

# Inventiva announces the publication of a scientific paper on the role of PPARs in the treatment of NASH in the medical journal *Nature Review Gastroenterology & Hepatology*

PPARs are shown to be attractive therapeutic targets for the treatment of NASH, producing beneficial effects on the liver, improving features of the metabolic syndrome and mitigating the risk of related extra-hepatic diseases

**Daix (France), November 2, 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 role of peroxisome proliferator-activated receptors (PPARs) in the treatment of NASH by the peer-reviewed medical journal *Nature Review Gastroenterology & Hepatology*.

Published in coordination with the panNASH<sup>™</sup> initiative, the article, entitled "*Non-alcoholic steatohepatitis: the role of peroxisome proliferator-activated receptors*", discusses the current literature on Non-Alcoholic Fatty Liver Disease (NAFLD), describes the role of PPARs in NASH and related metabolic diseases, and summarizes the preclinical and clinical data on the use of PPAR agonists.

NAFLD is a multisystem disease with extra-hepatic disease implications, including the development of type two diabetes (T2DM) and cardiovascular diseases (CVDs). As the paper highlights, patients with NAFLD tend to present many features of the metabolic syndrome, such as central obesity, atherogenic dyslipidemia, hypertension, abnormal glucose tolerance and insulin resistance, and, in progression of NAFLD towards NASH, develop hepatic inflammation and often fibrosis.

According to the article, PPARs are key regulators of many of the adversely affected mechanistic pathways involved, making them attractive therapeutic targets for the treatment of NASH. Reportedly, PPARs produce beneficial effects on the liver, improve various features of the metabolic syndrome and mitigate the risk of developing related extra-hepatic diseases such as T2DM and CVDs.

The paper also discusses the well-known side effects of PPARs, explaining that those, including excessive body weight gain and fluid retention, can be controlled by the use of biomarkers and recover after stopping the treatment.

**Jean-Louis Junien, Chairman of Inventiva's Scientific Advisory Board, commented:** "This scientific paper clearly illustrates that, although previous studies have shown limited efficacy of individual PPARs, ongoing clinical trials suggest a broader and more efficacious therapeutic potential especially of pan-PPAR agonists to treat the multisystem disease of NASH. This can in particular be attributed to their capacity to target different interrelated mechanisms in the pathophysiology of NASH. As such, lanifibranor, Inventiva's lead drug candidate and only pan-PPAR agonist currently in development for the treatment of NASH, is ideally positioned in this field as evidenced by the recent topline results of the Company's Phase IIb NATIVE clinical trial."



### **Publication details**

Title of scientific paper:	"Non-alcoholic steatohepatitis: the role of peroxisome proliferator-activated receptors"
Date of publication:	October 22, 2020
Authors:	Sven Francque <sup>1</sup> , Gyongyi Szabo <sup>2</sup> , Manal F. Abdelmalek <sup>3</sup> , Christopher D. Byrne <sup>4</sup> , Kenneth Cusi <sup>5</sup> , Jean-François Dufour <sup>6</sup> , Michael Roden <sup>7</sup> , Frank Sacks <sup>8</sup> and Frank Tacke <sup>9</sup>
Link to the article:	https://www.nature.com/articles/s41575-020-00366-5

# About panNASH<sup>™</sup>

The panNASH<sup>™</sup> initiative is a working group consisting of a committee of international independent experts that aims to increase the visibility and contribute to a better understanding of NASH, to share their expertise and to establish best practices for the treatment of the disease.

Established in 2018, the initiative is supported by Inventiva and includes European and American medical experts in areas related to NASH such as hepatology, diabetes and cardiology, along with renowned scientific experts dedicated to promoting a better understanding of the physiopathological mechanisms involved in the disease. Their aim is to play an active role in developing and disseminating their NASH expertise among the scientific community, patients and other key stakeholders within the healthcare system.

In particular, the experts group helps to develop and share new findings about NASH through publications, conferences and training sessions, focusing on the development of the disease, the identification of patients at risk, clinical markers and associated health risks, as well as the development of new treatments. Specifically, the committee contributes to increasing the knowledge of pathological mechanisms ranging from metabolic disorders to fibrosis and comorbidities, with a focus on the modulating role played by PPARs ( $\alpha,\delta,\gamma$  subtypes).

#### 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.

<sup>&</sup>lt;sup>1</sup> Sven Francque: Department of Gastroenterology and Hepatology, Antwerp University Hospital, Antwerp, Belgium.

<sup>&</sup>lt;sup>2</sup> Gyongyi Szabo: Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA.

<sup>&</sup>lt;sup>3</sup> Manal F. Abdelmalek: Division of Gastroenterology and Hepatology, Department of Medicine, Duke University Health System, Durham, NC, USA.

<sup>&</sup>lt;sup>4</sup> Christopher D. Byrne: Nutrition & Metabolism, Human Development & Health, Faculty of Medicine, University Hospital Southampton, Southampton, UK.

<sup>&</sup>lt;sup>5</sup> Kenneth Cusi: Division of Endocrinology, Diabetes and Metabolism, University of Florida, Gainesville, FL, USA.

<sup>&</sup>lt;sup>6</sup> Jean-François Dufour: Hepatology, Department of Clinical Research, University Hospital of Bern, Bern, Switzerland & University Clinic for Visceral Surgery and Medicine, Inselspital, Bern, Switzerland.

<sup>&</sup>lt;sup>7</sup> Michael Roden: Division of Endocrinology and Diabetology, Medical Faculty, Heinrich Heine University Düsseldorf, University Clinics Düsseldorf, Düsseldorf, Germany & Institute for Clinical Diabetology, German Diabetes Center (DDZ), Leibniz Center for Diabetes Research at Heinrich Heine University Düsseldorf, Düsseldorf, Germany.

<sup>&</sup>lt;sup>8</sup> Frank Sacks: Departments of Nutrition and Molecular Metabolism, Harvard T.H. Chan School of Public Health, Boston, MA, USA & Channing Division, Department of Medicine Harvard Medical School and Brigham and Women's Hospital, Boston, MA, USA.

<sup>&</sup>lt;sup>9</sup> Frank Tacke: Department of Hepatology & Gastroenterology, Charité University Medical Center, Berlin, Germany.



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. At the end of 2019, Inventiva published positive results from its Phase IIa clinical trial evaluating odiparcil for the treatment of MPS VI adult patients.

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 (Euronext: 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 <u>inventiva@brunswickgroup.com</u> +33 1 53 96 83 83 Westwicke, an ICR Company Patricia L. Bank Investor relations <u>patti.bank@westwicke.com</u> +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 halfyear 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 forwardlooking statements referred to above. Consequently, Inventiva accepts no liability for any consequences arising from the use of any of the above statements.