

## Inventiva announces the screening of the first patient in LEGEND, a Phase IIa combination trial with lanifibranor and empagliflozin in patients with NASH and T2D

- ▶ The Phase IIa Proof-of-Concept study is designed to assess the safety and efficacy of lanifibranor in combination with the SGLT2 inhibitor empagliflozin for the treatment of patients with non-cirrhotic non-alcoholic steatohepatitis (NASH) and type-2 diabetes (T2D)
- ▶ The primary efficacy endpoint will be based on improvement in HbA1c
- ▶ Secondary efficacy endpoints include changes in liver enzymes, markers of glycemic control, lipid metabolism, inflammation and body fat composition
- ▶ Publication of topline results is expected in the second half of 2023

**Daix (France), Long Island City (New York, United States), July 7, 2022** – Inventiva (Euronext Paris and Nasdaq: IVA), a clinical-stage biopharmaceutical company focused on the development of oral small molecule therapies for the treatment of NASH and other diseases with significant unmet medical needs, today announced the screening in the United States of America of the first patient in its LEGEND Phase IIa combination trial with lanifibranor and empagliflozin in patients with NASH and T2D <sup>1</sup>. Over 30 sites located in France, United Kingdom, Belgium, Netherlands and United States have already been qualified to participate in this clinical trial. Topline results are expected to be published in the second half of 2023.

**Prof. Michelle Lai, M.D., Ph.D., Beth Israel Deaconess Medical Center and co-principal investigator of the LEGEND Phase IIa clinical trial, said:** *“The LEGEND trial is expected to help us better understand the pathophysiology of patients we care for in our clinics who suffer of NASH and T2D. Insulin resistance is a root cause leading to the development of NASH, and the combination of lanifibranor and empagliflozin could potentially provide complementary effects and provide additional therapeutic benefits to improve the overall cardiometabolic health of our patients.”*

**Dr. Michael Cooreman, Chief Medical Officer of Inventiva, commented:** *“We are delighted to see the initiation of this Proof-of-Concept study, which we believe will further draw attention to NASH as a multisystemic liver disease with a highly relevant cardiometabolic aspect. This clinical trial is anticipated to not only add to the body of evidence demonstrating the therapeutic benefits of lanifibranor on the broad spectrum of the disease biology of NASH, but should also provide insights on how the complementary mechanisms of action of a pan-PPAR agonist and an SGLT2 inhibitor could enhance the therapeutic benefits of lanifibranor.”*

The Phase IIa trial, LEGEND, has been designed as a multi-center randomized, placebo-controlled trial to assess the safety and efficacy of lanifibranor in combination with the SGLT2 inhibitor empagliflozin for the treatment of adult patients with non-cirrhotic NASH and T2D. The trial is double-blind for the placebo and lanifibranor arms and open-label for the combination of lanifibranor and empagliflozin arm.

<sup>1</sup> For more details, please refer to: [clinicaltrials.gov/NCT05232071](https://clinicaltrials.gov/NCT05232071).

LEGEND is expected to recruit a total of 63 patients with non-cirrhotic NASH and T2D. In the trial, the diagnosis of non-cirrhotic NASH will be based on a historic histology evaluation or a combination of non-invasive methods including imaging and serum-based metabolic diagnostic tests.

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, inflammatory markers and body fat composition. The trial is designed to provide valuable information on body weight evolution and body fat composition in patients with NASH and T2D when treated with lanifibranor and empagliflozin. Magnetic resonance imaging (MRI) based imaging will allow the collection of non-invasive data on hepatic fat, inflammation and fibrosis.

### 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 $\alpha$  and PPAR $\delta$ , and a partial activation of PPAR $\gamma$ . 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. 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 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'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.

The Company has established a strategic collaboration with AbbVie in the area of autoimmune diseases that resulted in the discovery of the drug candidate cedirogant (ABBV-157), an oral ROR $\gamma$  inverse agonist which is being evaluated in a Phase IIb clinical trial, led by AbbVie, in adult patients with moderate to severe chronic plaque psoriasis. Inventiva's pipeline also includes odiparcil, a drug candidate for the treatment of adult mucopolysaccharidoses (MPS) VI patients. As part of Inventiva's decision to focus clinical efforts on the development of lanifibranor, it suspended clinical efforts relating to odiparcil and is reviewing available options with respect to its potential further development. Inventiva is 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: FRO013233012) and on the Nasdaq Global Market in the United States (ticker: IVA). [www.inventivapharma.com](http://www.inventivapharma.com).

## Contacts

### Inventiva

Pascaline Clerc  
VP of Global External Affairs  
[media@inventivapharma.com](mailto:media@inventivapharma.com)  
+1 240 620 9175

### Brunswick Group

Laurence Frost /  
Tristan Roquet Montegon /  
Aude Lepreux  
Media relations  
[inventiva@brunswickgroup.com](mailto:inventiva@brunswickgroup.com)  
+33 1 53 96 83 83

### Westwicke, an ICR Company

Patricia L. Bank  
Investor relations  
[patti.bank@westwicke.com](mailto: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 recruitment, screening and enrolment for those trials, including LEGEND, clinical trial data releases and publications, the information, insights and impacts that may be gathered from clinical trials, including LEGEND, the potential therapeutic benefits of lanifibranor in combination with empagliflozin, the design of trials, including LEGEND, pipeline and preclinical and clinical development plans, milestone payments, royalties and product sales, future activities, expectations, plans, growth and prospects of Inventiva and the sufficiency of Inventiva’s cash resources and cash runway. 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” 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, 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 and related impacts and potential impacts on the initiation, enrolment and completion of Inventiva’s clinical trials on anticipated timelines. 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 and 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 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.*