

Inventiva announces the decision by the investigator to reduce the number of patients in the ongoing Phase II trial evaluating lanifibranor in type 2 diabetes patients (T2DM) with Non-Alcoholic Fatty Liver Disease (NAFLD)

- ▶ Following higher than expected effects on steatosis reduction during the Phase IIb NATIVE trial in NASH, the number of patients to be recruited in the trial evaluating lanifibranor in patients with T2DM and NAFLD has been reduced to 34 (vs. 64 initially)
- ▶ The Phase II trial results are expected in 2021

Daix (France), July 6, 2020 – Inventiva (Euronext: IVA) ("Inventiva" or the "Company"), a clinical-stage biopharmaceutical company developing 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 decision by the investigator to reduce the number of patients to be enrolled in the investigator-initiated Phase II clinical trial of lanifibranor in patients with TD2M and NAFLD being conducted by Prof. Cusi at the University of Florida.

This trial aims to evaluate the metabolic effects of lanifibranor and its potential efficacy on liver triglycerides in T2DM patients with NAFLD and provide additional clinical data supporting lanifibranor's potential for the treatment of NASH.

Originally, the trial was expected to enroll 64 patients to be treated with a single daily dose of lanifibranor (800 mg/day) or placebo for a 24-week period and 10 subjects in a healthy, non-obese control group. However, given the observed effects of lanifibranor in reducing steatosis during the Phase IIb NATIVE clinical trial evaluating lanifibranor for the treatment of NASH, the investigator Prof. Cusi has decided to reduce the number of patients to be evaluated to 34 patients from 64 originally, while maintaining the same statistical powering in the trial.

At present, this investigator-initiated trial has recruited 23 patients, 15 of which have completed the 24-week period of treatment. Results from this trial are currently expected in 2021. However, due to the COVID-19 pandemic, the recruitment and screening of new patients has been suspended at the University of Florida, where the trial is being conducted, and the results could therefore be delayed.

The table below sets forth data from the Phase IIb NATIVE clinical trial with respect to the pre-specified analysis of changes in CRN steatosis score in the subset of T2DM patients, as compared to the overall population of patients treated in the trial. These data contributed to the investigator's decision to reduce target enrollment in the ongoing investigator-initiated NAFLD trial.

	Intention to Treat Population (ITT)			Per Protocol Population (PP)		
	Placebo	Lanifibranor		Placebo	Lanifibranor	
		800mg	1200mg		800mg	1200mg
Improvement of CRN Steatosis score at week 24 (all patients)	N = 81 26%	N = 83 55% <i>P<0.001*</i>	N = 83 65% <i>P<0.001*</i>	N = 62 34%	N = 63 67% <i>P<0.001*</i>	N = 69 71% <i>P<0.001*</i>
Improvement of CRN Steatosis score at week 24 (patients with T2DM)	N = 35 26%	N = 33 73% <i>P<0.0001*</i>	N = 35 69% <i>P<0.0004*</i>	N = 26 35%	N = 27 81% <i>P<0.0006*</i>	N = 28 75% <i>P<0.0031*</i>

* Statistically significant in accordance to the statistical analysis plan (SAP)

Prof. Ken Cusi, M.D., F.A.C.P., F.A.C.E., Professor of Medicine, Chief, Division of Endocrinology, Diabetes and Metabolism, University of Florida, said: *“The results recently shown by lanifibranor in NASH patients with respect to its ability to reduce steatosis and significantly improve insulin sensitivity and glycemic control are higher than I expected and support lanifibranor’s potential for the treatment of patients with NASH. I now look forward to advancing this trial and developing data to support the hypothesis that lanifibranor can have a significant impact on hepatic triglycerides in patients with type 2 diabetes and NAFLD.”*

Pierre Broqua, CSO and cofounder of Inventiva, stated: *“We are very pleased with this decision following the positive results of lanifibranor during the Phase IIb clinical trial in NASH. Type 2 diabetes patients with NASH are generally exposed to an increased risk of poor clinical outcomes and are therefore in a critical need for an efficacious NASH treatment. We were thus particularly pleased to see significant improvements in CRN steatosis scores in patients with type 2 diabetes in the NATIVE trial and look forward to data from Prof. Cusi’s trial, which could further support lanifibranor’s potential in this population.”*



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 α and PPAR δ , and a partial activation of PPAR γ . 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.

About the study of lanifibranor in type 2 diabetes (T2DM) patients with non-alcoholic fatty liver disease (NAFLD)

The trial being conducted by Prof. Kenneth Cusi, Chief of the Division of Endocrinology, Diabetes & Metabolism in the Department of Medicine at the University of Florida, Gainesville, is expected to enroll 34 patients treated for a 24-week period with a single daily dose of lanifibranor (800 mg/day) or placebo and 10 subjects in a healthy, non-obese control group. The study’s overall objective is to measure the metabolic effects of lanifibranor and its

potential efficacy on liver triglycerides in T2DM patients with NAFLD. The primary endpoint is the change in liver triglycerides as assessed by proton magnetic resonance spectroscopy. Secondary endpoints include changes in liver fibrosis, evidence of metabolic improvements in insulin resistance, de novo lipogenesis, free fatty acids and lipids, as well as safety. Results from this trial are currently expected in 2021. However, due to the COVID-19 pandemic, the recruitment and screening of new patients has been suspended at the University of Florida, where the trial is being conducted, and the results could therefore be delayed.

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.

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. A Phase I/II clinical trial in children with MPS VI is currently under preparation following the release of positive results of the Phase IIa clinical trial in adult MPS VI patients at the end of 2019.

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). www.inventivapharma.com

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Please refer to the Universal Registration Document filed with the Autorité des Marchés Financiers on June 19, 2020 under n° D.20-0551 for additional information in relation to such factors, risks and uncertainties.

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