Inventiva announces positive outcomes of biomarker study measuring intracellular GAGs in leukocytes from MPS VI patients

Data confirm highly promising biomarker for MPS VI and limited enzyme replacement therapy (ERT) efficacy in reducing leukoGAGs

Daix (France), February 26, 2018 – Inventiva, a biopharmaceutical company developing innovative therapies in nonalcoholic steatohepatitis (NASH), systemic sclerosis (SSc) and mucopolysaccharidosis (MPS), today announced the positive outcomes of a biomarker study to evaluate intracellular glycosaminoglycans (GAGs) levels in leukocytes as a disease activity biomarker in MPS VI. Conducted at UCSF Benioff Children's Hospital in Oakland, California by Dr Paul R. Harmatz, and analyzed by the Greenwood Genetic Center Biochemical Genetics Laboratory in South Carolina, an international leader in the diagnosis of lysosomal storage disorders, this biomarker study has enabled the development of a new and robust quantification method of intracellular heparan sulfate (HS), chondroitin sulfate (CS) and dermatan sulfate (DS) in leukocytes (leukoGAG). These leukoGAGs may provide compelling surrogate markers to be used in clinical trials, and for patient monitoring. In addition, patients treated with galsulfase, the enzyme replacement therapy (ERT) approved for MPS VI patients, maintained a high level of leukoGAGs compared to age-matched healthy volunteers suggesting the possibility to further reduce this level with a new treatment such as odiparcil.

The study enrolled 12 subjects: six MPS VI patients, who have been treated with galsulfase for 10 ± 3.1 years (range 6-14 years), and six age-matched control subjects not affected with MPS. Urinary GAGs (uGAGs) and leukoGAGs were measured and the results show that all MPS VI patients receiving ERT have total uGAGs above the upper limit of normal (ULN) and leukoGAGs above control subjects values. In MPS VI patients receiving ERT, the most abundant GAG components are DS and CS in urine and CS in leucocytes. These two forms of GAGs are reduced in MPS VI patient cells treated with odiparcil. Finally, data on the arylsulfatase B activity (the deficient enzyme in MPS VI) in leukocytes, showed that one hour after completion of galsulfase infusion, enzyme activity is increased nearly eightfold but that the CS content in leucocytes remains more than 12-fold above basal level.

Dr. Paul R. Harmatz, the principal investigator of this study, said: *"The high level of leukoGAG in patients receiving ERT is a clear signal of the limitations of this therapeutic strategy. Our ability to use a new and robust quantification method to measure intracellular HS/CS/DS will enrich our analysis of the Phase IIa iMProveS trial and are suggestive of the high medical need that can be addressed by odiparcil."*

About odiparcil

Odiparcil is the first new treatment in development for MPS VI in over a decade. The current standard of care is ERT, which requires weekly infusions. An orally available therapeutic such as odiparcil would greatly increase the quality of life of patients. More importantly, thanks to its optimal distribution in the body, odiparcil has shown efficacy in tissues and organs where current ERT is not effective. Inventiva believes odiparcil could meaningfully improve the lives of MPS VI patients, and become the new standard of care. On December 30th, 2017, the first patient was enrolled in the Phase IIa iMProveS (improve MPS treatment) trial of odiparcil in MPS VI patients. Results from this study are expected in 1H 2019. Odiparcil has received orphan drug designation for MPS VI in the

United States and Europe in August 2017. Given its mechanism of action, odiparcil could address several forms of MPS 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.

About MPS VI

MPS VI (Maroteaux-Lamy syndrome), is a rare, pediatric, genetic, degenerative disease characterized by the abnormal functioning of the enzyme N-acetylgalactosamine 4-sulphatase (arylsulphatase B; ASB) leading to the accumulation of chondroitin sulfate and dermatan sulfate in the cells, tissues and organs. Patients suffer from short stature, corneal clouding, hearing loss, dysostosis multiplex, hepatosplenomegaly, cardiac valve disease and reduced pulmonary function without intellectual deficit. As with other MPS, the time of onset, rate of progression and extent of the disease may vary between the affected individuals. The life expectancy of MPS VI patients, if untreated, is approximately 20 years in patients with severe forms of the disease, or longer in patients with less severe forms. The prevalence of MPS VI is estimated to be 1 in 225,000 live births and varies between countries. There is no cure for MPS VI and current treatment options such as ERT or hematopoietic stem cell transplant (HSCT) leave the patients with high unmet medical needs.

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.

About The Greenwood Genetic Center: www.ggc.com

The Greenwood Genetic Center (GGC), founded in 1974, is a nonprofit organization advancing the field of medical genetics and caring for families impacted by genetic disease and birth defects. At its home campus in Greenwood, South Carolina, a talented team of physicians and scientists provides clinical genetic services, diagnostic laboratory testing, educational programs and resources, and research in the field of medical genetics. GGC's faculty and staff are committed to the goal of developing preventive and curative therapies for the individuals and families they serve. The Greenwood Genetic Center's vision is to be a center of excellence in medical genetics serving as a resource for all persons who need genetic services or information and working to reduce the prevalence and impact of genetic disorders.

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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.

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