PRESS RELEASE

Inventiva announces the publication in *Biomedicine & Pharmacotherapy* of the results from a preclinical study showing improvement of portal hypertension with lanifibranor treatment

- The study demonstrated that lanifibranor improved Portal Hypertension (PH) in mouse models of fibrotic PH and prehepatic non-fibrotic PH
- Lanifibranor was observed to decrease portal pressure by improving Liver Sinusoidal Endothelial Cell (LSEC) dysfunction and fibrosis, and by directly targeting the splanchnic vasculature through its anti-angiogenetic effects
- These findings suggest that lanifibranor may be a promising therapeutic candidate that could potentially address PH-related complications typically associated with MASLD, MASH, and other advanced chronic liver diseases, including cirrhosis

Daix (France), New York City (New York, United States), February 26, 2025 – Inventiva (Euronext Paris and Nasdaq: IVA) ("Inventiva" or the "Company"), a clinical-stage biopharmaceutical company focused on the development of oral small molecule therapies for the treatment of metabolic dysfunction-associated steatohepatitis ("MASH") and other diseases with significant unmet medical needs, today announced the publication in *Biomedicine & Pharmacotherapy*, a peer-reviewed, scientific journal, of the results from a preclinical study demonstrating that lanifibranor may reduce Portal Hypertension ("PH").

The study, a grant-supported collaboration with Ghent University Hospital researchers, evaluated the effect of lanifibranor on PH independently of hepatic condition.

The preclinical study utilized two distinct mouse models to investigate portal hypertension through different mechanisms. The first model, Partial Portal Vein Ligation ("PPVL"), induced an increase in portal pressure with vascular modifications in the splanchnic compartment, without affecting the liver itself. The second model, common Bile Duct Ligation ("cBDL"), resulted in liver fibrosis and cirrhosis, leading to an elevation in portal pressure. Mice in the PPVL and cBDL models received daily treatments of lanifibranor for 7 days and 14 days, respectively, at two doses (10 and 30 mg/kg) to assess the effect of lanifibranor on PH, as measured by portal pressure.

In the PPVL model, lanifibranor was observed to reduce portal pressure in a dose-dependent manner and with a statistically significant effect, with a decrease of 28% at 10mg/kg ($p=0.03$) and 39% at 30mg/kg ($p=0.001$). This improvement of PH is attributed to the vascular amelioration within the splanchnic compartment, including a reduced blood flow in the superior mesenteric artery ($p=0.07$), a significant decrease in endothelial cells staining (indicative of reduced angiogenesis), and a statistically significant reduction in vascular wall thickness, which correlates with the decrease in portal pressure.

Furthermore, analysis of the mesenteric vascular architecture through vascular corrosion casting revealed structural modifications in the mesenteric vasculature demonstrating angiogenesis and vascular arborization that were reversed following treatment with lanifibranor.

In the cBDL model, lanifibranor was observed to reduce, in a dose-dependent manner, portal pressure and spleen weight with a concurrent improvement of fibrosis. In addition, LSEC dysfunction and hepatic angiogenesis, as associated with fibrotic PH, were shown to decrease. These results suggest that lanifibranor has the potential to ameliorate PH through its direct antifibrotic effect.

PH is a significant complication of advanced chronic liver disease, including cirrhosis and MASH, and can also develop in the earlier stages of Metabolic dysfunction Associated Liver Disease ("MASLD"). It is expected that a reduction of portal pressure would be most beneficial in patients with advanced fibrosis or patients with cirrhosis and could contribute to the prevention of decompensation events. The preclinical study suggests that lanifibranor treatment improves PH in both fibrotic and non-fibrotic models. These results underscore the potential of lanifibranor to prevent PH by addressing both intra-hepatic conditions such as fibrosis and LSEC dysfunction but also extra-hepatic condition such as mesenteric vasculature expansion through its anti-angiogenetic effects. These findings suggest that lanifibranor may hold potential as a therapeutic option for patients with clinically significant PH.

Prof. Sven Francque, M.D., Ph.D., Antwerp University Hospital, said: "The study's results highlight the potential of lanifibranor in addressing the challenging issue of portal hypertension, which is a major driver of decompensation in advanced chronic liver disease such as MASH, but also occurs early in MASLD. The interrelationship between portal hypertension and clinical complications in liver disease is critical but we have few therapeutic options. A treatment protocol addressing portal hypertension may pave a way to better address the complex multimodalities leading to the development of MASH, of fibrosis and of advanced chronic liver disease. We thank our colleagues from Ghent University Hospital for their participation, support and expertise in leading this important study."

Publication details

Publication title:	*"The pan-PPAR agonist lanifibranor reduces portal pressure independent of fibrosis reduction through the splanchnic vasculature."*
Authors:	Anneleen Heldens, Christophe Casteleyn, Louis Onghena, Milton Antwi, Sara Neyt, Benedicte Descamps, Christian Vanhove, Xavier Verhelst, Sarah Raevens, Hans Van Vlierberghe, Lindsey Devisscher, Ruth De Bruyne, Jean-Louis Junien, Guillaume Wettstein, Anja Geerts, Sander Lefere.
Online version:	doi: 10.1016/j.biopha.2025.117826. Online ahead of print. PMID: 39805191.

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 and other diseases with significant unmet medical need. 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.

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). 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, Inventiva's pipeline and preclinical and clinical development plans, the clinical development of and regulatory plans and pathway for lanifibranor, 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, to enter into potential transactions, Inventiva's ability to satisfy in part or full the closing conditions for subsequent tranches of the structured financing announced on October 14, 2024 (the "Structured Financing"), on the expected timing or at all, and whether and to what extent the prefunded warrants issued in connection with the Structured Financing may be exercised and by which holders, 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 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 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 global inflation, fluctuations in 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, 2023 filed with the Autorité des Marchés Financiers on April 3, 2024 as amended on October 14, 2024 and the Annual Report on Form 20-F for the year ended December 31, 2023 filed with the Securities and Exchange Commission (the "SEC") on April 3, 2024 and the Half-Year Report for the six months ended June 30, 2024 on Form 6-K filed with the SEC on October 15, 2024 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.

Please note that this press release does not pertain to conditions precedent relating to the €348 million Structured Financing announced on October 14, 2024. Important information relating to the second tranche of the financing will be the subject of a press release from the Company at the applicable time.