News Release

February 10, 2021

JCR Pharmaceuticals Co., Ltd.

Translation

JCR Pharmaceuticals Receives FDA IND Clearance to Initiate Global Phase 3 Clinical Trial of JR-141 for Mucopolysaccharidosis Type II (Hunter Syndrome)

Feb. 10, 2021 -- JCR Pharmaceuticals Co., Ltd. (TSE 4552; Chairman and President: Shin Ashida; "JCR") announced today that it has received clearance of its Investigational New Drug (IND) application from the US Food and Drug Administration (FDA) to initiate a phase 3 clinical trial of JR-141 (INN: pabinafusp alfa) for the treatment of Mucopolysaccharidosis (MPS) II (Hunter syndrome) in the US.
JR-141 is a blood-brain-barrier (BBB)-penetrating recombinant iduronate-2-sulfatase product candidate for the treatment of patients with Hunter syndrome, to which J-Brain Cargo®, JCR's proprietary BBB technology, is applied.
As a global clinical trial, we are preparing to start this trial in Brazil and Europe, following the U.S.

Hunter syndrome is an X-linked recessive Lysosomal storage disorders caused by a deficiency of iduronate-2-sulfatase, an enzyme that breaks down glycosaminoglycans (mucopolysaccharides) in the body. Hunter syndrome gives rise to a wide range of somatic and central nervous system (CNS) symptoms. A major limitation to the current enzyme replacement therapy (ERT) is that it does not address CNS symptoms because of the enzyme's inability cross the BBB.

In this study, 50 patients with Hunter syndrome will be treated with JR-141 or the standard treatment for up to 105 weeks under a standard of care controlled, parallel-group trial design. The summary of this study is registered on clinicaltrials.gov.

JCR filed an application for marketing approval of JR-141 in Japan in September 2020 and in Brazil in December 2020 based on comprehensive evidence supported by the robust data generated from non-clinical and clinical trials in Japan and Brazil. JR-141 received orphan drug designation from the FDA in October 2018, from the European Medicines Agency (EMA) in February 2019 and from the Ministry of Health, Labor and Welfare in September 2020.

Following JR-141, JCR plans to harness its J-Brain Cargo® technology platform and progress its robust pipeline of innovative ERT products for other lysosomal storage disorders (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.

This new drug development is expected to have a minor impact on JCR's consolidated financial results for the year ending on March 31, 2021.

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]

About J-Brain Cargo® Technology

JCR's first-in-class proprietary technology, J-Brain Cargo®, enables the development of therapies that cross the BBB and penetrate the CNS. The CNS complications of diseases are often severe, resulting in developmental delays, an impact on cognition and, above all, poor prognosis, which affect patients' independence as well as the quality of life of patients and their caregivers. With J-Brain Cargo®, JCR seeks to address the unresolved clinical challenges of LSDs by delivering the enzyme to both the body and the brain.

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.

References

[1] Sonoda H, Morimoto H, Yoden E, et al. A blood-brain-barrier-penetrating anti-human transferrin receptor antibody fusion protein for neuronopathic mucopolysaccharidosis II. Molecular Therapy. 2018;26(5):1366-1374. (DOI: https://doi.org/10.1016/j.ymthe.2018.02.032)

[2] Morimoto H, Kida S, Yoden E, et al. Clearance of heparan sulfate in the brain prevents neurodegeneration and neurocognitive impairment in MPS II mice. Molecular Therapy. 2021 Jan 25;S1525-0016(21)0027-7. (DOI: https://doi.org/10.1016/j.ymthe.2021.01.027)

[3] Okuyama T, Eto Y, Sakai N, et al. Iduronate-2-sulfatase with anti-human transferrin receptor antibody for neuropathic mucopolysaccharidosis II: a phase 1/2 trial. Molecular Therapy. 2019;27(2):456-464. (DOI: https://doi.org/10.1016/j.ymthe.2018.12.005)

Contact:

Investors & Media:

JCR Pharmaceuticals Co., Ltd.

Corporate Communications

ir-info@jcrpharm.co.jp

###