

Inventiva announces further progress achieved in the clinical development of lanifibranor for the treatment of NASH

- ▶ First patient screened in the United States for the NATIVE trial in NASH
- ▶ 155 patients randomized to date, 70% of the total target
- ▶ Results for the NATIVE trial in NASH expected in the first half of 2020
- ▶ Second DSMB meeting recommends that the trial continue as planned

Daix (France) February 21st, 2019 – Inventiva (Euronext: IVA), a clinical-stage biopharmaceutical company developing oral small molecule therapies for the treatment of diseases in the areas of fibrosis, lysosomal storage disorders and oncology, today announced the screening of the first patient in the United States for its Phase IIb NATIVE (*NASH Trial to Validate IVA337 Efficacy*) clinical trial evaluating lanifibranor, the Company's lead product candidate, for the treatment of non-alcoholic steatohepatitis (NASH), a common and progressive chronic liver disease for which there is currently no approved therapy. Inventiva also announced that the NATIVE Data Safety Monitoring Board (DSMB) held its second meeting and recommended that the trial continue as planned.

The screening of the first patient in the United States follows the positive review by the U.S. Food and Drug Administration (FDA) of the NATIVE trial protocol and the inclusion of 14 sites in the United States in the trial, which brought the total number of sites involved to 91. Out of 225 patients expected to be enrolled in the trial, 155 patients have been randomized, and 71 patients have already completed the six-months treatment. The NATIVE trial continues to progress as planned and results are anticipated in the first half of 2020.

Pr Sven Francque, M.D., Ph.D. from the Antwerp University Hospital and Co-Principal Investigator, said: *"The news of the first patient screened in the U.S. and the opening of 14 sites represents great progress. We expect to open 5 additional sites in Europe to further accelerate patient recruitment. Given the study design and lanifibranor's mechanism of action, we believe that the results of the NATIVE trial, if positive, will support lanifibranor's move into the pivotal Phase III trial."*

Pr Manal Abdelmalek, M.D., M.P.H. from Duke University, who agreed to act as Co-Principal Investigator with Pr Sven Francque, stated: *"I am very pleased to be a part of this important trial and am excited by the profile of lanifibranor, a drug that is designed to act on many features of NASH by combining anti-fibrotic and anti-inflammatory activities with metabolic benefits, including improvement of insulin sensitivity."*

"The NATIVE trial is rolling out in the United States as planned and we are excited to add U.S. sites to the study, making NATIVE a truly international trial. We are thrilled to welcome Pr Abdelmalek, a renowned hepatologist, to the Steering Committee of the NATIVE trial and we look forward to finalizing recruitment over the coming months," added Inventiva's Chief Medical Officer, Marie-Paule Richard, M.D.

In addition, the NATIVE DSMB has reviewed the available safety data from the trial and recommended, for the second time, that the trial continue without modification to the protocol. The positive outcome of this second DSMB review is consistent with the results of long-term toxicological studies, as well as of Phase I and Phase II clinical trials, which have shown that lanifibranor is associated with a favorable safety profile.

About lanifibranor

Lanifibranor, Inventiva's lead product candidate, is an orally-available small molecule that acts to induce anti-fibrotic, anti-inflammatory and beneficial 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, 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 safety and tolerability profile that has been observed in clinical trials and pre-clinical studies to date.

About the NATIVE Phase IIb trial

The NATIVE (NASH Trial to Validate IVA337 Efficacy) clinical trial is a 24-week treatment, randomized, double-blind, placebo-controlled Phase IIb clinical trial evaluating lanifibranor in the treatment of patients with non-alcoholic steatohepatitis ("NASH"). The goal of the trial is to assess the effect of lanifibranor on the improvement in liver inflammation and ballooning, which are two of the markers of the resolution of NASH. To be considered for inclusion, patients must have: a diagnosis of NASH confirmed by liver biopsy; a cumulative score of inflammation and ballooning (as measured using the steatosis, activity and fibrosis, or "SAF", scoring system) of three or four out of four, indicating the presence of moderate to severe inflammation and ballooning; a steatosis score greater than or equal to one, indicating the presence of moderate to severe steatosis; and a fibrosis score less than four, indicating the absence of cirrhosis. The primary endpoint of the trial is a reduction in the combined inflammation and ballooning score of two points compared to baseline, without worsening fibrosis. Secondary endpoints include NASH resolution, improvements in each of the steatosis, inflammation, ballooning and fibrosis scores from baseline as measured using the SAF score, improvements in various other fibrosis measures, improvements in several metabolic markers, improvements in steatosis, inflammation and ballooning as measured using the "NAS" score, and safety.

The trial is expected to enrol 225 patients with NASH at more than 90 sites in Europe, the United States, Canada, Australia and Mauritius. Results of the trial are expected in the first half of 2020.

About Inventiva

Inventiva is a clinical-stage biopharmaceutical company focused on the development of oral small molecule therapies for the treatment of diseases with significant unmet medical needs in the areas of fibrosis, lysosomal storage disorders and oncology.

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 – lanifibranor and odiparil in non-alcoholic steatohepatitis ("NASH") and mucopolysaccharidosis ("MPS"), respectively, 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. Inventiva is currently evaluating lanifibranor in a Phase IIb clinical trial for the treatment of this disease for which there are currently no approved therapies.

Inventiva is also developing odiparil, a second clinical-stage asset, for the treatment of patients with MPS, a group of rare genetic disorders. The Company is currently investigating odiparil in a Phase IIa clinical trial for the treatment of adult patients with the MPS VI subtype.

In parallel, Inventiva is in the process of selecting an oncology development candidate for its Hippo signaling pathway program and is advancing pre-clinical programs for the treatment of autoimmune diseases and idiopathic pulmonary fibrosis (“IPF”) in collaboration with AbbVie and Boehringer Ingelheim International respectively. AbbVie is investigating ABBV-157, a clinical development candidate resulting from its collaboration with Inventiva, in a Phase I clinical trial for the treatment of moderate to severe psoriasis. Both collaborations entitle 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 partnerships.

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. It also owns an extensive library of approximately 240,000 pharmacologically relevant molecules, 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 “Document de référence” filed with the Autorité des Marchés Financiers on April 13, 2018 under n° R.18-013 for additional information in relation to such factors, risks and uncertainties.

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