

## Inventiva announces positive results from Phase IIa clinical study with odiparcil in mucopolysaccharidosis type VI

- ▶ Safety primary objective of the study met
- ▶ Positive results observed regarding the efficacy of odiparcil, especially in hard-to-reach tissues
- ▶ Decision to continue the clinical development of odiparcil for the treatment of mucopolysaccharidosis (MPS) type VI
- ▶ Study results to be presented during a dedicated conference call and webcast on December 19, 2019

**Daix (France), December 18, 2019** – Inventiva (Euronext: IVA), a clinical-stage biopharmaceutical company developing oral small molecule therapies for the treatment of diseases in the areas of fibrosis, lysosomal storage disorders and oncology, today announced the results from its Phase IIa iMProveS (*improve MPS treatment*) clinical study evaluating odiparcil for the treatment of mucopolysaccharidosis (MPS) type VI, a rare, progressive genetic disorder with high unmet medical need.

The 26-week Phase IIa clinical trial included 20 patients aged 16 years or older suffering from advanced stages of MPS VI. 15 patients were randomized in a double-blind, placebo-controlled cohort and received an oral dose of 250mg or 500mg of odiparcil or placebo twice a day for six months, in addition to enzyme replacement therapy (ERT), the current standard of care. The remaining five patients were included in an open-label cohort and received an oral dose of 500mg of odiparcil twice a day for six months, without being treated with ERT. 13 patients completed the study: four patients who received placebo in addition to ERT and nine patients equally distributed in each of the three odiparcil groups.

**Frédéric Cren, Chairman, Chief Executive Officer and cofounder of Inventiva, commented:** *“We are very pleased with today’s positive results and would like to thank all patients, caregivers, investigators and our team for their commitment and dedication to this study and the overall program. We believe that the efficacy shown after only six months of treatment and its oral formulation could make odiparcil a treatment of choice for MPS VI patients, particularly given the high unmet medical need in this disease field. Based on the observed efficacy data and odiparcil’s good safety profile, we have decided to move forward with the clinical development of odiparcil in MPS VI with a focus on children, the target population for this compound.”*

**Chris Hendriksz, member of the iMProveS clinical study steering committee and extraordinary professor of Paediatrics and Child Health, University of Pretoria, South Africa, said:** *“This is an exciting moment in the MPS field as we now have the first data for an oral compound which shows efficacy results in hard-to-reach tissues for MPS disorders. Despite the current approved therapies, there is still a huge unmet medical need related to eye, heart and bone manifestations and seeing positive changes in this study in a very short treatment time is very exciting for patients.”*

The clinical study met its safety primary objective further supporting the good overall safety profile of odiparcil already observed in previous Phase I and Phase II clinical studies conducted for the prevention of thrombosis. All

investigators of the iMProveS study reported positive experience with odiparcil in terms of safety. The majority of adverse events were mild or moderate. One death occurred in the placebo group and three serious adverse events (SAEs) were assessed as treatment-related in patients in the odiparcil groups. Two of these SAEs were biological findings qualified as laboratory false-positive. The third SAE was a skin reaction, which is frequently observed in ERT-treated MPS VI patients. Compared to previous Phase I and II clinical studies conducted with odiparcil for the prevention of thrombosis, no new safety findings were observed.

Considering the short study duration and the advanced status of the disease in patients included in the study, the iMProveS study showed positive results regarding the efficacy of odiparcil:

- Improvements were observed in patients treated with odiparcil, in addition to ERT, with regards to corneal clouding as well as cardiac and respiratory functions.
- Consistent with odiparcil's mechanism of action, a dose-dependent urinary clearance of glycosaminoglycans (GAGs), used as an activity biomarker, was clearly demonstrated in the entire patient population treated with odiparcil. Similarly to ERT, odiparcil did not induce a reduction of leukocyte glycosaminoglycans (leukoGAGs), which was therefore not confirmed as a biomarker for the decrease of GAG accumulation in this study. Work is planned regarding skin GAG analysis.
- Regarding locomotor function, no clear difference was observed among the different patient groups.

Results from the pharmacokinetics analysis were in line with expectations and will be used for dose selection in the next study planned with MPS VI children. In the iMProveS study, the pharmacokinetic profile obtained in MPS VI patients treated with odiparcil is not impacted by ERT and is consistent with profiles previously observed in Phase I and Phase II studies in prevention of thrombosis.

Based on the iMProveS clinical study results, Inventiva has decided to continue the clinical development of odiparcil for the treatment of MPS VI. To this end, the Company aims to launch, as planned, a clinical study evaluating odiparcil in MPS VI children, the target population for this treatment. Inventiva is currently finalizing the study design to take into account today's results. Details will be posted on [clinicaltrials.gov](https://clinicaltrials.gov) once the study protocol has been finalized and validated with the relevant regulatory authorities.

### Results presentation

Inventiva's management team will present today's study results during a dedicated conference call and webcast on **Thursday, December 19, 2019 at 2:00 pm (Paris time)**.

To join the conference call, please use the code **9149459** after dialling one of the following numbers:

France: +33 1 70 73 27 27

Belgium: +32 10 39 12 06

Denmark: +45 32 72 75 18

Germany: +49 69 22 22 49 10

Netherlands: +31 20 71 57 366

Switzerland: +41 44 58 04 873

United Kingdom: +44 203 00 95 710

United States: +1 917-720-0178

The presentation accompanying this conference call will be simultaneously accessible on Inventiva's website in the "Investors" – "Financial Results & Presentations" section. It can be followed live or by replay in the same section of the Company's website and at: <https://edge.media-server.com/mmc/p/z5gurvfg>.

### About the Phase IIa iMProveS trial

The iMProveS (*improve MPS treatment*) study was a 26-week Phase IIa clinical trial taking place in four European sites and evaluating odiparcil for the treatment of patients with mucopolysaccharidosis (“MPS”) type VI. The primary endpoint of the trial was safety, as assessed by clinical and biological standard tests. Secondary endpoints included changes from baseline in leukocyte, skin and urinary glycosaminoglycan (“GAG”) content, improvements of activity and mobility, evaluation of cardiovascular, lung and respiratory function and vision and hearing impairments.

For this trial, 20 patients, aged 16 years or older, had been enrolled. Patients receiving enzyme replacement therapy (ERT) and one of two odiparcil doses (500mg or 250mg twice a day) or placebo had been randomized in the double-blind placebo-controlled cohort. Patients not being treated with ERT and only receiving the high dose of odiparcil (500mg twice a day) had been enrolled in the open label cohort.

### About odiparcil and mucopolysaccharidoses

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.

Odiparcil has been granted Orphan Drug Designation (ODD) by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) and has also obtained Rare Pediatric Disease Designation (RPDD) 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 diseases with significant unmet medical needs in the areas of fibrosis, lysosomal storage disorders and oncology.

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 – lanifibranor and odiparcil – in non-alcoholic steatohepatitis (“NASH”) and mucopolysaccharidosis (“MPS”), respectively, 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.

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 partnership with AbbVie in the area of

autoimmune diseases. AbbVie has started the clinical development phase of ABBV-157, a drug candidate for the treatment of moderate to severe psoriasis resulting from its collaboration with Inventiva. This collaboration entitles 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 this partnership.

The Company has a scientific 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, around 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: FR0013233012). [www.inventivapharma.com](http://www.inventivapharma.com)

## Contacts

### Inventiva

Frédéric Cren  
Chairman & CEO  
[info@inventivapharma.com](mailto:info@inventivapharma.com)  
+33 3 80 44 75 00

### Brunswick Group

Yannick Tetzlaff / Tristan Roquet  
Montegon / Aude Lepreux  
Media relations  
[inventiva@brunswickgroup.com](mailto:inventiva@brunswickgroup.com)  
+33 1 53 96 83 83

### LifeSci Advisors

Monique Kosse  
Investor relations  
[monique@lifesciadvisors.com](mailto:monique@lifesciadvisors.com)  
+1 212 915 3820

## Important Notice

*This press release contains forward-looking statements, forecasts and estimates with respect to the clinical development plans, business and regulatory strategy, and anticipated future performance of Inventiva and of the market in which it operates. Certain of these statements, forecasts and estimates can be recognized by the use of words such as, without limitation, “believes”, “anticipates”, “expects”, “intends”, “plans”, “seeks”, “estimates”, “may”, “will” and “continue” and similar expressions. Such statements are not historical facts but rather are statements of future expectations and other forward-looking statements that are based on management's beliefs. These statements reflect such views and assumptions prevailing as of the date of the statements and involve known and unknown risks and uncertainties that could cause future results, performance or future events to differ materially from those expressed or implied in such statements. Actual events are difficult to predict and may depend upon factors that are beyond Inventiva's control. There can be no guarantees with respect to pipeline product candidates that the candidates will receive the necessary regulatory approvals or that they will prove to be commercially successful. Therefore, actual results may turn out to be materially different from the anticipated future results, performance or achievements expressed or implied by such statements, forecasts and estimates. Given these uncertainties, no representations are made as to the accuracy or fairness of such forward-looking statements, forecasts and estimates. Furthermore, forward-looking statements, forecasts and estimates only speak as of the date of this press release. Readers are cautioned not to place undue reliance on any of these forward-looking statements.*

*Please refer to the “Document de référence” filed with the Autorité des Marchés Financiers on April 12, 2019 under n° R.19-006 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.*