News Release

January 24, 2024

JCR Pharmaceuticals Co., Ltd.

JCR Pharmaceuticals to Present at the 20th Annual WORLD*Symposium*™ 2024

Hyogo, Japan, January 24, 2024 -- JCR Pharmaceuticals Co., Ltd. (TSE 4552; Chairman and President: Shin Ashida; "JCR") announced today that it will present six presentations at the 20th Annual WORLD*Symposium*™ 2024, to be held February 4-9, 2024 in San Diego, Calif. These presentations demonstrate the potential benefits of the investigational therapies in JCR's development pipeline and of J-Brain Cargo®, JCR's proprietary technology that delivers medicine across the blood-brain barrier (BBB) for the treatment of lysosomal storage disorders and neurodegenerative disorders.

Three of the presentations will highlight JCR's lead product candidate, JR-141 (pabinafusp alfa, intravenous infusion), a recombinant fusion protein consisting of a humanized anti-transferrin receptor antibody and iduronate-2-sulfatase for the treatment of patients with mucopolysaccharidosis type II (MPS II, or Hunter syndrome). The Ministry of Health, Labour and Welfare (MHLW) in Japan approved JR-141 under the brand name IZCARGO® in March 2021 for the treatment of MPS II. In addition to posters available for each of the presentations,two of them will be shared as oral presentations given by a clinical investigator and a researcher from JCR Pharmaceuticals.

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

Title	A global phase III study of pabinafusp alfa (JR-141) for neuronopathic mucopolysaccharidosis type II: updated study design (Ikeda, et al.)
Presented on	Poster No. 154: Thursday, Feb. 8 at 3pm

Title	Integrated long-term efficacy and safety data on enzyme replacement therapy with pabinafusp alfa for neuronopathic mucopolysaccharidosis type II (MPS-II): Updated clinical data from Japan and Brazil (Eto, et al.)
Presented on	Oral: Wednesday, Feb. 7 at 9am Poster No.81: Wednesday, Feb. 7 at 3pm

Title	Recovery of retinal function in MPS II mice by treatment with pabinafusp alfa (Imakiire, et al.)
Presented on	Oral: Thursday, Feb. 8 at 1pm Poster No. 155: Thursday, Feb. 8 at 3pm

WORLD*Symposium*™ 2024 will also feature two posters highlighting JR-171 (lepunafusp alfa), an investigational, BBB-penetrating, recombinant α-L-iduronidase enzyme replacement therapy ERT that JCR is developing for the treatment of patients with mucopolysaccharidosis type I (MPS I, or Hurler, Hurler-Scheie, or Scheie syndrome).

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

Title	Efficacy and safety data (52-week) from a phase 1/2 trial and extension study of JR-171 (lepunafusp alfa) used in enzyme replacement therapy for patients with MPS I (Giugliani, et al.)
Presented on	Oral: Wednesday, Feb. 7 at 1pm Poster No. 113: Wednesday, Feb. 7 at 3pm

Title	Enzyme replacement therapy with a blood brain barrier-penetrating antibody-fused alpha-L-iduronidase prevents bone deformities in a mouse model of mucopolysaccharidosis type I (Morioka, et al.)
Presented on	Poster No.229: Thursday, Feb.8 at 3pm

In addition, JCR will present the following poster from its research and development pipeline:

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

Title	A phase I/II clinical trial of JR-441 for treatment of Sanfilippo syndrome type A (MPS IIIA) (Muschol, et al.)
Presented on	Poster No. 234: Wednesday, Feb. 7 at 3pm

WORLD*Symposi*um™ attendees who would like to receive more information about JCR Pharmaceuticals can visit JCR's on-site conference booth (#207) or visit its virtual booth on the WORLD*Symposium*™ conference website.

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 20th Annual WORLD*Symposium*™, please visit https://worldsymposia.org/.

About Pabinafusp Alfa
Pabinafusp alfa 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 blood-brain barrier (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 IZCARGO® effective against the Central nervous system (CNS) symptoms of Hunter syndrome.

In pre-clinical trials, JCR has confirmed both high-affinity binding of pabinafusp alfa 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 Hunter syndrome.[1,2]

In several clinical trials of pabinafusp alfa, JCR obtained evidence of reducing heparan sulfate (HS) concentrations in the cerebrospinal fluid (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 the positive effects of pabinafusp alfa on CNS symptoms.[3,4,5,6]

Pabinafusp alfa was approved by the Ministry of Health, Labour and Welfare and 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 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 the J-Brain Cargo® Platform Technology
JCR Pharmaceuticals has developed a proprietary BBB-penetrating technology J-Brain Cargo®, to bring biotherapeutics into the CNS. The first drug developed based on this technology and approved in Japan for the treatment of MPS II (mucopolysaccharidosis type II) is IZGARGO® (INN: pabinafusp alfa). Based on the same platform technology, JR-141 (INN: pabinafusp alfa), JR-171 (INN:lepunafusp alfa) and JR-441 are advancing into global clinical stage. JCR intends to start clinical trials on four additional programs from its LSD pipeline by FY2028.

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 3,000 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 Mucopolysaccharidosis I (Hurler, Hurler-Scheie, Scheie syndrome)
MPS I is an autosomal recessive LSD caused by a deficiency of α-L-iduronidase, an enzyme that breaks down glycosaminoglycans (mucopolysaccharides) in the body. The current worldwide prevalence of MPS I is estimated to be approximately 4,000 (according to JCR research). MPS I gives rise to a wide range of somatic and neurological symptoms. A major limitation of current ERT is that it does not address CNS symptoms because of the enzyme's inability cross the BBB. MPS I is the only LSD in which hematopoietic stem cell transplantation ("HSCT") is part of the standard of case in the severe form of the disease. Significant unmet medical need persists in all forms of MPS I.

About Sanfilippo Syndrome (MPS III)
Sanfilippo syndrome is an autosomal recessive disease caused by a deficiency of the enzymes that metabolize mucopolysaccharides within the body. The disease is classified into four subtypes (A, B, C, and D) according to the respective deficient enzymes. Symptoms include accumulation of heparan sulfate in tissues throughout the body. Notably, the rapidly progressive form of the disease frequently affects neurocognitive development, which peaks around 2 or 3 years of age, before subsequently deteriorating, resulting in a complete loss of speech by the age of 7 or 8. Progression further gives rise to symptoms such as sleep disorders, hepatosplenomegaly, seizures, and neurobehavioral abnormalities.

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 46-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, MPS II (Hunter syndrome), 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), 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, 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.

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