News Release

May 19, 2021
JCR Pharmaceuticals Co., Ltd.

Translation

Launch of IZCARGO® I.V. Infusion 10mg (JR-141: Pabinafusp Alfa) for Treatment of MPS II (Hunter Syndrome) in Japan

May 19, 2021-- JCR Pharmaceuticals Co., Ltd. (TSE 4552; Chairman and President: Shin Ashida; "JCR") announced today that IZCARGO® I.V. infusion 10mg (JR-141: Pabinafusp Alfa (Genetical Recombination)) for the treatment of mucopolysaccharidosis II (MPS II, or Hunter syndrome), approved in March 2021, is being placed on the National Health Insurance (NHI) reimbursement price list and launched as of today.

This product is the first-ever approved enzyme replacement treatment that penetrates the blood-brain-barrier (BBB) via intravenous administration for the treatment of MPS II (Hunter syndrome), a lysosomal storage disorder (LSD). By delivering the enzyme to both the body and the brains, this product is expected to treat not only the systemic symptoms but also the neurological complications of MPS II.

Currently, JR-141 is also under review for manufacturing and marketing approval by the Brazilian Health Surveillance Agency (Agência Nacional de Vigilância Sanitária [ANVISA]). JCR is also preparing to initiate a global Phase 3 clinical trial for JR-141 in the US, Brazil and Europe (UK, Germany and France).

JCR, as a specialty pharma in the rare disease arena, will continue to proactively engage in research and development of transformative treatment options for patients with rare diseases.

In terms of impact on JCR's consolidated financial results for the fiscal year ending March 31, 2022, the figures in the forecast will remain unchanged as this item was factored into JCR's plans at the beginning of the fiscal year.



IZCARGO® I.V. infusion 10mg

IZCARGO® I.V. Infusion 10mg

- Product Name: IZCARGO® I.V. infusion 10mg
- International Nonproprietary Name: pabinafusp alfa
- Indications: Mucopolysaccharidosis II
- Dosage and administration: An intravenous infusion administered once every other week at a dose of 2.0 mg per kg of body weight
- Approval date: March 23, 2021
- NHI reimbursement price listing date: May 19, 2021
- NHI reimbursement price: 251,030 yen / 10mg 1vial

Lysosomal storage disorders (LSDs)

LSDs are diseases in which genetic defects or mutations in hydrolytic enzymes, membrane proteins that serve as enzyme transporters and other proteins within lysosomes, which are organelles found in cells, result in the accumulation of substrates that cannot be broken down within the lysosomes as the enzyme activity decreases. This condition causes disorders in cells and tissues. There is a wide range of clinical symptoms that can appear depending on the specific substrates that accumulate. CNS manifestations are present in many cases of LSDs.

About JR-141

JR-141 is a recombinant fusion protein of an antibody against the human transferrin receptor and idursulfase, the enzyme that is missing or malfunctioning in subjects with Hunter syndrome. It is expected to be effective against CNS symptoms by crossing the BBB through transferrin receptor-mediated transcytosis using J-Brain Cargo®, JCR's proprietary BBB technology. Uptake into cells is mediated through the mannose-6-phosphate receptor. JCR has advanced development activities by establishing the necessary evidence from the molecular design stage to the non-clinical and clinical trial phases.

In non-clinical trials, JCR has confirmed both high affinity binding of JR-141 to transferrin receptors, and passage across the BBB into neuronal cells as evidenced by electron microscopy. In addition, JCR has confirmed that using J-Brain Cargo® technology, enzymes are taken up into various brain tissues. A decrease in substrate accumulation has also been confirmed in an animal model of Hunter syndrome.*[1,2,3]

In several clinical trials with JR-141, JCR obtained evidence of reduction of heparan sulfate concentrations in the CSF, a biomarker for assessing effectiveness against CNS symptoms, consistent with the results obtained from non-clinical studies. JCR also obtained clinical results that demonstrate positive effects of JR-141 on CNS symptoms.*[4,5,6]

About mucopolysaccharidosis II (Hunter syndrome)

Mucopolysaccharidosis II (MPS II； Hunter syndrome) is designated as an intractable disease by the Ministry of Health, Labour and Welfare, and classified as specificpediatric chronic disease. Hunter syndrome is an X-linked recessive LSD caused by a deficiency of iduronate-2-sulfatase, an enzyme that breaks down glycosaminoglycans (mucopolysaccharides) in the body. The number of patients with Hunter syndrome in Japan is estimated at approximately 250 (according to JCR research). MPS II gives rise to a wide range of somatic and neurological symptoms. A major limitation to current ERT is that it does not address CNS symptoms because of the enzyme's inability cross the BBB.

<Publications about JR-141>

*[1]: Sonoda, et al. A Blood-Brain-Barrier-Penetrating Anti-human Transferrin Receptor Antibody Fusion Protein for Neuronopathic Mucopolysaccharidosis II. Mol Ther. 2018; 26(5): 1366-74.
*[2]: Morimoto, et al. Clearance of heparin sulfate in the brain prevents neurodegeneration and neurocognitive impairment in MPS II mice. Mol. Ther. 2021; https://doi.org/10.1016/j.ymthe.2021.01.027
*[3]: Yamamoto et al. Nonclinical Safety evaluation of pabinafusp alfa, an anti-human transferrin receptor antibody and iduronate-2-sulfatase fusion protein, for the treatment of neuronopathic mucopolysaccharidosis type II. Mol Genet Metab Rep. 2021; https://doi.org/10.1016/j.ymgmr.2021.100758
*[4]: Okuyama, et al. Iduronate-2-sulfatase with Anti-human Transferrin Receptor Antibody for Neuropathic Mucopolysaccharidosis II: A Phase 1/2 Trial. Mol Ther. 2020; 27(2): 456-464.
*[5]: Okuyama, et al. A Phase 2/3 Trial of Pabinafusp Alfa, IDS Fused with Anti-Human Transferrin Receptor Antibody, Targeting Neurodegeneration in MPS-II. Mol Ther. 2020; 29(2): 671-679.
*[6]: Giugliani, et al. Iduronate-2-sulfatase fused with anti-human transferrin receptor antibody, pabinafusp alfa, for treatment of neuronopathic and non-neuronopathic mucopolysaccharidosis II: Report of a phase 2 trial in Brazil. Mol Ther. 2021; https://doi.org/10.1016/j.ymthe.2021.03.019

About JCR Pharmaceuticals Co., Ltd.

JCR Pharmaceuticals Co., Ltd. (TSE 4552) is a global specialty pharmaceuticals company that is redefining expectations and expanding possibilities for people with rare and genetic diseases worldwide. We continue to build upon our 45-year legacy in Japan while expanding our global footprint into the US, Europe, and Latin America. We improve patients' lives by applying our scientific expertise and unique technologies to research, develop, and deliver next-generation therapies. Our approved products in Japan include therapies for the treatment of growth disorder, Fabry disease, acute graft-versus host disease, and renal anemia. Our investigational products in development worldwide are aimed at treating rare diseases including MPS I (Hurler, Hurler-Scheie and Scheie syndrome), MPS II (Hunter syndrome), Pompe disease, and more. JCR strives to expand the possibilities for patients while accelerating medical advancement at a global level. Our core values – reliability, confidence, and persistence – benefit all our stakeholders, including employees, partners, and patients. Together we soar. For more information, please visit https://www.jcrpharm.co.jp/en/site/en/.

Cautionary Statement Regarding Forward-Looking Statements

This document contains forward-looking statements that are subject to known and unknown risks and uncertainties, many of which are outside our control. Forward-looking statements often contain words such as "believe," "estimate," "anticipate," "intend," "plan," "will," "would," "target" and similar references to future periods. All forward-looking statements regarding our plans, outlook, strategy and future business, financial performance and financial condition are based on judgments derived from the information available to us at this time. Factors or events that could cause our actual results to be materially different from those expressed in our forward-looking statements include, but are not limited to, a deterioration of economic conditions, a change in the legal or governmental system, a delay in launching a new product, impact on competitors' pricing and product strategies, a decline in marketing capabilities relating to our products, manufacturing difficulties or delays, an infringement of our intellectual property rights, an adverse court decision in a significant lawsuit and regulatory actions.

This document involves information on pharmaceutical products (including those under development). However, it is not intended for advertising or providing medical advice. Furthermore, it is intended to provide information on our company and businesses and not to solicit investment in securities we issue.

Except as required by law, we assume no obligation to update these forward-looking statements publicly or to update the factors that could cause actual results to differ materially, even if new information becomes available in the future.

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