

## Lanifibranor carcinogenicity studies: Progressing as planned and interim results in rats indicate no compound related urinary bladder tumors

- ▶ 104-week in-life period completed
- ▶ Rat preliminary results indicate no compound related neoplastic effect in the urinary bladder
- ▶ Mice carcinogenicity study analysis ongoing
- ▶ Final peer-reviewed results expected for both species by end of Q2 2018

**Daix (France), March 28, 2018** – Inventiva, a biopharmaceutical company developing innovative therapies in nonalcoholic steatohepatitis (NASH), systemic sclerosis (SSc), and mucopolysaccharidosis (MPS), today reported preliminary results of the two-year carcinogenicity studies with the pan-PPAR agonist lanifibranor in rats. Two carcinogenicity studies in rats and in mice were started in October 2015 after study protocol approval by the US Food and Drug Administration (FDA) and executed by Envigo (UK), a Contract Research Organization (CRO) with previous expertise in running similar studies, particularly with compounds from the PPAR class. These studies tested the effects of three doses of lanifibranor administered daily for a 104-week period, compared to control groups. This first in-life phase was conducted as planned and histopathology evaluation of the two studies is nearly completed. The peer-review phase of the two studies in rats and mice is expected to be finalized by the end of the second quarter 2018.

The peer-review is ongoing and preliminary results of the study in rats are already available, indicating that there are no compound-related incidences of neoplastic lesions, and in particular no increased incidence of urinary bladder cancer, a finding that was reported for several single or dual PPAR compounds. Lanifibranor's moderate and balanced panPPAR profile and different chemical structure could explain the benign profile of the compound.

Doctor J. Armstrong, senior pathologist in charge of the peer-review, commented: *"The peer-review is ongoing and preliminary results of the study in rats from the incident tables indicate a very benign safety profile of lanifibranor. I am particularly pleased that no primary urinary bladder neoplasms were diagnosed in the treated rats, a finding that was reported for several other PPAR compounds."*

Pierre Broqua, Chief Scientific Officer and a co-founder of Inventiva, added: *"These preliminary results in rats are in line with the good safety profile of the moderately potent and well-balanced pan-PPAR agonist lanifibranor, demonstrated in long-term toxicological studies as well as in clinical Phase I and Phase II studies. Since bladder tumors have been associated with several different PPAR compounds, the carcinogenicity studies of lanifibranor are a critical part of the overall development package. While the study is not yet completed for both species, we are encouraged by the clean lanifibranor profile in the rat study, where there were no signs of increased bladder tumor incidence in any of the lanifibranor dose groups. We look forward to reviewing the full results from both species within the coming months."*

These two carcinogenicity studies are being carried out as part of the lanifibranor development plan and are a regulatory requirement for lanifibranor commercialization.

**About lanifibranor:**

Lanifibranor is a next generation pan-PPAR modulator designed as a moderately potent and well-balanced PPAR  $\alpha$ ,  $\delta$  and  $\gamma$ . This unique profile was conceived in order to obtain an optimal therapeutic margin with strong efficacy and tolerance. Lanifibranor displayed an antifibrotic efficacy superior to selective PPAR- $\alpha$ , PPAR- $\delta$  or PPAR- $\gamma$  agonists in several relevant preclinical models. Inventiva is conducting two Phase IIb clinical studies in NASH and SSc with lanifibranor.

**About Inventiva:** <http://www.inventivapharma.com>

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

Lanifibranor, its lead product, is an anti-fibrotic treatment with a strong action mechanism permitting 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 initial indications with substantial unmet medical need: NASH, a severe and increasingly prevalent liver disease already affecting over 30 million people 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 developing in parallel, a second clinical product, odiparcil (formerly IVA336), a treatment for several forms of mucopolysaccharidosis where dermatan and/or chondroitin sulfates GAGs accumulate: MPS I or Hurler/Scheie syndromes, MPS II or Hunter syndrome, MPS IVa or Morquio syndrome, MPS VI or Maroteaux-Lamy syndrome and MPS VII or Sly syndrome. Inventiva is also developing a preclinical stage oncology portfolio.

Inventiva benefits from partnerships with world-leading research entities such as the Institut Curie. Two strategic R&D partnerships have also been established with AbbVie and Boehringer Ingelheim, making Inventiva eligible for preclinical, clinical, regulatory and commercial milestone payments, in addition to royalties on the products resulting from the partnerships.

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

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*Please refer to the "Document de référence" filed with the Autorité des Marchés Financiers on April 26, 2017 under n° R.17-025 for additional information in relation to such factors, risks and uncertainties.*

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