PRESS RELEASE

Inventiva's paper on the discovery and synthesis of its panPPAR agonist lanifibranor accepted and published in the *Journal of Medicinal Chemistry* of the American Chemical Society

Lanifibranor is in Phase IIb development for non-alcoholic steatohepatitis (NASH) and systemic sclerosis (SSc)

Daix (France) March 13, 2018 – Inventiva, a biopharmaceutical company developing innovative therapies in nonalcoholic steatohepatitis (NASH), systemic sclerosis (SSc) and mucopolysaccharidosis (MPS), today announced the publication of an article online, ahead of print, describing the discovery of its promising panPPAR agonist, lanifibranor, in the *Journal of Medicinal Chemistry* of the American Chemical Society. The *Journal of Medicinal Chemistry* is one of the most important journals in medicinal chemistry.

Pierre Broqua, Chief Scientific Officer and Inventiva's co-founder, said: *"We're delighted to have our paper published by the prestigious Journal of Medicinal Chemistry. Of particular interest is the data showing how lanifibranor has a specific binding into the PPARγ pocket, a further explanation to the excellent safety profile demonstrated so far by lanifibranor, our lead clinical candidate currently in Phase IIb trials in NASH and SSc."*

Background

Peroxisome proliferator-activated receptors (PPARs) play a key role in controlling the fibrotic process. Inventiva's lead program lanifibranor is an anti-fibrotic treatment with a powerful mechanism of action that activates all three alpha, gamma and delta PPARs. Currently two lanifibranor Phase IIb trials are ongoing in NASH and SSc. Inventiva has been granted orphan drug designation for lanifibranor in the treatment of SSc by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA).

***Journal of Medicinal Chemistry* publication**

The study now published in the *Journal of Medicinal Chemistry* sets out in detail how Inventiva's research team discovered lanifibranor, and what they believe are the benefits of this novel compound.

Starting from a high-throughput screening hit, an extensive medicinal chemistry optimization campaign led to the discovery of lanifibranor. Xray co-crystal structure of lanifibranor bound to PPARγ displayed a new atypical binding mode in comparison to rosiglitazone. The compound's head to tail positioning stabilizes a conformationally active form of PPARγ without interacting directly with Helix H12. The authors believe that lanifibranor's non-classical binding mode, its different coregulator recruitment profile and its balanced activity for the three PPAR isoforms may well explain its good safety profile relative to other PPAR agonists.

Furthermore, lanifibranor demonstrated excellent anti-hyperglycemic and hypolipidemic efficacy in a relevant mouse model, and a significant anti-fibrotic activity in a mouse model for liver fibrosis. Compared to other PPARγ agonists, lanifibranor had no effect on hematocrit, plasma volume or heart weight in rats. These encouraging results provide ample rationale for the further development of lanifibranor in NASH.

Link to publication & reference:

Design, synthesis and evaluation of a novel series of indole sulfonamide Peroxisome Proliferator Activated Receptors (PPAR)α/δ/γ triple activators: discovery of lanifibranor a new anti-fibrotic clinical candidate

https://pubs.acs.org/doi/10.1021/acs.jmedchem.7b01285

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About Inventiva: 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 also developing in parallel, a second clinical product, odiparcil (formerly IVA336), a treatment for several forms of mucopolysaccharidosis where dermatan and/or chondroïtin 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, ADME and pharmacology platforms.

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Please refer to the "Document de reference" 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.

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.