News Release

February 14, 2023
JCR Pharmaceuticals Co., Ltd.

Translation

JCR Pharmaceuticals to Present at the 19th Annual WORLD*Symposium*™ 2023

Hyogo, Japan, Feb. 14, 2023 -- JCR Pharmaceuticals Co., Ltd. (TSE 4552; Chairman and President: Shin Ashida; "JCR") announced today that it will host ten presentations at the 19th Annual WORLD*Symposium*™ 2023, to be held February 22-26, 2023 in Orlando, FL, USA. The presentations demonstrate the potential benefits of the investigational therapies in JCR's development pipeline which is using J-Brain Cargo®, JCR's proprietary technology that delivers medicines across the blood-brain barrier (BBB), and JCR's approach for the treatment of lysosomal storage disorders (LSDs). Four of the ten presentations will be held as oral presentations during the plenary sessions and as posters.

Four of the presentations will focus on JCR's lead product candidate, JR-141 (INN: pabinafusp alfa), a BBB penetrating recombinant iduronate-2-sulfatase for the treatment of patients with mucopolysaccharidosis type II (MPS II, or Hunter syndrome). It includes an oral presentation on real world experience with JR-141 in Japan.

In addition, JCR will present phase I/II clinical data on JR-171 (INN: lepunafusp alfa), a BBB-penetrating recombinant α-L-iduronidase for the treatment of MPS I (Hurler, Hurler-Scheie, or Scheie syndrome), on JR-441, a BBB-penetrating recombinant heparan N-sulfatase for MPS IIIA (Sanfilippo A), JR-471, a BBB-penetrating recombinant α-L-fucosidase for treating fucosidosis and data on drug candidates for the treatment of Krabbe's disease and CLN1, respectively.

An overview of all presentations is shown below:

JR-141 (INN: pabinafusp alfa), (BBB-penetrating iduronate-2-sulfatase (rDNA origin))
Target disease: Mucopolysaccharidosis type II (Hunter syndrome)

Title	Real-world data of enzyme replacement therapy with pabinafusp alfa for neuronopathic MPS-II: Updated clinical data from Japan
Date	Oral: Friday, Feb. 24, 2:00 PM - 3:00 PM Poster No.110: Friday, Feb. 24, 4:00 PM - 5:00 PM
Presenter	Yoshikatsu Eto, M.D.

Title	Changes in quality of life reflecting neurobehavioral improvements observed by caregivers/physicians of patients with neuronopathic mucopolysaccharidosis: An interview-based survey from Brazil following clinical trials with pabinafusp alfa
Date	Poster No.239: Friday, Feb. 24, 3:00 PM - 4:00 PM
Presenter	Ana Maria Martins, M.D., Ph.D.

Title	Long-term neurodevelopmental changes in subjects with MPS II following long-term treatment with pabinafusp alfa: An integrated analysis from pre- and post-approval clinical trials in Brazil and Japan
Date	Poster No.133: Friday, Feb. 24, 4:00 PM - 5:00 PM
Presenter	Roberto Giugliani, M.D., Ph.D.

Title	Intravenous treatment with pabinafusp alfa dose-dependently prevents neurological impairment and bone deformities in a mouse model of mucopolysaccharidosis type II
Date	Poster No.247: Saturday, Feb. 25, 4:00 PM - 5:00 PM
Presenter	Hideto Morimoto

JR-171 (INN: lepunafusp alfa), (BBB-penetrating α-L-iduronidase (rDNA origin))
Target disease: Mucopolysaccharidosis type I (Hurler, Hurler-Scheie and Scheie syndrome)

Title	Interim results of a phase 1/2 study of JR-171 (lepunafusp alfa), a novel brain-penetrant enzyme replacement therapy for MPS I
Date	Oral: Friday, Feb. 24, 9:00 AM - 10:00 AM Poster No.157: Friday, Feb. 24, 3:00 PM - 4:00 PM
Presenter	Paul Harmatz, M.D.

JR-441 (BBB-penetrating heparan N-sulfatase (rDNA origin))
Target disease: Mucopolysaccharidosis type III A (Sanfilippo A syndrome)

Title	Nonclinical pharmacodynamics, pharmacokinetics and safety profiles of anti-human transferrin receptor antibody-fused N-sulfoglucosamine sulfohydrolase for mucopolysaccharidosis type IIIA
Date	Oral: Saturday, Feb. 25, 8:00 AM - 9:00 AM Poster No.180: Saturday, Feb. 25, 3:00 PM - 4:00 PM
Presenter	Asuka Inoue, Ph.D.

JR-471 (BBB-penetrating α-L-fucosidase (rDNA origin))
Target disease: Fucosidosis

Title	A fusion protein of anti-human transferrin receptor antibody and alfa-L-fucosidase 1 is a prospective candidate for the treatment of the symptoms in CNS and visceral tissues of fucosidosis
Date	Poster No.381: Saturday, Feb. 25, 4:00 PM - 5:00 PM
Presenter	Eiji Yoden

Title	International online survey of fucosidosis: Key symptoms and the family experience
Date	Poster No.154: Saturday, Feb. 25, 3:00 PM - 4:00 PM
Presenter	Kohtaro Hamauchi

Other Programs
Target disease: Krabbe disease

Title	Life-span extension in Krabbe disease mice by treatment with a transferrin receptor-targeted galactocerebrosidase
Date	Poster No.179: Saturday, Feb. 25, 3:00 PM - 4:00 PM
Presenter	Atsushi Imakiire

Target disease: CLN1

Title	Treatment of CLN1 disease with a blood-brain barrier penetrating lysosomal enzyme AGT-194
Date	Oral: Thursday, Feb. 23, 2:00 PM - 3:00PM Poster No.153: Thursday, Feb. 23, 3:00 PM - 4:00 PM
Presenter	Andreas Hahn, M.D., Ph.D.

WORLD*Symposi*um™ attendees who would like to receive more information about JCR Pharmaceuticals can visit JCR's on-site conference booth.

About the Annual WORLD*Symposium*™
The WORLD*Symposium*™ is designed for basic, translational and clinical researchers, patient advocacy groups, clinicians, and all others who are interested in learning more about the latest discoveries related to lysosomal diseases and the clinical investigation of these advances. For additional information on the 19th Annual WORLD*Symposium*™, please visit https://worldsymposia.org/.

About JR-141 (Pabinafusp Alfa)
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 withMPS II. It incorporates J-Brain Cargo®, JCR's proprietary blood-brain barrier (BBB)-penetrating technology, to cross the BBB through transferrin receptor-mediated transcytosis. Its uptake into cells is mediated through the mannose-6-phosphate receptor and the transferrin receptor. This novel mechanism of action is expected to make JR-141 effective against the CNS symptoms of MPS II. 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. In addition, JCR has confirmed enzyme uptake in various brain tissues. The company has also confirmed a reduction of substrate accumulation in the CNS and peripheral organs in an animal model of MPS II.[1,2]

In several clinical trials of JR-141, JCR obtained evidence of reducing heparan sulfate (HS) concentrations in the CSF, a biomarker used for the assessment of substrate reduction in the CNS; 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] Several studies are currently ongoing to investigate the long-term effect of JR-141 in individuals with MPS II.

JR-141 was approved by the Ministry of Health, Labour and Welfare for the treatment of MPS IIand 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 global 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.

Important Safety Information
INDICATION:

IZCARGO® is indicated for the treatment of mucopolysaccharidosis type II (MPS II), which is also known as Hunter syndrome. IZCARGO® is approved in Japan only.

CONTRAINDICATION:

IZCARGO® is contraindicated in patients with a history of anaphylactic shock to its any components.

WARNINGS AND PRECAUTIONS:

Warnings
Since serious anaphylaxis and shock may occur with use of IZCARGO®, adequate emergency measures should be made ready for execution before initiation of administration, and the patient should be closely monitored during and after the administration. If a serious infusion associated reaction (IAR) occurs, administration of IZCARGO® should be discontinued, and appropriate actions should be taken.

When IZCARGO® is administered to patients with severe respiratory failure or acute respiratory disease, an IAR may lead to acute exacerbation of symptoms. Patient's condition should be closely monitored and appropriate actions should be taken as needed.

Precautions for Use
IZCARGO® is a protein medicinal product and may cause anaphylactic shock, for which close monitoring is required. If any signs of anaphylaxis are noted, discontinue the infusion, and take appropriate actions. Considering the onset of such symptoms, emergency measures should be made ready for execution.

IZCARGO® may cause IARs such as headache, chills, syncope, fatigue, dizziness, pyrexia, rash, erythema, urticaria, or other symptoms. If an IAR occurs, reduce the rate or temporarily discontinue the infusion, and initiate appropriate drug treatment (e.g., corticosteroids, antihistamines, antipyretic analgesics, anti-inflammatory drugs) or emergency procedures (e.g., oxygen administration, securing of airway, adrenaline administration). Premedication with antihistamines, corticosteroids, etc. should be considered for the subsequent infusion of IZCARGO®.

ADVERSE REACTIONS:
The most commonly reported adverse reactions were pyrexia and urticaria.

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 complex carbohydrates called glycosaminoglycans (GAGs, also known as mucopolysaccharides) in the body. Hunter syndrome, which affects an estimated 7,800 individuals worldwide (according to JCR research), gives rise to a wide range of somatic and neurological symptoms. The current standard of care for Hunter syndrome is ERT. CNS symptoms related MPS II have been unmet medical needs so far.

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 48-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), MPS III A and B (Sanfilippo type A and B), 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, et al. A blood-brain-barrier-penetrating anti-human transferrin receptor antibody fusion protein for neuronopathic mucopolysaccharidosis II. Mol. Ther. 2018; 26(5):1366-1374.
2: Morimoto, et al. Clearance of heparin sulfate in the brain prevents neurodegeneration and neurocognitive impairment in MPS II mice. Mol. Ther. 2021; 29(5): 1853-1861.
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; 29(7): 2378-2386.
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.

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

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