News Release

21 December, 2018
JCR Pharmaceuticals Co., Ltd.

Translation

A blood-brain-barrier-penetrating recombinant iduronate-2-sulfatase (JR-141):
Notice on The Publication of The Phase 1/2 Clinical Trial Results for Hunter Syndrome in *Molecular Therapy*

JCR Pharmaceuticals Co., Ltd. (TSE 4552; Chairman and President: Shin Ashida; "JCR") announced today that the results of the Phase 1/2 clinical trial of JR-141 conducted in Japan for Hunter Syndrome have been published in the electronic edition of *Molecular Therapy*, the official journal of The American Society of Gene & Cell Therapy (ASGCT). 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. A summary of the article is as follows.

◆ Title:
Iduronate-2-sulfatase with anti-human transferrin receptor antibody for neuropathic mucopolysaccharidosis II: a phase 1/2 trial

◆ Digital Object Identifier: https://doi.org/10.1016/j.ymthe.2018.12.005

◆ Summary:
JR-141 was administered for 4 weeks to 14 Japanese MPS II patients, to whom a recombinant IDS product (idursulfase) had been continuously administered, to evaluate its safety and pharmacokinetics as well as exploratory efficacy.

- Safety: Tolerability up to a maximum dosage of 2.0 mg/kg a week was confirmed, with no adverse events that required discontinuation of the drug administration or were considered life-threatening.
- Pharmacokinetics: The plasma concentration showed a dose-dependent increase in AUC and Cmax. Plasma clearance was confirmed within 21 hours after the start of administration.
- Exploratory efficacy: The biomarker data and an amelioration of neurocognitive and motor functions in two patients suggested improvements in the central nervous system (CNS) symptoms, and systemic efficacy non-inferior to idursulfase.

[Biomarker for CNS symptoms]
Levels of heparan sulfate (HS) in cerebrospinal fluid decreased in all patients following 3 weeks of intravenous administration of JR-141 at 1.0 mg/kg/week or 2.0 mg/kg/week.

[Biomarker for systemic symptoms]
Subjects were switched from idursulfase to JR-141 at 1.0 or 2.0 mg/kg/week, and showed no notable changes in the serum and urinary levels of HS and DS and in the urinary glycosaminoglycans before and after the switching.

[About JCR Pharmaceuticals]

JCR is a specialty pharma engaged in the research, development, manufacture 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 community.

[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.

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