PRESS RELEASE

Inventiva announces the publication in the *Journal of Hepatology* of new pre-clinical data showing the beneficial effects of lanifibranor on cirrhosis

- The underlying studies aimed at characterizing the effects of the pan-PPAR agonist lanifibranor in two pre-clinical models of cirrhosis and in liver cells from cirrhotic patients
- Lanifibranor showed clear beneficial effects leading to a marked improvement of fibrosis, portal hypertension and liver vascular resistance, three key elements of cirrhosis pathophysiology
- Results in hepatic cells from cirrhotic patients further encourage the clinical evaluation of lanifibranor for the treatment of cirrhosis

Daix (France), December 7, 2020 – Inventiva (Euronext Paris and Nasdaq: IVA), a clinical-stage biopharmaceutical company focused on the development of oral small molecule therapies for the treatment of non-alcoholic steatohepatitis (NASH), mucopolysaccharidoses (MPS) and other diseases with significant unmet medical need, today announced the publication of a scientific paper on the beneficial effects of lanifibranor on experimental advanced chronic liver disease (ACLD) by the peer-reviewed scientific journal *Journal of Hepatology*.

The article, entitled "*The pan-PPAR agonist lanifibranor improves portal hypertension and hepatic fibrosis in experimental advanced chronic liver disease"*, discusses the effects of Inventiva's lead drug candidate lanifibranor, a pan-peroxisome proliferator-activated receptor (pan-PPAR) agonist, in two distinct pre-clinical models of cirrhosis and in human liver cells from cirrhotic patients. The objective of the underlying studies was to evaluate the therapeutic potential of lanifibranor for the treatment of advanced cirrhosis.

Cirrhosis originates from a sustained hepatic injury that can vary in nature, with excessive alcohol consumption, unhealthy dietary habits and hepatitis B and C virus infections being the most common causes. As a consequence of long-term liver injury, tissue wound healing mechanisms may become deregulated, leading to hepatic fibrosis, which can ultimately progress to decompensated cirrhosis and, in some cases, hepatocellular carcinoma.[1]

The results of the pre-clinical studies show that lanifibranor improved portal hypertension, fibrosis and liver vascular resistance, three frequent and severe clinical syndromes associated with cirrhosis. The drug candidate also reduced ascites, sinusoidal capillarization, liver sinusoidal endothelial cells (LSEC) and hepatic stellate cells (HSC) activated phenotypes as well as microvascular function and liver inflammation. Furthermore, the results show that all three PPAR isoforms were downregulated in both cirrhotic patients as well as in the pre-clinical models.

Moreover, differential expression of PPAR isoforms was observed in different liver cell types, emphasizing the importance of targeting all three isoforms for the treatment of cirrhosis. Finally, the findings also indicate that lanifibranor improved the phenotypes of isolated hepatocytes and hepatic stellate cells from cirrhotic patients, suggesting that the positive effects observed in both pre-clinical models could be translated to these patients.

[1] Pellicoro A, Ramachandran P, Iredale JP, et al. Liver fibrosis and repair: Immune regulation of wound healing in a solid organ. Nat Rev Immunol 2014;14:181–194.

Pierre Broqua, CSO and cofounder of Inventiva, commented: *"We are very pleased to see our latest pre-clinical results on lanifibranor for the treatment of cirrhosis published in the renowned Journal of Hepatology. This scientific paper clearly illustrates that lanifibranor significantly improves key features of this severe disease, which still lacks a safe and effective treatment. The beneficial effects are based on our lead drug candidate lanifibranor's capacity to target all three PPAR isoforms concomitantly and further encourage its clinical evaluation for the treatment of cirrhosis."*

Dr Jordi Gracia-Sancho, Head of the Liver Vascular Biology Team of IDIBAPS – Hospital Clínic de Barcelona and co-author of the article, added: *"These studies, which combine two pre-clinical models of cirrhosis and human liver cells cultured in advanced in vitro systems, show that the pan-PPAR agonist lanifibranor improves the functionality of the cells that compose the liver microcirculatory system, leading to an improvement in portal hypertension and fibrosis. Considering the lack of treatments for advanced chronic liver disease, and its most deleterious complication portal hypertension, the findings included in this manuscript shed light on the way to develop novel therapies for patients with chronic hepatopathies."*

Publication details

Title of scientific paper:	*"The pan PPAR agonist lanifibranor improves portal hypertension and hepatic fibrosis in experimental advanced chronic liver disease"*
Date of publication:	December 2, 2020
Authors:	Zoe Boyer-Diaz[2], Peio Aristu-Zabalza[3], María Andrés-Rozas[4], Claude Robert[5], Martí Ortega-Ribera[6], Anabel Fernández-Iglesias[7], Pierre Broqua[8], Jean-Louis Junien[9], Guillaume Wettstein[10], Jaime Bosch[11], Jordi Gracia-Sancho[12]
Link to the article:	https://authors.elsevier.com/sd/article/S0168-8278(20)33832-0

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. 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 U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy and Fast Track designation to lanifibranor for the treatment of NASH.

2 Zoe Boyer-Diaz: MSc, Barcelona Liver Bioservices, Barcelona, Spain.
3 Peio Aristu-Zabalza: MSc, Barcelona Liver Bioservices, Barcelona, Spain.
4 María Andrés-Rozas: MSc, Barcelona Liver Bioservices, Barcelona, Spain.
5 Claude Robert: MSc, Inventiva, Daix, France.
6 Martí Ortega-Ribera: MSc, Liver Vascular Biology Research Group, IDIBAPS, Barcelona, Spain.
7 Anabel Fernández-Iglesias: PhD, Liver Vascular Biology Research Group, IDIBAPS, Barcelona, Spain & PhD, CIBEREHD, Madrid, Spain.
8 Pierre Broqua: PhD, Inventiva, Daix, France.
9 Jean-Louis Junien: PhD, Inventiva, Daix, France.
10 Guillaume Wettstein: PhD, Inventiva, Daix, France.
11 Jaime Bosch: MD & PhD, Liver Vascular Biology Research Group, IDIBAPS, Barcelona, Spain, CIBEREHD, Madrid, Spain, Hepatology, Department of Biomedical Research, University of Bern, Bern, Switzerland.
12 Jordi Gracia-Sancho: PhD, Barcelona Liver Bioservices, Barcelona, Spain, Liver Vascular Biology Research Group, IDIBAPS, Barcelona, Spain, CIBEREHD, Madrid, Spain, Hepatology, Department of Biomedical Research, University of Bern, Bern, Switzerland.

About Inventiva

Inventiva is a clinical-stage biopharmaceutical company focused on the development of oral small molecule therapies for the treatment of NASH, MPS and other diseases with significant unmet medical need.

Leveraging its expertise and experience in the domain of compounds targeting nuclear receptors, transcription factors and epigenetic modulation, Inventiva is currently advancing two clinical candidates, as well as a deep pipeline of earlier stage programs.

Lanifibranor, its lead product candidate, is being developed for the treatment of patients with NASH, a common and progressive chronic liver disease for which there are currently no approved therapies. Inventiva recently announced positive topline data from its Phase IIb clinical trial evaluating lanifibranor for the treatment of patients with NASH and obtained Breakthrough Therapy and Fast Track designation for lanifibranor in the treatment of NASH.

Inventiva is also developing odiparcil, a second clinical stage asset, for the treatment of patients with subtypes of MPS, a group of rare genetic disorders. Inventiva announced positive topline data from its Phase IIa clinical trial evaluating odiparcil for the treatment of adult MPS VI patients at the end of 2019 and received FDA Fast Track designation in MPS VI for odiparcil in October 2020.

In parallel, Inventiva is in the process of selecting an oncology development candidate for its Hippo signalling pathway program. Furthermore, the Company has established a strategic collaboration with AbbVie in the area of autoimmune diseases. AbbVie has started the clinical development of ABBV-157, a drug candidate for the treatment of moderate to severe psoriasis resulting from its collaboration with Inventiva. This collaboration enables Inventiva to receive milestone payments upon the achievement of pre-clinical, clinical, regulatory and commercial milestones, in addition to royalties on any approved products resulting from the collaboration.

The Company has a scientific team of approximately 70 people with deep expertise in the fields of biology, medicinal and computational chemistry, pharmacokinetics and pharmacology, as well as in clinical development. It also 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

Contacts

Inventiva
Frédéric Cren
Chairman & CEO
info@inventivapharma.com
+33 3 80 44 75 00

Brunswick Group
Yannick Tetzlaff /
Tristan Roquet Montegon /
Aude Lepreux
Media relations
inventiva@brunswickgroup.com
+33 1 53 96 83 83

Westwicke, an ICR Company
Patricia L. Bank
Investor relations
patti.bank@westwicke.com
+1 415 513-1284

Important Notice

This press release contains forward-looking statements, forecasts and estimates with respect to Inventiva's clinical trials, clinical trial data releases, clinical development plans and anticipated future activities 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" 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, or that candidates will receive the necessary regulatory approvals. 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 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, 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 control, Inventiva's product candidates may cause undesirable side effects 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, 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. 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 filed with the Autorité des Marchés Financiers on June 19, 2020 under n° D.20-0551 and its amendment filed on July 10, 2020 under n° D. 20-0551-A01 as well as the half-year financial report on June 30, 2020 for additional information in relation to such factors, risks and uncertainties.

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.