

Inventiva announces changes to the clinical development of lanifibranor, including plans for a new Phase III trial in patients with NASH and compensated cirrhosis

- ▶ Proposed changes are expected to be beneficial to the lanifibranor clinical program by reducing the number of biopsies and the trial duration, eventually offering all patients in the trial access to treatment and potentially expanding the addressable patient population to patients with NASH and compensated cirrhosis
- ▶ Confirmatory trial of lanifibranor clinical benefits, which was initially planned to be evaluated in Part 2 of NATiv3 trial in patients with NASH and F2/F3 fibrosis, is now planned to be evaluated in a new Phase III trial in patients with NASH and compensated cirrhosis in place of the previously planned Part 2 of the NATiv3 trial
- ▶ The ongoing Part 1 of the NATiv3 trial continues as planned and, if successful, is expected to provide the necessary data to support NDA submission for accelerated approval, based on liver histological endpoints; expected enrollment for Part 1 remains on track with last patient first visit expected to be completed H2 2023
- ▶ Approximately 200 screen-failed patients from Part 1 of the NATiv3 trial are expected to be included in a new 72-week exploratory cohort aimed at generating results based on non-invasive tests and contributing to the regulatory safety database
- ▶ All patients enrolled in Part 1 of the NATiv3 trial and the exploratory cohort could have access to lanifibranor treatment by being offered to participate in a new 48-week active treatment extension study
- ▶ The results of the new planned Phase III in patients with NASH and compensated cirrhosis, if successful, are expected to support the submission for FDA full approval and expand the addressable patient population beyond patients with F2 and F3 fibrosis to include patients with NASH and compensated cirrhosis

Daix (France), Long Island City (New York, United States), January 4, 2023 – 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 patients with non-alcoholic steatohepatitis (“NASH”), mucopolysaccharidoses (“MPS”) and other diseases with significant unmet medical needs, today announced that, following a consultation with the U.S. Food and Drug Administration (“FDA”), Inventiva has decided to modify the clinical development plan of lanifibranor for the treatment of NASH. Inventiva’s request for a consultation with

the FDA followed a public communication by the FDA¹ suggesting that an alternative approach to seek full approval in patients with NASH could be considered upon submission of positive results of a Phase III trial using a histology surrogate endpoint in patients with NASH and a Phase III clinical outcome trial in patients with NASH and compensated cirrhosis. The Company's proposed changes to the NATiV3 trial are designed to align with the alternative regulatory approach and are expected to be beneficial to the overall lanifibranor clinical program by 1) reducing the number of biopsies a patient undergoes during the trial from three to two, 2) reducing the trial duration a patient has to consent to from 7 years to 72 weeks, 3) offering all patients in the trial access to a lanifibranor treatment for at least 48 weeks by allowing them to enter into a new active treatment extension study, and 4) potentially expanding the addressable patient population to include patients with NASH and compensated cirrhosis.

The Company continues to anticipate submission of a new drug application ("NDA") to the FDA for accelerated approval with such planned submission based on liver histological endpoints of approximately 900 patients treated over a 72-week period. A placebo-controlled exploratory cohort is anticipated to be added in parallel to Part 1 of the NATiV3 trial and will include approximately 200 patients with NASH and fibrosis who are not eligible for Part 1 (screen failures). The Company anticipates that this exploratory cohort may allow the generation of additional results using non-invasive tests and contribute to the safety database requirement to support the planned submission for potential accelerated approval.

Under the newly planned trial design, the original Part 2 of the NATiV3 trial, a clinical outcome trial that was previously planned to be conducted in approximately 2,000 patients with F2 and F3 fibrosis for a maximum period of seven years will be replaced by a placebo-controlled Phase III outcome trial which will be event driven and is expected to last approximately three years. The Phase III outcome trial is expected to randomize approximately 800 patients with NASH and compensated cirrhosis.

If the results of the outcome trial in patients with NASH and compensated cirrhosis are positive, the Company anticipates they will support the submission of an NDA to the FDA for full approval and the potential expansion of the addressable patient population beyond patients with F2 and F3 fibrosis to include patients with NASH and compensated cirrhosis, a patient population at an increased risk of liver-related morbidity and mortality and for which the anti-fibrotic properties of lanifibranor could potentially prevent worsening of the disease. Lanifibranor has been granted both Fast Track and Breakthrough Therapy designations for the treatment of NASH, and the FDA confirmed last year that the Fast Track designation is also applicable to the treatment of NASH for patients with compensated cirrhosis.

The Company does not expect these trial design changes to have a significant impact on the funds originally anticipated to be needed to potentially secure accelerated approval in the U.S. or conditional approval in the EU based on the new trial design.

Michael Cooreman, M.D., Chief Medical Officer of Inventiva, commented: *"This is a promising evolution for our lanifibranor clinical development program. Not only are Inventiva's changes to the trial design expected to provide an opportunity for patients enrolled in the placebo arm to access a lanifibranor treatment arm, but also the changes are designed to reduce the number of biopsies. We believe these changes provide an opportunity to support the anticipated timeline to seek accelerated approval and potentially bring a treatment option to a larger population which could include patients with NASH and compensated cirrhosis."*

Prof. Arun Sanyal, M.D., Director of the Stravitz-Sanyal Institute for Liver Disease and Metabolic Health, Virginia Commonwealth University and co-principal investigator of the NATiV3 Phase III clinical trial, stated: *"This revised clinical trial design has been built on the latest thinking in the field. I believe that these changes to the program with an amended NATiV3 and Phase III trial in patients with compensated cirrhosis will reinforce the*

¹ FDA Webcast. "Regulatory Perspectives for Development of Drugs for Treatment of NASH." January 29, 2021. Available at <https://www.fda.gov/drugs/news-events-human-drugs/regulatory-perspectives-development-drugs-treatment-nash-01292021-01292021>

scientific rigour of the development program as it will now include a broader patient population in dire need of treatment options.”

Prof. Sven Francque, M.D., Ph.D., Antwerp University Hospital and co-principal investigator of the NATiV3 Phase III clinical trial, said: *“Lanifibranor has demonstrated a significant effect on the composite histological endpoint in the NATiVE Phase IIb trial. Given lanifibranor’s mechanism of action and the effects demonstrated on the broad spectrum of the disease, including its anti-fibrotic effect, I believe including patients with NASH and compensated cirrhosis in the program is extremely relevant.”*

Donna Cryer, President and CEO of the Global Liver Institute, said: *“Patients and caregivers commend Inventiva for making these changes in consultation with regulators. We believe limiting the number of biopsies and giving patients, both randomized and placebo, access to a treatment arm are invaluable measures for patients suffering with NASH and who still do not have access to any approved treatment options today.”*

Enrolment for Part 1 of the NATiV3 trial remains on track, with the last patient first visit expected to take place in the second half of 2023.

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 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 most-advanced 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, 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 80 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 C 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 enrolment for those trials, including the ongoing Part 1 of the NATiV3 Phase III clinical trial, and the planned new Phase III clinical trial and 48-week active treatment extension study with lanifibranor in NASH, 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 addressable patient population, the potential therapeutic benefits of lanifibranor for patients with F2 and F3 fibrosis, NASH and compensated cirrhosis, regulatory submissions and approvals, the benefit of having received the FDA’s Breakthrough Therapy and Fast Track designation for lanifibranor in the treatment of NASH or the impact thereof on Inventiva’s ability to obtain regulatory approval, the expectation that the revised Phase III clinical trial NATiV3 and new Phase III clinical trial will facilitate patient enrolment, the effect of the changes to the NATiV3 Phase III clinical trial on the results and timeline of the trial, that the trial is expected to provide the necessary data to support NDA submission for accelerated approval and the likelihood of regulatory approval, Inventiva’s pipeline and preclinical and clinical development plans, future activities, expectations, plans, growth and prospects of Inventiva and funds required to obtain approval in the U.S. and elsewhere. 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”, “plans”, “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. Future 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, 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 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 the current COVID-19 pandemic and 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, and macroeconomic conditions, including global inflation and uncertain financial markets. 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, 2021 filed with the Autorité des Marchés Financiers on March 11, 2022, the Annual Report on Form 20-F for the year ended December 31, 2021 filed with the Securities and Exchange Commission on March 11, 2022 and the financial report for the first half of 2022 filed with the Securities and Exchange Commission on September 22, 2022 for additional information in relation to such factors, risks and uncertainties.

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.