PRESS RELEASE

Inventiva announces the publication in *Journal of Hepatology Reports* on results of lanifibranor treatment on liver sinusoidal endothelial cells in patients with MASLD/MASH and in preclinical models of the disease

- Analysis of liver sinusoidal endothelial cells ("LSEC") from screening and end of treatment biopsies in the Phase 2b NATIVE study showed evidence of LSEC capillarization in patients without MASH, and a further increased capillarization in patients with MASH
- In addition, in the subgroup of patients without MASH, there was higher LSEC capillarization in patients with MASLD than those with normal histology
- LSEC capillarization observed in patients was strongly associated with liver fibrosis and to a lesser extent inflammation
- End of treatment biopsies from Phase 2b NATIVE showed improvement in LSEC capillarization in patients with MASH and treated with lanifibranor compared to placebo
- In addition, using two preclinical models, lanifibranor demonstrated effects extending beyond capillarization reversal, normalizing portal pressure and intrahepatic vascular resistance
- These effects in the preclinical models appear more pronounced than those observed with single PPAR agonists, suggesting that as a pan-PPAR agonist, lanifibranor could represent a comprehensive therapeutic approach for MASH, fibrosis regression, and the prevention of progression to cirrhosis

Daix (France), New York City (New York, United States), July 2, 2025 – Inventiva (Euronext Paris and Nasdaq: IVA) ("Inventiva" or the "Company"), a clinical-stage biopharmaceutical company focused on the development of oral therapies for the treatment of metabolic dysfunction-associated steatohepatitis ("MASH"), today announces the publication in *Journal of Hepatology Reports,* a peer-reviewed, scientific journal, of results from the Phase 2b NATIVE clinical trial and preclinical study evaluating the effects of lanifibranor on liver sinusoidal endothelial cells in Metabolic dysfunction-associated steatotic liver disease ("MASLD") and MASH.

Kris V. Kowdley MD, Director of the Liver Institute Northwest, Washington said: "The liver sinusoidal endothelial cells (LSECs) play a crucial role in the vascular changes seen in liver diseases, including MASH and cirrhosis. Capillarization of these cells appears early, even before the onset of MASH. The results from the Phase 2b NATIVE trial with lanifibranor show a correlation between LSEC capillarization and both the stage of fibrosis and inflammation, along with evidence suggesting that lanifibranor can reduce this capillarization. These findings strengthen our confidence in lanifibranor's potential to help prevent progression to cirrhosis and associated clinical events."

The LSEC alteration was evaluated using CD34 staining in the Phase 2b NATIVE biopsies, which showed a higher density of CD34 staining in patients with MASLD or MASH compared to patients without MASLD.

The CD34 staining was shown to be associated with liver fibrosis and to a lesser extent with inflammation. CD34 staining on the NATIVE liver biopsies was reduced in a dose-dependent manner following the treatment with lanifibranor for 24 weeks. These data suggest that lanifibranor potentially reduces LSEC capillarization, a key driver in the progression of cirrhosis, in patients with MASH and fibrosis.

Two preclinical models for MASLD and MASH showed that vascular modifications appear at early stages of disease development even before inflammation and fibrosis. Moreover, these models showed that the effects of lanifibranor potentially extend beyond capillarization reversal, normalizing intrahepatic vascular resistance (IHVR) demonstrated by normalization of portal vein pressure and the ex-vivo measured transhepatic pressure gradient. These effects were superior to those observed with single PPAR agonists.

LSEC dysfunction is increasingly recognized as a key contributor to the progression of chronic liver diseases. LSEC dysfunction is characterized by loss of fenestrations (defenestration) and by capillarization, which disrupts hepatic microcirculation, leading to impaired substrate exchange, increased intrahepatic vascular resistance, and elevated portal pressure. This dysfunction also promotes a pro-inflammatory and pro-fibrotic environment, facilitating the progression from early-stage liver disease to more advanced conditions such as fibrosis and cirrhosis.
The histological evaluation from the NATIVE Phase 2b trial demonstrated that LSEC capillarization occurs in the very early stage of the disease. We believe the robust dataset from the NATIVE Phase 2b trial combined with the additional data from preclinical models, points to potential benefits of lanifibranor as a pan-PPAR agonist targeting the multiple components of the disease.

Publication details

Publication title:	*"Altered liver sinusoidal endothelial cells in MASLD and their evolution following lanifibranor treatment."*
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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 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 MASH. 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 preclinical studies to date. The FDA has granted Breakthrough Therapy and Fast Track designation to lanifibranor for the treatment of MASH.

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. The Company is currently evaluating lanifibranor, a novel pan-PPAR agonist, in the NATiV3 pivotal Phase 3 clinical trial for the treatment of adult patients with MASH, a common and progressive chronic liver disease.

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). http://www.inventivapharma.com

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Important Notice

This press release contains certain "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, Inventiva's expectations with respect to forecasts and estimates with respect to Inventiva's pre-clinical programs and clinical trials, including design, protocol, duration, timing and costs of Inventiva's pre-clinical studies, and the results and timing thereof and regulatory matters with respect thereto, preclinical study data releases and publications, the information, insights and impacts that may be gathered from preclinical studies, clinical trials, the potential therapeutic benefits of lanifibranor, potential regulatory submissions, approvals and commercialization, the clinical development of and regulatory plans and pathway for lanifibranor, the expected benefit of having received Breakthrough Therapy Designation and Fast Track Designation, including its impact on the development and review timeline of Inventiva's product candidates and approvals, and future activities, expectations, plans, growth and prospects of Inventiva. 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 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 interim data or data from any interim analysis of ongoing clinical trials may not be predictive of future trial results, the recommendation of the DMC may not be indicative of a potential marketing approval, Inventiva cannot provide assurance on the impacts of the Suspected Unexpected Serious Adverse

Reaction 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 its product candidate, lanifibranor, 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 additional holds and/or additional amendments to Inventiva's clinical trials, Inventiva's expectations with respect to the clinical development plan for lanifibranor for the treatment of MASH may not be realized and may not support the approval of a New Drug Application, Inventiva's ability to identify additional products or product candidates with significant commercial potential, Inventiva's expectations with respect to its pipeline prioritization plan and related workforce reduction, including potential benefits, expenses and consequences relating thereto, Inventiva's ability to execute on its commercialization, marketing and manufacturing capabilities and strategy, Inventiva's ability to successfully cooperate with existing partners or enter into new partnerships, and to fulfill its obligations under any agreements entered into in connection with such partnerships, the benefits of its existing and future partnerships on the clinical development, regulatory approvals and, if approved, commercialization of its product candidates, and the achievement of milestones thereunder and the timing thereof, 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 pre-clinical studies and clinical development programs and timelines, its financial condition and results of operations could be materially and adversely affected by changes in law and regulations, unfavorable conditions in its industry, geopolitical events, such as the conflict between Russia and Ukraine and related sanctions, the conflict in the Middle East and the related risk of a larger conflict, health epidemics, and macroeconomic conditions, including developments in international trade policies, global inflation, financial and credit market fluctuations, tariffs and other trade barriers, political turmoil, and natural catastrophes, 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, 2024 filed with the Autorité des Marchés Financiers on April 15, 2025 and the Annual Report on Form 20-F for the year ended December 31, 2024 filed with the Securities and Exchange Commission (the "SEC") on April 15, 2025 for other risks and uncertainties affecting Inventiva, including those described under the caption "Risk Factors" and in future filings with the SEC. 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