News Release

September 29, 2020
JCR Pharmaceuticals Co., Ltd.

Translation

JCR Files for Marketing Approval of JR-141 (Pabinafusp Alfa) for Hunter Syndrome under the SAKIGAKE Designation System in Japan

JCR Pharmaceuticals Co., Ltd. (TSE 4552; Chairman and President: Shin Ashida; "JCR") announced today that it has filed an application with the Ministry of Health, Labour and Welfare of Japan (MHLW) for marketing approval of JR-141 (Pabinafusp Alfa) for the treatment of mucopolysaccharidosis II (Hunter syndrome). 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. In March 2018, MHLW designated JR-141 as a covered item under the SAKIGAKE Designation System in Japan.

This filing for marketing approval is based on evidence comprehensively supported by the results obtained to date from non-clinical and clinical trials of JR-141.
In a phase 3 clinical trial conducted in Japan, JR-141 was administered to patients for 52 weeks. The heparan sulfate (HS) concentrations in cerebrospinal fluid (CSF), the primary endpoint and a biomarker for effectiveness against central nervous system (CNS) symptoms, decreased in all patients, thereby meeting the primary objective of the trial. In the assessment of somatic symptoms, the trial confirmed that the therapeutic efficacy was maintained in patients switched from the current enzyme replacement therapy (ERT) to JR-141. The trial also confirmed an improvement in symptoms in naïve cases that had not previously received the current ERT prior to the start of the trial. Moreover, a neurocognitive development assessment demonstrated maintenance or improvement of age-equivalent function during the 52 weeks of treatment. With regard to the safety profile, no serious adverse events that were related to treatment were reported.

Following JR-141, JCR plans to harness its J-Brain Cargo® technology platform and develop a robust pipeline of innovative ERT products for additional lysosomal storage disorders (LSDs). JCR, as a specialty pharma in the rare disease arena, will continue to proactively engage in research and development of treatment options for patients with rare diseases.

This filing for marketing approval 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 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 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
In several clinical trials, JCR obtained evidence of reduction of heparin sulfate concentrations in the CSF, a biomarker for assessing effectiveness against CNS symptoms, consistent with the results obtained from the non-clinical studies. JCR also obtained clinical results that demonstrate positive effects of JR-141 on CNS symptoms.*2

About mucopolysaccharidosis II (Hunter syndrome)
Mucopolysaccharidosis II (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 (JCR research). Hunter syndrome 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.

<References>
*1: A Blood-Brain-Barrier-Penetrating Anti-human Transferrin Receptor Antibody Fusion Protein for Neuronopathic Mucopolysaccharidosis II
(DOI: https://doi.org/10.1016/j.ymthe.2018.02.032)
*2: Iduronate-2-sulfatase with anti-human transferrin receptor antibody for neuropathic mucopolysaccharidosis II: a phase 1/2 trial
(DOI: https://doi.org/10.1016/j.ymthe.2018.12.005)

[About JCR Pharmaceuticals]
JCR is a specialty pharma company engaged in the research, development, manufacturing and marketing of biopharmaceuticals and regenerative medicine with a focus on rare diseases. Its philosophy, "Contributing towards people's healthcare through pharmaceutical products" drives JCR to create innovative pharmaceutical products as value-added treatment options for the under-served patient populations.

[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 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.

Investors & Media:
JCR Pharmaceuticals Co., Ltd.
Corporate Communications
ir-info@jcrpharm.co.jp

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