

Inventiva Announces Results From Phase IIb Clinical Trial with Lanifibranor in Systemic Sclerosis

- ▶ Primary endpoint of the trial was not met, no statistically significant difference between the placebo and lanifibranor treated groups for the primary outcome
- ▶ Favorable safety profile of lanifibranor observed
- ▶ Decision to discontinue further developments in the treatment of Systemic Sclerosis ("SSc")
- ▶ Unchanged focus on lanifibranor's development for the treatment of NASH along with Inventiva's pipeline of product candidates
- ▶ Trial results to be presented during 2018 full-year results conference call and webcast on February 27, 2019

Daix (France), February 18, 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 results from the FASST (*For A Systemic Sclerosis Treatment*) clinical trial evaluating lanifibranor for the treatment of patients with diffuse cutaneous systemic sclerosis ("dcSSc"), a rare, progressive autoimmune, rheumatic disease with frequent serious adverse events and high unmet medical need.

The FASST clinical trial, a one-year, double-blind, randomized, placebo-controlled Phase IIb study, included 145 patients suffering from the early phase of dcSSc, who received lanifibranor in either two doses of 400mg per day or two doses of 600mg per day over 48 weeks in addition to their existing standard of care, which in most cases included immunosuppressive therapy.

The FASST clinical trial did not meet its primary endpoint of a mean absolute change from baseline to week 48, relative to placebo, in the modified Rodnan Skin Score ("mRSS"), which assesses skin thickness across 17 defined points on the body on a scale of zero, indicating normal skin, to three, indicating severe thickness. There was a decrease in the average mRSS observed in active and placebo arms with only four patients reporting to have increases in mRSS scores over the course of the trial.

	800mg lanifibranor	1200mg lanifibranor	Placebo
Number of patients	49	48	48
Mean baseline mRSS (SD ¹)	18.2 (3.8)	17.8 (3.9)	17.1 (-3.7)
Mean absolute change of mRSS from baseline to week 48 (SD ³)	-3.7 (4.2)	-4.3 (5.0)	-4.9 (4.6)

¹ Standard Deviation

While the trial did not meet any of the secondary endpoints, lanifibranor showed a favorable trend in patients' global assessment of disease activity with a mean absolute change in visual analog scale¹ ($p=0.08$) from baseline versus placebo indicating a perceived benefit by patients.

Within this fragile and poly-medicated population, lanifibranor was observed to be associated with a favorable safety profile, with no adverse interactions with immunosuppressive background therapies observed. The proportion of patients with at least one adverse event was similar across the three patient groups.

As reported in established literature, patients in the early phase of SSc population have an increased susceptibility to edema.² In the FASST clinical trial, fluid retention was observed related to lanifibranor but was only judged severe in one patient in each dose group, and a single serious adverse event of peripheral edema was observed at the highest lanifibranor dose. Furthermore, no cardiac or renal safety concerns were observed in the trial.

Yannick Allanore, co-principal investigator of the FASST clinical trial and professor of rheumatology at the Hôpital Cochin in Paris, commented: *"The FASST clinical trial was well-conducted and represents the first study in dcSSc with a stratified background on immunosuppressive therapy. It appears that the presence of background therapy produced a strong placebo effect and limited the number of patients progressing in dcSSc."*

Professor Christopher Denton, co-principal investigator of the FASST clinical trial and professor at the University College of London, added: *"We regret the study results but we are satisfied both by lanifibranor patients' well-being, expressed in their global assessment, and lanifibranor's favorable safety profile observed in the trial, including in combination with immunosuppressive drugs."*

Based on the FASST clinical trial results, Inventiva plans to discontinue lanifibranor's clinical development for the treatment of dcSSc in order to fully focus on the development of lanifibranor for the treatment of NASH, of odiparcil for the treatment of mucopolysaccharidoses (MPS), and of YAP-TEAD in the field of oncology.

Frédéric Cren, Chairman and CEO of Inventiva, said: *"We are disappointed by the results of the FASST clinical trial in dcSSc, a challenging disease as evidenced by the recent failure of three other late-stage trials. While we have decided to discontinue the lanifibranor program in SSc, we are very grateful for the dedication and commitment of patients, caregivers, investigators and our team to this program. We remain confident in lanifibranor's unique mechanism of action and will therefore continue to move forward, as planned, with its clinical development in the treatment of NASH. Beyond lanifibranor, we have a promising and diversified development pipeline, backed by a strong discovery engine, notably with odiparcil for the treatment of mucopolysaccharidoses, and look forward to the upcoming clinical milestones."*

Results presentation

Inventiva's management team will present the trial results in the context of the Company's 2018 full-year results which will be published on Wednesday February 27, 2018 at 5:45 pm (Paris time).

On that occasion, the Company will host a conference call in English at 6:15 pm (Paris time). The conference call will be simultaneously webcast and accessible on Inventiva's website in the "Investors" – "Financial Results & Presentations" section. A replay of the conference call and webcast will also be available following the event.

More details on the conference call and webcast will be provided in the Company's 2018 full-year results' press release.

About the FASST Phase IIb trial

¹ The visual analog scale (VAS) corresponds to a global assessment of wellbeing by patients in the last month of treatment.

² Cosimo Bruni, Tracy Frech, et al. "Vascular Leaking, a Pivotal and Early Pathogenetic Event in Systemic Sclerosis: Should the Door be Closed?", *Frontiers in Immunology*, 2018, (9): 1-9.

The FASST (For A Systemic Sclerosis Treatment) clinical trial was a one-year randomized, double-blind, placebo-controlled Phase IIb clinical trial evaluating lanifibranor in the treatment of patients with diffuse cutaneous systemic sclerosis (“dcSSc”), which affects approximately 35% of patients with systemic sclerosis (“SSc”). The primary endpoint of the trial was a mean absolute change from baseline to week 48 in the modified Rodnan Skin Score (“mRSS”), which assesses skin thickness across 17 defined points on the body on a scale of zero, indicating normal skin, to three, indicating severe thickness. The mRSS is a clinically validated and FDA-accepted endpoint measuring the evolution of skin fibrosis, which is known to be correlated with internal organ fibrosis. In addition, secondary endpoints for the trial included changes in forced vital capacity (“FVC”), which is an FDA-accepted endpoint measuring pulmonary function, overall progression of the disease (assessed as the absence of rescue therapy and of severe organ involvement, such as kidney failure), changes in gastrointestinal health, and safety.

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 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 safety and tolerability profile that has been observed in clinical trials and pre-clinical studies to date.

Inventiva is currently evaluating lanifibranor in a Phase IIb clinical trial for the treatment of non-alcoholic steatohepatitis (“NASH”), a common and progressive chronic liver disease, for which there is currently no approved therapy.

About Systemic Sclerosis

SSc is a rare, progressive and debilitating chronic autoimmune rheumatic disease that is characterized by microvascular damage, dysregulation of the immune system and generalized fibrosis in multiple organs. As such, SSc affects the skin, lungs, heart, gastrointestinal tract and kidneys, with the impairments of the internal organs the most disabling and life-threatening manifestations of the disease.

It causes patients to suffer from major disability, significantly impaired quality of life and shorter life expectancy, primarily due to organ failure. SSc is potentially fatal, with the cause typically being cardio-respiratory failure. SSc patients have a greater mortality rate than patients with any other rheumatic disease. The prevalence of SSc is estimated to be 154 people per million in each of the United States and Europe and women are five times more likely than men to develop the disease.

As of today, there are no approved treatments for SSc.

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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 Inc. and Boehringer Ingelheim International GmbH 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

Important Notice

This press release contains forward-looking statements, forecasts and estimates with respect to the clinical development plans, business and regulatory strategy, and anticipated future performance of Inventiva and of the market in which it operates. 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 candidates will receive the necessary regulatory approvals or that they will prove to be commercially successful. Therefore, 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. Given these 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 "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.

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.