Press release

IVA337 delivers significant therapeutic advances in fibrosis, a major public health challenge

- **Enrolment of the first systemic sclerosis patients in the Phase IIb trial of IVA337, one of Inventiva's lead products**
- **Preparation of a new Phase IIb study in the treatment of NASH[1]**

Daix (France), January 28, 2016 - Inventiva, a biopharmaceutical company specialized in nuclear receptors, transcription factors and epigenetics for the development of innovative therapies for fibrosis, oncology and rare diseases, is announcing today the enrolment of the first patients in its international Phase IIb FASST[2] trial of IVA337, its lead anti-fibrotic therapy, in the treatment of systemic sclerosis.

Systemic sclerosis is a severe auto-immune disease, which can prove fatal in many cases. It is characterized by significant progressive fibrosis of the skin and several vital organs such as the lungs, kidneys, digestive tract and heart, leading to their failure. It affects close to 170,000 patients around the world and represents a market estimated to be worth over €1 billion in the United States[3], with no effective treatment currently available.

IVA337, a highly promising drug candidate for the treatment of fibrotic diseases

Fibrotic diseases, which are responsible every year for close to 45% of deaths worldwide[4], pose a major public health challenge.

A distinguishing feature of IVA337 is that it activates a specific class of nuclear receptors – the PPARs (Peroxisome Proliferator Activated Receptors) – that are involved in the fibrotic process. IVA337 is a new-generation PanPPAR, which has demonstrated anti-fibrotic properties in several tissues alongside good clinical tolerance. Its unique mechanism of action goes through the activation of all three alpha, gamma and delta PPARs to slow, halt or reverse the progression of fibrosis.

The anti-fibrotic effects of IVA337 on the skin, lungs, kidneys and liver open up a pathway for the treatment of numerous fibrotic diseases. Inventiva therefore decided to pursue the development of IVA337 in the treatment of two fibrotic diseases with very high unmet medical needs: NASH and Systemic Sclerosis. NASH, is a severe liver fibrotic condition that may cause cirrhosis or even cancer and which affects over 30 million people in the United States[5]. Systemic sclerosis is an orphan disease with no available treatment to date, for which Inventiva has already obtained orphan drug status in Europe and the United States.

[1] Non-Alcoholic Steato-Hepatitis
[2] FASST: For A Systemic Sclerosis Treatment
[3] Corbus Investor Presentation; Cytori Therapeutics Investor Presentation
[4] The Journal of Clinical Investigation; Common and unique mechanisms regulate fibrosis in various fibroproliferative diseases; March 2007
[5] Angulo et al. Hepatology 1999; 30(6):1356-62. ; Minervini et al. J Hepatology 2009; 50:501–510.

Encouraging results obtained for the treatment of systemic sclerosis, a complex and severe disease with no known effective treatment

After successfully completing its Phase I and Phase IIa trials, Inventiva is advancing with the development of its anti-fibrotic lead drug candidate by launching the Phase IIb FASST trial for the treatment of systemic sclerosis.

Enrolments for this randomised, double-blind year-long trial have begun. It will include a total of 135 patients in 8 European countries, who will be given a placebo or one of the two doses of IVA337 being tested. The study protocol, which was endorsed by the European Medicines Agency, aims to demonstrate the positive impact of IVA337 on disease progression in patients who have contracted the most severe form of systemic sclerosis.

"To date, no drug has demonstrated an ability to either slow down or reduce fibrosis in the course of systemic sclerosis. Various therapeutic trials have failed. These results show the increasing need for a whole new generation of drugs. IVA337 developed by Inventiva is a moderate and balanced activator of the alpha, gamma and delta PPARs and has demonstrated very good tolerance and highly attractive anti-fibrotic properties in preliminary trials. These results and this original mechanism of action led to set-up Phase IIb trials and allow patients to carry on with their ongoing treatment, including immunosuppressive therapies. This should facilitate recruitment for the FASST trial", comments Yannick Allanore, Professor of Rheumatology at Hôpital Cochin in Paris and coordinator of the FASST study.

"With more than 50 hospitals taking part in the trial in 8 countries, the FASST study is to date one of the largest initiatives launched to develop an anti-fibrotic therapeutic strategy for systemic sclerosis. This trial was designed to establish IVA337 as the cornerstone treatment for systemic sclerosis patients", adds Pierre Broqua, CSO and co-founder of Inventiva.

"*The positive results generated during the pre-clinical and clinical studies with IVA337 represent a key step in the design of a new high-potential therapeutic approach against fibrosis*" concludes Frédéric Cren, Inventiva's CEO and co-founder. *"Thanks to the unique anti-fibrotic properties of our drug candidate IVA337, we aim to bring to market a curative treatment for systemic sclerosis and NASH, a disease for which another Phase IIb trial with IVA337 is due to be launched this year.*"

About systemic sclerosis:

Systemic sclerosis is a rare and complex disease affecting the auto-immune system, the microvascular system and conjunctive tissues. This fibrotic disease mainly affects the skin, but also the lungs, the heart, the gastro-intestinal tract and the kidneys. Due to the progressive failure of different organs, systemic sclerosis is a severe disease with a high mortality rate. Once patients are diagnosed with systemic sclerosis, generally between the ages of 40 and 50, the median survival period is of 11 years. Close to 170,000 people suffer from systemic sclerosis, with women outnumbering men by a ratio of more than five to one[6].

The disease owes its original name of scleroderma, which derives from the Greek words skleros (hard) and derma (skin), to the skin condition it provokes. The disease causes severe physical and psycho-social consequences that may be deadly for patients whose vital organs are affected. The extension of this skin fibrosis has led to the classification of two sub-categories, respectively called limited systemic sclerosis and diffuse systemic sclerosis. The latter is more serious and is targeted in the FASST trial.

To date, only symptomatic drugs with limited therapeutic effects are available in order to attenuate the consequences of fibrosis progression. However, they do not prevent, delay nor reverse the disease's devastating process.

About Inventiva: www.inventivapharma.com

Inventiva is a biopharmaceutical company specialized in the development of drugs interacting with nuclear receptors, transcription factors and epigenetic modulation. Inventiva opens up novel breakthrough therapies against fibrotic diseases, cancers and orphan diseases with substantial unmet medical needs.

[6] Journal of Rheumatology, 2013

IVA337, its lead product, is an anti-fibrotic treatment with a unique mechanism of action going through the activation of all three alpha, gamma and delta PPARs (peroxisome proliferator-activated receptors), which play key roles in controlling the fibrotic process. Its anti-fibrotic action targets two indications with substantial unmet medical needs: NASH, a severe and increasingly prevalent liver disease already affecting over 30 million people[7] in the United States, and systemic sclerosis, a disease with a very high mortality rate and for which there is no approved treatment to date.

Inventiva is also developing IVA336, a clinical program for the treatment of three different forms of mucopolysaccharidosis (MPS I or Hurler-Sheie syndrome, MPS II or Sly syndrome and MPS VI also known as Maroteaux-Lamy syndrome), as well as an oncology portfolio. Inventiva benefits from partnerships with world-leading research entities such as the Institut Curie. A strategic partnership has also been put in place with AbbVie, providing Inventiva with eligibility to preclinical, clinical, regulatory and commercial milestone payments and royalties on the products resulting from the partnership.

Inventiva employs over 100 highly qualified scientists and owns state-of-the-art R&D facilities, acquired from the international pharmaceutical group Abbott, comprising, near Dijon, a library of over 240,000 molecules as well as biology, chemistry and pharmacology platforms.

For further information: www.inventivapharma.com

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[7] Angulo et al. Hepatology 1999; 30(6):1356-62. ; Minervini et al. J Hepatology 2009;50:501–510.