News Release

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JCR Pharmaceuticals Co., Ltd.

JCR Pharmaceuticals Receives the WORLD*Symposium*™ New Treatment Award for IZCARGO® (Pabinafusp Alfa)

- Award Recognizes Japanese Regulatory Approval of IZCARGO® for Treatment of MPS II (Hunter Syndrome) and Promise of JCR's J-Brain Cargo® Technology -

Hyogo, Japan, February 3, 2022 – JCR Pharmaceuticals Co., Ltd. (TSE 4552; Chairman and President: Shin Ashida; "JCR") today announced that WORLD*Symposium*™ 2022 has bestowed its New Treatment Award to IZCARGO® (pabinafusp alfa 10 mL, intravenous infusion), which the Ministry of Health, Labour and Welfare (MHLW) approved last year for the treatment of mucopolysaccharidosis type II (MPS II, or Hunter syndrome) in Japan. IZCARGO® (formerly known as JR-141) is a recombinant iduronate-2-sulfatase enzyme replacement therapy (ERT) that relies on J-Brain Cargo®, a proprietary technology developed by JCR, to deliver therapeutics across the blood-brain barrier (BBB). It is the first-ever approved ERT in any country that penetrates the BBB via intravenous administration, a potentially life-changing benefit for individuals with lysosomal storage disorders (LSDs) such as MPS II.

The New Treatment Award will be presented to IZCARGO® on Thursday, Feb. 10, 2022, at 7:30 AM PST at the WORLD*Symposium*™ 2022 live meeting in San Diego, Calif. The award honors new treatments that are viewed as providing value to patients with lysosomal diseases, with general acceptance as evidenced by regulatory approval. In announcing this year's award recipients, the symposium organizers specifically saluted JCR for providing clinical data meriting approval by the MHLW.

"We are honored to receive such a prestigious award from WORLD*Symposium*™ 2022," commented Shin Ashida, Chairman, and President of JCR Pharmaceuticals. "The New Treatment Award is an important recognition of the promise of our J-Brain Cargo® technology in addressing the central nervous system complications. The award provides fresh momentum to our ongoing efforts in the global Phase 3 program with JR-141 (IZCARGO®) for the treatment of Hunter syndrome in collaboration with Takeda. It is my strong desire to bring this transformative therapy to Hunter patients around the world as quickly as possible."

The MHLW approved IZCARGO® (pabinafusp alfa) under SAKIGAKE designation in March 2021, the culmination of several recent regulatory milestones that also included receipt of Fast Track designation from the US Food and Drug Administration (FDA), orphan drug designation and PRIME designation from the European Medicines Agency (EMA), and the FDA's acceptance of the IZCARGO® Investigational New Drug application. In addition, JCR filed an application in 2020 with the Brazilian Health Surveillance Agency (Agência Nacional de Vigilância Sanitária [ANVISA]) for marketing approval of pabinafusp alfa for the treatment of patients with MPS II. The global Phase 3 clinical trial is open for recruitment.

"The approval of IZCARGO® is a milestone in the treatment of the brain in lysosomal storage disease,

such as MPSII," said William M. Pardridge, M.D., distinguished professor emeritus at the University of California, Los Angeles, who first invented the concept of BBB Trojan horse technology. "IZCARGO® is biologic drug that is engineered as a dual-purpose monoclonal antibody-lysosomal enzyme fusion protein. The antibody domain acts as a molecular Trojan horse to ferry into brain the missing lysosomal enzyme via receptor-mediated transport across the BBB. The BBB Trojan horse technology can be deployed to re-engineer any number of biologic drugs, which normally do not cross the BBB. As BBB Trojan horse fusion proteins, these new therapeutics will enable treatment of the brain for both rare genetic diseases, such as MPSII, and the more common brain diseases, such as Alzheimer's disease."

"JCR has a long history of commitment to the rare diseases including LSD." commented Hiroyuki Sonoda, Vice President of JCR Pharmaceuticals and inventor of J-Brain Cargo®. "From the experience, we became to believe that our mission is to find a solution for CNS symptoms. We succeeded in developing our own BBB technology and IZCARGO® became the first approved product of its kind. We would like to express our gratitude to everyone who have supported development of IZCARGO®, especially to Dr. Pardridge, regarding the success of developing BBB penetration technology, and also to many patients and physicians for their devotion to the clinical trials. JCR will further continue to focus on new drug development for rare diseases."

WORLD*Symposium*™ 2022 is an annual research conference dedicated to lysosomal diseases. The WORLD name is an acronym that stands for We're Organizing Research on Lysosomal Diseases. Since its inception in 2002, WORLD*Symposium*™ has grown into an international research conference that attracts over 2000 participants from more than 50 countries around the globe.

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 sujects 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.
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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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