News Release

October 18, 2021
JCR Pharmaceuticals Co., Ltd.

Translation

EMA grants PRIME Designation for JR-141 for the treatment of Mucopolysaccharidosis Type II (Hunter Syndrome)

Oct. 18, 2021 -- JCR Pharmaceuticals Co., Ltd. (TSE 4552; Chairman and President: Shin Ashida; "JCR") announced today that the European Medicines Agency (EMA) has granted PRIME designation for the investigational drug JR-141 (INN: pabinafusp alfa) for the treatment of Mucopolysaccharidosis (MPS) II (Hunter syndrome). PRIME is a scheme launched by the EMA to enhance support for the development of medicines for unmet medical needs. This voluntary scheme is based on enhanced interaction and early dialogue with developers of promising medicines, to optimize development plans and speed up evaluation so these medicines can reach patients earlier.

MPS II is a lysosomal storage disorder (LSD) characterized by multiple somatic and central nervous system (CNS) signs and symptoms.JR-141 is a recombinant fusion protein of antibody against the human transferrin receptor and idursulfase, the enzyme missing or malfunctioning in subjects with MPS II. By crossing the blood-brain barrier (BBB) through transferrin receptor mediated transcytosis, it is expected to be effective against CNS symptoms of the disease, thereby addressing a significant unmet need in the treatment of MPS II.

Currently, JCR is preparing to start a global Phase 3 clinical trial for JR-141 in the U.S., Brazil and Europe.

With PRIME designation, JCR can expect to be eligible for accelerated assessment of JR-141 at the time of application for a marketing authorization in Europe.

Following JR-141, JCR plans to harness its J-Brain Cargo® technology platform and progress its robust pipeline of innovative enzyme replacement therapies (ERTs) for other LSDs. 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.

There is no impact on our consolidated business results for the year ending on March 31, 2022 related to the matter.

EMA PRIME (PRIority MEdicines) Designation

PRIME is a scheme launched by the European Medicines Agency (EMA) to enhance support for the development of medicines that target an unmet medical need. This voluntary scheme is based on enhanced interaction and early dialogue with developers of promising medicines, to optimize development plans and speed up evaluation so these medicines can reach patients earlier. Through PRIME, the Agency offers early and proactive support to medicine developers to optimize the generation of robust data on a medicine's benefits and risks and enable accelerated assessment of medicines applications. Developers of a medicine that benefitted from PRIME can expect to be eligible for accelerated assessment at the time of application for a marketing authorization. To be accepted for PRIME, a medicine has to show its potential to benefit patients with unmet medical needs based on early clinical data.

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 incorporates J-Brain Cargo®, JCR's proprietary BBB-penetrating technology, to cross the BBB through transferrin receptor-mediated transcytosis, and its uptake into cells is mediated through the mannose-6-phosphate receptor. This novel mechanism of action is expected to make JR-141 effective against the CNS symptoms of Hunter syndrome.

In pre-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 enzyme uptake in various brain tissues. The company has also confirmed a decrease in substrate accumulation in an animal model of Hunter syndrome.[1,2]

In several clinical trials of JR-141, JCR obtained evidence of reduced HS concentrations in the CSF, a biomarker for assessing effectiveness against CNS symptoms; these results were consistent with those obtained in pre-clinical studies. Clinical studies have also demonstrated positive effects of JR-141 on CNS symptoms.[3,4,5,6]

JR-141 was approved by the Ministry of Health, Labour and Welfare and marketed since May 2021 under the brand name "IZCARGO® I.V. Infusion 10mg."

In September 2021, JCR and Takeda announced a geographically-focused exclusive collaboration and license agreement to commercialize JR-141. Under the agreement, Takeda will exclusively commercialize JR-141 outside of the United States, including Canada, Europe, and other regions (excluding Japan and certain other Asia-Pacific countries). Takeda also received an option for an exclusive license to commercialize JR-141 in the U.S. upon completion of the Phase 3 program. The two companies will collaborate to bring this therapy to patients as quickly as possible upon completion of the global Phase 3 program, which will be conducted by JCR.

About mucopolysaccharidosis II (Hunter syndrome)

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

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 46-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, MPS II (Hunter syndrome), 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), 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.

References

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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: 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.
4: 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. 2021; 29(2): 671-679.
5: 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.
6: Giugliani, et al. Enzyme Replacement Therapy with Pabinafusp Alfa for Neuronopathic Mucopolysaccharidosis II; an Integrated Analysis of Preclinical and Clinical Data. Int. J. Mol. Sci. 2021, Volume 22, Issue 20, 10938.

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