

Inventiva announces that screening in the NATiV3, Phase III, clinical trial evaluating lanifibranor in NASH has resumed

- ▶ Inventiva has lifted the voluntary pause on screening and randomization in the NATiV3 clinical trial following the approval from the US central IRB of the amended protocol and ICF.
- ▶ Screening of patients is resuming in sites operating under central IRB in the US.
- ▶ Other sites and countries are expected to resume screening and randomization activities progressively over the next weeks.
- ▶ Last Patient First Visit is currently targeted for first half 2024.

Daix (France), Long Island City (New York, United States), March 7, 2024 – Inventiva (Euronext Paris and Nasdaq: IVA) (the “Company”), a clinical-stage biopharmaceutical company focused on the development of oral small molecule therapies for the treatment of non-alcoholic steatohepatitis (NASH) and other diseases with significant unmet medical needs, today announced that it has lifted the previously disclosed¹ voluntary pause on screening and randomization of its NATiV3 clinical trial and that sites are resuming screening activities.

Following the Suspected Unexpected Serious Adverse Reaction (“SUSAR”) in a patient enrolled in the study, Inventiva chose to voluntarily pause screening and randomization of new patients in the NATiV3 trial to implement the recommendations of the independent Data Monitoring Committee (“DMC”), which included liver monitoring every 6 weeks for each patient enrolled in the trial, and amending the protocol to exclude newly screened patients diagnosed or with a predisposition to autoimmune liver and thyroid disease. In addition, the Company has made amendments to the Informed Consent Form (“ICF”) in line with the DMC recommendations. During the pause, the DMC has continued to receive updates on the patient status and has reviewed and approved the amendments made to Inventiva’s study documents.

Inventiva received the first approval from the central IRB overseeing clinical research in the United States. Clinical sites located in the United States operating under central IRB have meanwhile resumed screening and randomization activities. This is an important milestone as 152 sites of the NATiV3 clinical trial sites are operating under central IRB and have so far randomized over 60% of the patients in the main cohort. Inventiva expects to progressively obtain the approvals required by local authorities to restart screening and randomization in other countries over the next few weeks.

Frédéric Cren, Chairman, Chief Executive Officer and cofounder of Inventiva, stated: *“The well-being of our patients is paramount in our clinical research, and we are delighted to see that the patient who experienced the SUSAR is expected to make a full recovery. We want to thank all sites and all patients currently enrolled and in screening for their dedication to our study. Our team has worked diligently, and we are pleased to see screening and randomization resuming in our American sites under central IRB. Our sites operating under central IRB have contributed to more than 60% of all patients randomized in the trial and we expect them to be key in securing the last patients needed to finalize enrollment. Our ongoing interactions with the NATiV3 sites give us confidence*

¹ [Inventiva - PR - Full Year 2023 Revenue et Cash - EN - 02 15 2024- final.pdf \(inventivapharma.com\)](#)

in their strong commitment to resume the recruitment activities and we are looking forward to completing enrollment in the NATiV3 study with their support.”

Prior to the voluntary pause, 913 patients were already randomized in the NATiV3 clinical trial including 731 in the main cohort and over 550 patients were in screening. Inventiva anticipates the last patient first visit for the NATiV3 clinical trial in the first half of 2024.

About lanifibranor

Lanifibranor, Inventiva’s lead product candidate, is an orally-available small molecule that acts to induce antifibrotic, 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 PPAR α and PPAR δ , and a partial activation of PPAR γ . 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 the NATiV3 Phase III trial

NATiV3 is a randomized, double-blind, placebo-controlled clinical trial designed to evaluate the long-term efficacy and safety of lanifibranor (800mg/daily and 1200mg/daily) in adult patients with biopsy-proven non-cirrhotic NASH and F2/F3 stage of liver fibrosis. The trial takes place in 24 countries and in more than 400 clinical sites and to recruit approximately 900 patients to be treated over a 72-week period. The effect of lanifibranor will be assessed on several histological endpoints, including NASH resolution and improvement of fibrosis of at least one stage.

An exploratory cohort is anticipated to enrol approximately 200 patients with NASH and fibrosis screen-failed on histology for the main NATiV3 clinical trial. Inventiva anticipates that this exploratory cohort may allow the generation of additional data using non-invasive tests and contribute to the regulatory safety database requirement to support the planned submission for potential accelerated approval to the Food and Drug Administration (FDA) and potential conditional approval to the European Medicines Agency (EMA) of lanifibranor for the treatment of NASH.

Topline results of NATiV3 are expected for the half 2026. For more information about NATiV3, visit clinicaltrials.gov.

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 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

Contacts

Inventiva

Pascaline Clerc
EVP, Strategy and Corporate Affairs
media@inventivapharma.com
+1 202 499 8937

Brunswick Group

Tristan Roquet Montegon /
Aude Lepreux /
Julia Cailleateau
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 enrollment for those trials, including the ongoing NATiV3 Phase III clinical trial with lanifibranor in patients with NASH and the LEGEND Phase IIa combination trial with lanifibranor and empagliflozin in patients with NASH, the impact of the SUSAR and the protocol amendments on clinical trials, including NATiV3 and LEGEND, and the results and timing thereof and regulatory matters with respect thereto, expectations with respect to patients in clinical trials, including the SUSAR patient, the potential for regulatory authorities to institute clinical holds and/or otherwise implement additional requirements and/or cause further delays in clinical trials, including in the NATiV3 and LEGEND trials, the 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 of Inventiva's product candidates, including lanifibranor, potential regulatory submissions, approvals and commercialization, Inventiva's pipeline and preclinical and clinical development plans, 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", "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 the impact of the SUSAR on its clinical trials may prove to be wrong and regulatory authorities may require additional holds and/or additional amendments to Inventiva's clinical trials, 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 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.