Inventiva announces the randomization of the first patient in China in the NATiV3 clinical trial and provides an update on its clinical development program

- The first patient was randomized in China in the NATiV3 Phase III clinical trial, triggering a milestone payment of $3 million from CTTQ to Inventiva.
- With this milestone payment Inventiva expects to have met the operational and financial conditions precedent to draw the second €25 million tranche of the EIB loan.[1]
- China's National Medical Products Administration has granted "Breakthrough Therapy Designation" to lanifibranor for the treatment of NASH. Lanifibranor is believed to be the first drug candidate to receive such designation from both the FDA and the NMPA.
- As of December 20, 2023, a total of 793 patients have been randomized in NATiV3 of which 657 in the main cohort and 136 in the exploratory cohort. 607 patients are currently in the screening process.
- The last patient first visit in the NATiV3 Phase III clinical trial is now expected in the first quarter of 2024, and the target number of randomized patients in the main cohort is expected to be reached in the second quarter of 2024.
- Analysis of the baseline characteristics of all patients randomized in the main cohort suggests a patient profile aligned with those of patients randomized in the NATIVE Phase II clinical trial.
- Lanifibranor continues to show a favorable tolerability profile as confirmed by the third Data Monitoring Committee[2] of November 2023.
- Topline results of the proof-of-concept Phase II clinical trial, LEGEND, evaluating lanifibranor in combination with empagliflozin are expected in the first quarter of 2024.

[1] The disbursement of the second tranche of €25 million is subject to, among other conditions, (i) the Company issuing warrants to EIB in accordance with the terms and conditions of the warrant agreements entered into July 1, 2022 in connection with the EIB credit facility, (ii) the receipt by the Company from the date of the EIB credit facility of an aggregate amount of at least €70.0 million ((as of today, the Company has received 68.5 million of euros, which includes the August 2023 financing, the Hepalys upfront payment of $10.0 million and the €18.0 million that was a condition for the disbursement of the first tranche of the EIB loan), paid either in exchange for Company shares, or through upfront or milestone payments; and (iii) operational conditions, including criteria based on patient enrolment and number of sites activated in the Company's NATiV3 Phase III clinical trial of lanifibranor in patients with NASH a condition that the Company believes it has met in December 2023.

[2] Inventiva-PR-3rd-DMC-NATiV3-EN-12-04-2023.pdf (inventivapharma.com)

Daix (France), Long Island City (New York, United States), December 20, 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 non-alcoholic steatohepatitis ("NASH") and other diseases with significant unmet medical needs, today announced that the first patient has been randomized in China in the global NATiV3 Phase III clinical trial and provided an update on its clinical development program.

Milestone payment from CTTQ and EIB loan

Following the randomization of the first patient in China, Inventiva is eligible to receive a $3 million milestone payment from Chia Tai Tianqing Pharmaceutical Group Co., Ltd. ("CTTQ"). This would be the second of the two short-term milestone payments following the $2 million milestone payment from CTTQ received on July 19, 2023, under the license and collaboration agreement with CTTQ. Upon the anticipated receipt in January 2024 of this $3 million milestone, Inventiva is expected to have met all financial and operational conditions precedent required to draw the second €25 million tranche under the finance contract with the European Investment Bank ("EIB") dated May 16, 2022 (the "Finance Contract"). The Company expects to draw this second tranche in early 2024, following the issuance of warrants to the EIB as provided in the Finance Contract.

Breakthrough Therapy Designation for lanifibranor in NASH by China's NMPA

Lanifibranor was granted Breakthrough Therapy Designation for NASH by China's National Medical Products Administration (NMPA). Similar to the U.S. Food and Drug Administration's (FDA) Breakthrough Therapy Designation, this designation is intended to accelerate the development and review of drugs for serious or life-threatening conditions. The NMPA granted "Breakthrough Therapy Designation" based on the results of Inventiva's Phase IIb NATIVE clinical trial. Inventiva believes that lanifibranor is the first drug candidate to receive "Breakthrough Therapy Designation" from both the FDA and the NMPA for the treatment of NASH.

NATiV3 update

Frederic Cren, CEO and co-founder of Inventiva said: *"While we are not reaching the first visit of the last patient by the end of 2023 as previously projected, the improvements in the randomization, screening numbers and screen failure rate give us confidence that we can reach this milestone in the first quarter of 2024. The recommendation of our third Data Monitoring Committee (DMC) in November 2024[2] to continue the trial without modification to the protocol is further confirmation of the good safety profile of lanifibranor. Furthermore, we have high hopes that the results of the LEGEND trial will show benefit of the combination of lanifibranor with empagliflozin in patients with NASH."*

As of December 20, 2023, 468 clinical sites have been activated in 24 countries, including China, and a total of 793 patients have been randomized, of which 657 in the main cohort and 136 in the exploratory cohort. 607 patients are in the screening process and, based on the recent screen failure rate of approximately 80%, Inventiva expects 121 additional patients to be randomized in the main cohort in the next 10 weeks.

Since July, with limited contribution from the sites in China, the newly opened sites and a third party clinical network in Mexico, between 250 to 300 patients are screened and approximately 50 patients are randomized in the main cohort each month, and the monthly enrolment rate is averaging 0.14 patient/site/month in the main cohort. Therefore, if the current screen failure rate for the main cohort and the number of patients entering the screening process are maintained, Inventiva now expects the first visit of the last patient to be in the first quarter of 2024 and to complete randomization in the second quarter of 2024.

Topline results for the Phase III NATiV3 clinical trial are now expected to be published in the first half of 2026 versus the second half of 2025, as previously communicated.

If the results of the trial confirm sufficient clinical benefit and a continued good safety profile, Inventiva plans to submit an application for accelerated approval in the United States and conditional approval in the European Union for the marketing of lanifibranor. In addition, CTTQ would also be in capacity to submit an application for a marketing authorization in Greater China.

NATiV3 patients distribution and characteristic

Approximately 70% of the patients randomized in the main and exploratory cohorts are from the United States, ~20% from Europe and ~10% from Latin America and the rest of the world.
At baseline, 13% of patients randomized in the main cohort are receiving a stable dose GLP1 receptor agonists and 8% are receiving stable SGLT2 inhibitors.
The baseline characteristics of the patients enrolled so far in the main cohort are in line with expectations and the patient population in the NATIVE Phase IIb clinical trial. The main difference in patient characteristics observed thus far is that there is a higher percentage of patients with type 2 diabetes (T2D) in the main cohort of the NATiV3 Phase III trial compared to the NATIVE Phase IIb trial (55% vs 42%, respectively). The effect size of lanifibranor therapy over placebo in the Phase IIb clinical trial on the composite endpoint "NASH resolution and fibrosis improvement" (which corresponds to the primary efficacy endpoint in the NATiV3 Phase III clinical trial), was higher in patients with T2D than in patients without diabetes: 21% and 26% for lanifibranor 800 and 1200 mg/day, respectively, in patients with T2D compared to 7% and 22%, respectively, in patients without T2D. Given the higher risk of hepatic and extrahepatic morbidity in patients with T2D and NASH[3], the higher effect size observed in patients with NASH and T2D treated with lanifibranor in the Phase IIb trial is an important result for this specific patient population if confirmed in the larger clinical trial.

As of December 20, 2023, 136 patients are randomised in the exploratory cohort including approximately 30% of patients with fibrosis stage F4. Inventiva believes that this subgroup of patients will provide valuable data on lanifibranor efficacy and safety.

Lanifibranor continues to show a favorable tolerability profile as confirmed by the third Data Monitoring Committee (DMC) that took place late November 2023[2]. This safety assessment was based on the review of safety data from more than 500 patients, including patients that have been treated with lanifibranor for more than 72 weeks.

Update on Phase II clinical trial LEGEND

Enrolment in the proof of concept, LEGEND Phase II clinical trial evaluating lanifibranor in combination with the SGLT2 inhibitor empagliflozin in patients with NASH has been stopped, and data collection and cleaning is ongoing. The first topline results on primary and secondary endpoints are expected for the end of the first quarter of 2024. The primary efficacy endpoint of the trial is a change in Hemoglobin A1c ("HbA1c") at the end of the 24-week treatment compared to baseline. Secondary endpoints include changes in liver enzymes, glycaemic and lipids parameters, and inflammatory markers. The trial has been designed to provide valuable information on body weight evolution in patients with NASH and T2D when treated with lanifibranor and empagliflozin, and on the reduction of hepatic steatosis using magnetic resonance imaging (MRI).

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

[3] Kenneth Cusi; Time to Include Nonalcoholic Steatohepatitis in the Management of Patients With Type 2 Diabetes. **Diabetes Care** 1 February 2020; 43 (2): 275–279. https://doi.org/10.2337/dci19-0064

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 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 an oncology development candidate for its Hippo signalling 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, preliminary analysis of clinical trials, regulatory plans, forecasts and estimates with respect to Inventiva's pre-clinical programs and clinical trials, including design, protocols, duration, timing, recruitment costs, screening and enrolment for those trials, including the ongoing NATiV3 Phase III clinical trial with lanifibranor in patients with NASH and the ongoing LEGEND Phase II clinical trial evaluating lanifibranor in combination with the sSGLT2 inhibitor empagliflozin in patients with NASH, including the possibility for patients to participate in those trials, the clinical development and regulatory plans and pathway for lanifibranor of Sino Biopharm and its affiliates, including the Phase III clinical trial in patients with 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 potential therapeutic benefits of Inventiva's product candidates, including lanifibranor and its safety and tolerability profile, expectations with respect to clinical development and commercialization by CTTQ, including with respect to potential clinical trials and regulatory approvals, expectations with respect to the benefits of the agreement with CTTQ, including potential acceleration of lanifibranor commercialization in the event required regulatory approvals are obtained, potential regulatory submissions and approvals, including a potential NDA filing in China, the United States and Europe, the expected benefit of having received Breakthrough Therapy Designation from the FDA and NMPA, including its impact on the development and review timeline of Inventiva's product candidates, Inventiva's future activities, expectations, plans, growth and prospects of Inventiva, and achievement of milestones, potential and expected milestone payments, including milestone payments from CTTQ, potential regulatory submissions and approvals, including potential accelerated approval in the United States and conditional approval Europe, the potential of Sino Biopharm's products and future activities, expectations, plans, growth and prospects of Sino Biopharm, and Inventiva's ability to satisfy the conditions precedent for the drawing of the second tranche of the EIB loan facility and the expected timing of the disbursement of the second tranche. 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 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 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 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, 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 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, enrolment 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 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 statement.