment of adult patients with MASH/NASH, a common and progressive chronic liver disease.

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](http://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 3 clinical trial with lanifibranor in MASH/NASH, clinical trial data releases and publications, the information, insights and impacts that may be gathered from clinical trials, the potential therapeutic benefits of Inventiva's product candidates, including lanifibranor, potential regulatory submissions, approvals and commercialization, Inventiva's pipeline and preclinical and clinical development plans, the expected benefit of having received Breakthrough Therapy Designation, including its impact on the development and review timeline of Inventiva's product candidates, 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 Suspected Unexpected Serious Adverse Reaction (SUSAR) on enrollment 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 ability to obtain financing and to enter into potential transactions, 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, 2023, filed with the Autorité des Marchés Financiers on April 3, 2024, and the Annual Report on Form 20-F for the year ended December 31, 2023, filed with the Securities and Exchange Commission on April 3, 2024. Other risks and uncertainties of which Inventiva is not currently aware may also affect its forward-looking statements and may cause actual results and the timing of events to differ materially from those anticipated. All information in this 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.*