PRESS RELEASE

Inventiva announces design of Phase III clinical trial with lanifibranor in NASH

- A single global Phase III clinical trial evaluating two doses of lanifibranor (800mg and 1200mg once daily) versus placebo is intended to support U.S. New Drug Application (NDA) / EU marketing authorization
- Seeking of U.S. accelerated approval and EU conditional approval for lanifibranor to be based on 72-week histology analysis in approximately 900 patients
- Use of primary composite endpoint combining NASH resolution and fibrosis improvement
- Inventiva confirms planned initiation of pivotal Phase III clinical trial in H1 2021

Daix (France), January 5, 2021 – 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 details of the Phase III clinical trial with its lead drug candidate lanifibranor in NASH following the end-of-phase II meeting with the U.S. Food and Drug Administration (FDA) and the receipt of the Scientific Advice letter from the European Medicines Agency (EMA). The Phase III trial design and clinical strategy have been discussed with both regulatory authorities and the following key points can be confirmed:

- **Seeking of U.S. accelerated approval and EU conditional approval for lanifibranor to be based on a 72-week histology analysis** – Inventiva will seek to obtain accelerated approval in the U.S. and conditional approval in the EU for lanifibranor based on a pre-specified histology analysis in approximately 900 patients after 72 weeks establishing a positive benefit-risk ratio.

- **Use of a primary composite endpoint combining NASH resolution and fibrosis improvement** – The primary composite endpoint of patients having both NASH resolution and fibrosis improvement of at least one stage will be used for the 72-week histology analysis. The endpoint is designed to predict a significant improvement of prognostic risk and, if met, may support a label for the treatment of NASH and the improvement in liver fibrosis in adult non-cirrhotic NASH patients. During Inventiva's NATIVE Phase IIb clinical trial, this endpoint was met with statistical significance, including in NASH patients with F2/F3 fibrosis, the patient population that will be included in the Phase III trial, as well as in NASH patients with type two diabetes (TD2M). Endpoints of NASH resolution and no worsening of fibrosis, and improvement of fibrosis with no worsening of NASH will be included as key secondary endpoints. Additional supportive histologic endpoints, non-invasive markers of liver fibrosis and steatohepatitis as well as effects on lipids and insulin resistance will also be evaluated.

Results from the NATIVE Phase IIb trial: ITT (intention-to-treat) population	**Placebo (N = 81)**	**800mg (N = 83)**	**1200mg (N = 83)**
Patients with both resolution of NASH and improvement of fibrosis [(1)]	7%	21% *P=0.017**	31% *P<0.001**
Results from the NATIVE Phase IIb trial: ITT population and patients with F2/F3 fibrosis	**Placebo (N = 57)**	**800mg (N = 68)**	**1200mg (N = 63)**
Patients with both resolution of NASH and improvement of fibrosis [(1)]	7%	24% *P = 0.012**	33% *P < 0.001**
Results from the NATIVE Phase IIb trial: ITT population and patients with TD2M	**Placebo (N = 35)**	**800mg (N = 33)**	**1200mg (N = 35)**
Patients with both resolution of NASH and improvement of fibrosis [(1)]	3%	24% *P = 0.012***	29% *P = 0.003****

** Two-sided p-values were calculated using Cochran Mantel Haenszel test, stratified on T2DM status*
*** Two-sided p-value from Fisher exact test*
**** Two-sided p-value from Chi-square test*

- **Adequacy of long-term use to be established after 72 weeks** – The duration of 72 weeks was considered adequate by both the FDA and EMA to establish long-term use as well as dose and cumulative drug exposure. With this trial, the proposed size of the safety database required for marketing application would be consistent with regulatory guidelines**.**

Named NATIVE3 (NASH lanifibranor Phase 3 trial), the planned trial has been designed as a double-blind, placebo-controlled global pivotal Phase III clinical trial to assess the potential benefit of lanifibranor treatment on liver-related clinical outcomes. Patients will be randomized 1:1:1 to receive lanifibranor (800mg once daily or 1200mg once daily) or placebo.

The trial will remain blinded after the pre-specified histological analysis and continue in a total of approximately 2,000 patients until the occurrence of a pre-specified number of adverse liver-related clinical events, including progression to cirrhosis. The trial would be completed on a post-marketing basis in the event that accelerated (U.S.) / conditional (EU) approval is received. Statistical powering of 90% was considered for the sample size calculations of the Phase III clinical trial.

The trial preparations are progressing according to schedule and Inventiva plans to initiate the trial in the first half of 2021.

Pierre Broqua, Chief Scientific Officer and cofounder of Inventiva, commented: *"We are very pleased to communicate today the design of our single pivotal Phase III trial evaluating lanifibranor in NASH with the perspective of seeking accelerated (U.S.) and conditional (EU) approvals in case of positive intermediary trial results. The primary endpoint, if met, would position lanifibranor as a drug that induces both NASH resolution and fibrosis improvement, which we believe would support its potential commercial success. Additional supportive efficacy analyses on lipids and insulin resistance are planned in order to further demonstrate the effect of lanifibranor in NASH patients. The preparation of this pivotal Phase III trial is well on track and we are looking forward to its initiation in the first half of 2021, as previously announced."*

(1) *Resolution of NASH and improvement of fibrosis at week 24: CRN-Inflammation = 0 or 1, CRN-Ballooning = 0 and an improvement of CRN-Fibrosis ≥ 1 stage compared to baseline. Patients with missing data were handled as non-responders.*

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. In addition to Fast Track designation, the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy to lanifibranor for the treatment of NASH based on Phase IIb data.

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

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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.