News Release

February 3, 2022

JCR Pharmaceuticals Co., Ltd.

JCR Pharmaceuticals to Present at the 18th Annual WORLD*Symposium*™ 2022

Hyogo, Japan, Feb. 3, 2022 -- JCR Pharmaceuticals Co., Ltd. (TSE 4552; Chairman and President: Shin Ashida; "JCR") announced today that it will present six posters at the 18th Annual WORLD*Symposium*™ 2022, to be held February 7-11, 2022 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.

Two of the presentations will highlight JCR's lead product candidate, JR-141 (pabinafusp alfa, intravenousinfusion), 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. These presentations will be available both as oral presentations given by clinical investigators during the plenary sessions and as posters.

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

Title	[Poster No]. Presented on
Long term efficacy and safety of pabinafusp-alfa (JR-141) in Hunter syndrome (MPS-II): 104-week data from the clinical trials in Japan and Brazil (Giugliani et al.)	[99] Feb. 9 (In-person) 9:00 - 10:00 PM PST
Behavioral improvement in a 9-year-old patient with MPS II undergoing enzyme replacement therapy with pabinafusp alfa: A case report. (Souza et al)	[289] Feb. 9 (In-person) 3:00 - 5:00 PM PST

WORLD*Symposium*™ 2022 will also feature two posters highlighting JR-171, an investigational, BBB-penetrating, recombinant α-L-iduronidase 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 (BBB-penetrating α-L-iduronidase (rDNA origin))
Target disease: Mucopolysaccharidosis type I (Hurler, Hurler-Scheie and Scheie syndrome)

Title	[Poster No.] Presented on
Enzyme replacement with a blood-brain barrier penetrating antibody-fused α-L-iduronidase prevents neurobehavioral performance of Mucopolysaccharidosis type I mice (Morimoto et al.)	[205] Feb. 10 (virtual) 3:00 - 5:00 PM PST
A phase I/II clinical study of intravenous administration of JR-171, a blood-brain barrier-crossing enzyme, in mucopolysaccharidosis type I: an update (Hamazaki et al.)	[113] Feb. 9 (virtual) 3:00 - 5:00 PST

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

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

Title	[Poster No.] Presented on
Efficacy of an anti-human transferrin receptor antibody-fused N-sulfoglucosamine sulfohydrolase in Mucopolysaccharidosis type IIIA mice (Inoue et al.)	[135] Feb. 9 (virtual) 3:00 - 5:00 PM PST

Early-Stage Research and Development Program
Target disease: Fabry disease

Title	[Poster No.] Presented on
Suppression of anti-alpha-GalA antibody production by blockade of T-cell costimulation in mice (Fukatsu et al.)	[89] Feb. 10 (virtual) 3:00 - 5:00 PM PST

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 18th 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 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 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 J-Brain Cargo® Technology
JCR's first-in-class proprietary technology, J-Brain Cargo®, enables the development of therapies that cross the blood-brain barrier (BBB) and penetrate the CNS. The CNS complications of diseases are often severe, resulting in developmental delays, an impact on cognition, and, above all, poor prognosis, which affect patients' independence and the quality of life of patients and their caregivers. With J-Brain Cargo®, JCR seeks to address the unresolved clinical challenges of lysosomal storage disorders (LSDs) by delivering the therapy to both the body and the brain.

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 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, acute graft-versus host disease, and renal anemia. Our investigational products in development worldwide are aimed at treating rare diseases including MPS I (Hurler syndrome, Hurler-Scheie, and Scheie syndrome), MPS II (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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