

## Inventiva's latest research on odiparcil's mechanism of action published in leading peer-reviewed scientific journal *PLOS ONE*

- ▶ The scientific paper reviewed the latest non-clinical pharmacology data obtained from skin fibroblasts from MPS VI patients (*in vitro*) and MPS VI mouse model (*in vivo*)
- ▶ The results show that odiparcil was associated with decreased glycosaminoglycan (GAG) accumulation as well as increased GAG excretion, and highlight its distribution in MPS VI disease-relevant tissues and organs
- ▶ This publication is consistent with positive results previously observed in odiparcil's clinical development for the treatment of MPS VI

**Daix (France), May 18, 2020** – Inventiva (Euronext: IVA), a clinical-stage biopharmaceutical company developing oral small molecule therapies for the treatment of non-alcoholic steatohepatitis (NASH), mucopolysaccharidoses (MPS) and other diseases with significant unmet medical need, announced today the publication of its latest research supporting Inventiva's understanding of the mechanism of action of odiparcil, the Company's product candidate for the treatment of MPS VI, in the scientific journal *PLOS ONE*. Published by the US-based Public Library of Science (PLOS) since 2006, *PLOS ONE* is one of the leading peer-reviewed, open access scientific journals worldwide.

The non-clinical studies conducted by Inventiva showed that *in vitro*, treatment with odiparcil was associated with reduced intracellular GAG content in skin fibroblasts isolated from MPS VI patients and concomitant the secretion of GAGs outside the cells in the culture media. Furthermore, Inventiva's research team observed *in vivo* in wild-type rats that odiparcil was well distributed in MPS VI disease-relevant tissues and organs such as bone, cartilage, heart and cornea, where enzyme replacement therapy (ERT), the current standard of care for MPS VI, has shown poor penetration. In a mouse genetic model of MPS VI, treatment with odiparcil was consistently associated with urinary excretion of GAGs throughout the treatment period and significantly reduced GAG accumulation in tissues such as liver and kidney. In addition, treatment with odiparcil was also associated with diminished pathological cartilage thickening of trachea and femoral growth plates of MPS VI mice.

The data set obtained with this latest study supports Inventiva's understanding of the mechanism of action of odiparcil, which acts to divert the synthesis of cellular GAGs into secreted soluble species. This data set is also consistent with positive results observed in the clinical development of odiparcil, which is undergoing clinical trials as a potential orally-delivered GAG clearance therapy for MPS VI patients.

**Pierre Broqua, CSO and cofounder of Inventiva, commented:** "We are very pleased to see our latest *in vitro* and *in vivo* research on odiparcil published in the renowned *PLOS ONE* scientific journal, which testifies to our innovative R&D approach in the field of MPS. Our results support our hypothesis about the mechanism of action of odiparcil, following the release of positive results from our Phase IIa iMProveS clinical trial with odiparcil in MPS VI at the end of last year. We are excited by these latest findings, further encouraging the development of our drug candidate for the treatment of MPS VI, as we prepare the Phase I/II clinical trial with odiparcil in MPS VI children."

### Publication details

**Title of scientific paper:** *“Odiparcil, a potential glycosaminoglycans clearance therapy in mucopolysaccharidosis VI - evidence from in vitro and in vivo models”*

**Date of publication:** May 15, 2020

**Link to the article:** <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0233032>

### About odiparcil

Odiparcil is an orally-available small molecule that acts on the underlying cause of the symptoms of mucopolysaccharidosis (MPS), a group of rare, progressive genetic disorders. MPS is characterized by the accumulation of glycosaminoglycans (GAGs), polysaccharides which are important for the modulation of cell to cell signalling and the maintenance of tissue structure and function, in the lysosomes of cells. Due to genetic mutations, lysosomes in patients with MPS contain deficient versions of the enzymes necessary to break down GAGs. As a result, GAGs accumulate within the lysosomes, causing the latter to swell and interfere with the ordinary functioning of cells, leading to the symptoms associated with MPS. MPS is categorized by subtypes, depending on the enzyme that is deficient and the corresponding GAGs that accumulate. By modifying how GAGs are synthesized, odiparcil facilitates the production of soluble GAGs that can be excreted in the urine, rather than accumulating in cells. Specifically, odiparcil acts on chondroitin sulfate (CS) and dermatan sulfate (DS), either or both of which accumulate in patients with MPS I, II, IVa, VI and VII.

A Phase I/II clinical trial in children with MPS VI is currently under preparation following the positive results of a Phase IIa clinical trial in adult MPS VI patients published at the end of 2019.

Odiparcil has been granted orphan drug designation by the U.S. Food and Drug Administration and the European Medicines Agency and has also obtained rare pediatric disease designation in the U.S. for the treatment of MPS VI.

### About Inventiva

Inventiva is a clinical-stage biopharmaceutical company focused on the development of oral small molecule therapies for the treatment of NASH, MPS and other diseases with significant unmet medical need.

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, 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 odiparcil, a second clinical stage asset, for the treatment of patients with MPS, a group of rare genetic disorders. A Phase Ib/II clinical trial in children with MPS VI is currently under preparation following the release of positive results of the Phase IIa clinical trial in adult MPS VI patients at the end of 2019.

In parallel, Inventiva is in the process of selecting an oncology development candidate for its Hippo signalling pathway program. Furthermore, the Company has established a strategic collaboration with AbbVie in the area of autoimmune diseases. AbbVie has started the clinical development of ABBV-157, a drug candidate for the

treatment of moderate to severe psoriasis resulting from its collaboration with Inventiva. This collaboration enables 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 collaboration.

The Company has a R&D team of approximately 70 people with deep expertise in the fields of biology, medicinal and computational chemistry, pharmacokinetics and pharmacology, as well as in clinical development. It also owns an extensive library of approximately 240,000 pharmacologically relevant molecules, approximately 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: FRO013233012). [www.inventivapharma.com](http://www.inventivapharma.com)

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