

## Inventiva Announces Peer Review Publication of IVA337 Data in Pre-Clinical NASH Models

### Data support therapeutic potential of IVA337 for the treatment of patients with NASH

**Daix (France), June 20, 2017 – 6:00pm CEST** – Inventiva, a biopharmaceutical company developing innovative therapies, particularly to treat fibrosis, today announced the peer review publication of data on the effects of its lead drug candidate IVA337, a pan-PPAR agonist currently in phase IIb clinical development in Non-Alcoholic Steatohepatitis (NASH), in various preclinical models of NASH. The paper [\*The New-Generation Pan-Peroxisome Proliferator-Activated Receptor Agonist IVA337 Protects the Liver From Metabolic Disorders and Fibrosis\*](#) is published in the June 19<sup>th</sup>, 2017 edition of *Hepatology Communications*. *Hepatology Communications* is a peer-reviewed, online-only open access journal for fast dissemination of high quality basic, translational, and clinical research in hepatology supported by Wiley's network of prestigious journals and societies.

The authors of the paper include several leading experts on NASH, including Professor Isabelle Leclerc from the University of Leuven (Belgium), Professor Derek Mann from the University of Newcastle (United Kingdom), Professor Sven Francque from the University Hospital of Antwerp (Belgium), as well as company scientists.

*"We are pleased to announce this peer review publication of our IVA337 data. These studies demonstrate that the molecule improves metabolic parameters and NASH histopathologic features, such as steatosis, ballooning, inflammation, and fibrosis, in several relevant animal models,"* said Pierre Broqua, Ph.D., Chief Scientific Officer and Co-Founder of Inventiva. *"Based on these results, together with a good safety profile differing from previously developed PPAR agonists, we believe that IVA337 is a promising candidate for NASH treatment. We are currently enrolling patients in a Phase IIb trial in NASH."*

#### Summary of Key Findings from Preclinical NASH Studies:

The effects of IVA337 on several preclinical models reproducing the main metabolic and hepatic features associated with NASH were investigated. These models comprised a diet-induced obesity model (high-fat/high-sucrose diet); a methionine- and choline-deficient diet (MCD model); the foz/foz model; the CCl<sub>4</sub>-induced liver fibrosis model (prophylactic and therapeutic) and human primary hepatic stellate cells.

In the two latter models, IVA337 displayed an antifibrotic efficacy superior to selective PPAR $\alpha$ , PPAR $\delta$  or PPAR $\gamma$  agonists.

**HF/HS model:** This diet-induced obesity model was used to evaluate the effect of IVA337 on insulin resistance and other parameters linked to metabolic syndrome. IVA337 dose dependently reduced body weight gain, normalized insulinemia and non-fasting glucose and reduced circulating leptin levels.

**MCD model:** In mice fed with a methionine- and choline-deficient diet, IVA337 completely prevented steatosis and to a large extent reduced necroinflammatory changes.

**HFD foz/ foz model:** The effect of IVA337 was investigated in the Alsm1 mutant foz/foz mice in which steatohepatitis occurs as a complication of severe obesity and insulin resistance. This model closely reproduces the natural history of NASH in humans. IVA337 largely attenuated steatosis and ballooning and reduced macrophage recruitment and fibrotic gene expression.

**CCL<sub>4</sub>- liver fibrosis:** IVA337 demonstrated both preventive and curative effects on fibrosis induced by CCl<sub>4</sub>.

IVA337 inhibited the expression of profibrotic and inflammasome genes while increasing the expression of  $\beta$ -oxidation-related and fatty acid desaturation-related genes in both the methionine and choline-deficient diet and the foz/foz model.

In vitro experiments were conducted to investigate the effect of IVA337 on human hepatic stellate cells (HSCs) which are the key cells driving liver fibrogenesis in NASH. IVA337 was shown to inhibit proliferation and activation of these cells.

**About Inventiva:** [www.inventivapharma.com](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.

IVA337, 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, IVA336, which is a treatment for three different forms of mucopolysaccharidosis: MPS I or Hurler/Scheie syndromes, MPS II or Hunter syndrome and MPS VI also known as Maroteaux-Lamy syndrome. Inventiva has a preclinical stage oncology portfolio.

Inventiva benefits from partnerships with world-leading research entities such as the Institut Curie. Two strategic commercial partnerships, one of which is at clinical stage, have also been developed 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.

## Contacts

### Inventiva

Frédéric Cren  
Chief Executive Officer  
[info@inventivapharma.com](mailto:info@inventivapharma.com)  
+33 (0)3 80 44 75 00

### NewCap

Julien Perez /  
Mathilde Bohin  
Investor Relations  
[inventiva@newcap.eu](mailto:inventiva@newcap.eu)  
+33 (0)1 44 71 98 52

### NewCap

Nicolas Merigeau /  
Arthur Rouillé  
Media Relations  
[inventiva@newcap.eu](mailto:inventiva@newcap.eu)  
+33 (0)1 44 71 94 98

### LifeSci Advisors

Chris Maggos  
Investor Relations  
[chris@lifesciadvisors.com](mailto:chris@lifesciadvisors.com)  
+41 79 367 6254

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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.*

*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.*