News Release

February 13, 2020
JCR Pharmaceuticals Co., Ltd.

Translation

JCR Announces Presentations on JR-141 for Hunter Syndrome and JR-162 for Pompe Disease at the 16th Annual WORLD*Symposium*™ 2020

JCR Pharmaceuticals Co., Ltd. (TSE 4552; Chairman and President: Shin Ashida; "JCR") announced today that it has given two oral and three poster presentations at the 16th Annual WORLD*Symposium*™ 2020*1 in Orlando, Florida, USA (February 10-13, 2020). These presentations highlight two candidates from JCR's development pipeline for lysosomal storage disorders; JR-141, a blood-brain barrier (BBB)-penetrating iduronate-2-sulfatase for Hunter syndrome, and JR-162, J-Brain Cargo®*2-applied acid α-glucosidase for Pompe disease. (Click here for related news release.)

1. Oral presentations (One oral presentation added since last news release.)

Title	Presented on
Results from a phase 2 trial of a blood-brain barrier penetrating enzyme (JR-141) in patients with MPS II in Brazil	February 12th 15:45-16:00 EST
Therapy for mucopolysaccharidosis II with an intravenous blood-brain barrier-crossing enzyme (JR-141): 26-week results from a phase 3 study in Japan suggesting significant efficacy against central nervous system and systemic symptoms	February 12th 16:00-16:15 EST

2. Poster presentations

Title	Presented on
Results from a phase 2 trial of a blood-brain barrier penetrating enzyme (JR-141) in patients with MPS II in Brazil	February 10th 16:30-18:30 EST
Therapy for mucopolysaccharidosis II with an intravenous blood-brain barrier-crossing enzyme (JR-141): 26-week results from a phase 3 study in Japan suggesting significant efficacy against central nervous system and systemic symptoms	February 11th 16:30-18:30 EST
A novel approach to CNS dysfunction of Pompe disease with a fusion protein consisting of anti-transferrin receptor antibody and GAA enzyme	February 12th 16:30-18:30 EST

Developing Therapeutics for Lysosomal Storage Disorders (LSDs)

JCR harnesses its J-Brain Cargo® as proprietary technology platform to develop a robust pipeline of innovative therapeutics for LSDs. Regarding JR-141, a blood-brain barrier (BBB)-penetrating iduronate-2-sulfatase for Hunter syndrome, JCR is conducting a phase 3 clinical trial in Japan and a phase 2 clinical trial in Brazil. During 2020, it aims to file an application for marketing approval of JR-141 in Japan. **Clinical studies of the following diseases are also in preparation to be initiated within 3 years.**

Hurler / Hurler-Scheie / Scheie syndrome（JR-171）	
Pompe disease（JR-162）	**Sanfilippo A syndrome（JR-441）**
Sanfilippo B syndrome	**Sly syndrome**

Succeeding these development pipeline, JCR is accelerating R&D to proceed to the clinical studies of the following LSDs to deliver new medicines for these currently untreated rare diseases as swiftly as possible.

GM1 gangliosidosis	**Fucosidosis**	**Krabbe disease**
α-Mannosidosis	**Gaucher disease**	**Niemann-Pick disease**
Batten disease (late infantile)	**Batten disease (infantile type)**	
Metachromatic leukodystrophy	**GM2 gangliosidosis**	

***1 WORLD*Symposium*™**

An international symposium held annually in the United States with a focus on the basic research to clinical application in the lysosomal diseases.
http://www.worldsymposia.org/

***2 J-Brain Cargo®**

J-Brain Cargo® is the innovative drug delivery system utilizing anti-transferrin receptor antibodies. In JR-141, being developed as a product candidate for the treatment of patients with Hunter syndrome, we expect improvement of not only systemic symptoms but also central nervous system (CNS) symptoms with J-Brain Cargo®, which allows penetrating BBB. In JR-162, being developed as a product candidate for the treatment of patients with Pompe disease, which mainly shows impairment of muscle tissues, we expect not only direct therapeutic effects on muscle tissues via transferrin receptor but also, by penetrating BBB, on nerve cells that regulate the muscles.

Summary of the Presentations at the 16th Annual WORLD*Symposium*™ 2020

Forward-looking Statement

This document contains forward-looking statements that are subject to a number of risks and uncertainties, many of which are outside our control. All forward-looking statements regarding our plans, outlook, strategy and future performance are based on judgments derived from the information available to us at this time.

All forward-looking statements speak only as of the date of this document.
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.

The clinical development data published in this document is the result at the time of the interim analysis. It does not guarantee future results, nor does it guarantee the efficacy, effects of products under development. This document is not intended to advertise the efficacy of the product under development. The clinical development data published in this document includes data not yet published in academic journals that have been peer-reviewed.

In accordance with the Fair Disclosure Rules, data other than those listed in this document will not be disclosed in questions and answers. We appreciate your understanding.

Code	Title
JR-141 (Brazil)	Results from a phase 2 trial of a blood-brain barrier penetrating enzyme (JR-141) in patients with MPS II in Brazil

Presentation URL：
Oral: https://www.jcrpharm.co.jp/ir/pdf/200213/141_br01.pdf
Poster: https://www.jcrpharm.co.jp/ir/pdf/200213/141_br02.pdf

Outline
JR-141 is an anti-human transferrin receptor (J-Brain Cargo®) antibody fused IDS (iduronate-2-sulfatase) expected to cross the blood-brain barrier (BBB). A pivotal 26-week phase 2 study in Brazil is designed to evaluate the efficacy and safety of JR-141 in targeting both central nervous system (CNS) and systemic symptoms in 20 patients with Hunter syndrome. It also evaluated dose responses among 1.0 mg/kg/week, 2.0 mg/kg/week and 4.0 mg/kg/week of intravenous administration of JR-141.

Summary of results
- After 26 weeks, the heparan sulfate (HS) concentrations in cerebrospinal fluid (CSF) decreased in all patients in the 2.0 and 4.0 mg groups. The dermatan sulfate (DS) concentrations in serum decreased in naïve patients in the 2.0 and 4.0 mg groups.

- Developmental assessment at week 26 showed maintenance or improvement of Age Equivalence (AE) in 10 of 12 severe patients (83.3%), and also of Developmental Quotient (DQ) in all 4 attenuated patients compared to the assessment made prior to JR-141 administration.

- No drug-related serious adverse events were reported at 26 weeks. IARs were reported only in the 4.0 mg group, where discontinuation, temporary cessation or addition of important combination therapy was required.

- These results suggest 2.0 mg/mg/week as the optimal dose for JR-141.

Code	Title
JR-141 (Japan)	Therapy for mucopolysaccharidosis II with an intravenous blood-brain barrier-crossing enzyme (JR-141): 26-week results from a phase 3 study in Japan suggesting significant efficacy against central nervous system and systemic symptoms

Presentation URL：
Oral: https://www.jcrpharm.co.jp/ir/pdf/200213/141_jp01.pdf
Poster: https://www.jcrpharm.co.jp/ir/pdf/200213/141_jp02.pdf

Outline
JR-141 is an anti-human transferrin receptor antibody (J-Brain Cargo®) fused IDS (iduronate-2-sulfatase) expected to cross the blood-brain barrier (BBB). A pivotal 52-week Phase 3 study is designed to evaluate the efficacy and safety of 2.0 mg/kg/week intravenous administration of JR-141 in 28 patients with Hunter syndrome in targeting both central nervous system (CNS) and systemic symptoms. This presentation reports 26-week results.

Summary of the results

- After 26 weeks, the primary endpoint, heparan sulfate concentrations in cerebrospinal fluid (CSF-HS), decreased in all of the patients (Mean 58.4±9.5 %). 10 patients who participated in this study had been also enrolled in the phase 1/2 study in Japan. The CSF-HS levels of these patients increased from the end of the phase 1/2 study until the start of this study. Their CSF-HS levels decreased again after the resumed administration of JR-141. These results support the effects of JR-141 on CNS by crossing the BBB.

- CSF-HS at baseline (week 0) showed variable distributions between the severe and the attenuated patients, with a threshold of approximately 4,000 ng/mL. This suggests that CSF-HS is an appropriate biomarker of the severity of Hunter syndrome.

- Developmental assessment at week 26 showed maintenance or improvement of Age Equivalence (AE) in all 17 severe patients, and also of Developmental Quotient (DQ) in all 8 attenuated patients in comparison with those prior to JR-141 administration. Behavioral improvements in each patient were also reported, e.g. "Vocabulary increased," "Started counting numbers," "Has become calmer," "Improvement of facial expression," "Improvement of concentration," and "Smile again."

- The serum concentrations of HS and dermatan sulfate (DS) levels, considered as biomarkers of the systemic symptoms, were maintained in the patients switched from the current ERT, and decreased in the naïve patients at 4 weeks. Comparable efficacy of JR-141 to the current ERT on systemic symptoms was thus supported.

- No drug-related serious adverse events were reported at 26 weeks. Safety profile of JR-141 was comparable to that of the current ERT.

Code	Title
JR-162	A novel approach to CNS dysfunction of Pompe disease with a fusion protein consisting of anti-transferrin receptor antibody and GAA enzyme

Presentation URL：
Poster: https://www.jcrpharm.co.jp/ir/pdf/200213/162_01.pdf

Back ground and outline
Pompe disease, a type of lysosomal storage disorders, is caused by the absence or deficiency of acid alpha-glucosidase (GAA). Patients with infantile-onset Pompe disease, if untreated, die of cardiac failure before 2 years of age following cardiac hypertrophy and muscle weakness caused by glycogen accumulation. Symptoms of late-onset Pompe disease are usually milder than those of the infantile-onset type, but most patients with the former experience progressive muscle weakness, leading to respiratory disorders. JR-162, a fusion protein consisting of anti-human transferrin receptor antibody (named J-Brain Cargo®) and recombinant human GAA (rhGAA), was designed to be delivered efficiently to muscles by the mannose-6-phosphate (M6P) receptors as well as the transferrin receptors (TfR). In addition, this drug can be delivered to central nervous system (CNS) tissues by crossing the blood-brain barrier (BBB) through the mechanism of receptor-mediated transcytosis. We evaluated the efficacy of JR-162 in the KO control mice (*hTfR*-KI/*Gaa*-KO) administered intravenously at a periodical interval for 40 weeks

Summary of results
- The glycogen levels in the brain of *hTfR*-KI/*Gaa*-KO mice reduced significantly by JR-162 compared to those in the untreated and the rhGAA-treated model mice.

- JR-162 suppressed histopathological changes in the CNS tissues.

- After the administration of JR-162, the accumulated glycogen levels in the type I dominant muscle (soleus) and the heart decreased as effectively as rhGAA, while they decreased more effectively than rhGAA in the type II dominant muscle (quadriceps and tibialis anterior) and the diaphragm.

- JR-162 has potentials to exert therapeutic effects on muscle weakness and respiratory dysfunctions caused by both myogenic as well as neurogenic myopathies.

[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 communities.

[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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