News Release

January 28, 2025
JCR Pharmaceuticals Co., Ltd.

JCR Pharmaceuticals to Present at the 21st Annual WORLD*Symposium*™ 2025

- Data to be presented in two poster presentations -

Hyogo, Japan – January 28, 2025 – JCR Pharmaceuticals Co., Ltd. (TSE 4552; "JCR") announced today that it will present at the 21st Annual WORLD*Symposium*™ 2025, held February 3-7, 2025, in San Diego, Calif. The poster presentations will 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.

Details of the presentations are as follows:

Presentation Title: *Treatment with a transferrin receptor-targeted β-hexosaminidase A prolongs life span of GM2 gangliosidosis mice*
Date/Time: *February 4, 2025, 15:30-17:30 PST*
Presenter: *Kazuki Miyauchi, Scientist (JCR Pharmaceuticals)*
Poster Number: *LB-33*

Presentation Title: *Long-term impact of pabinafusp alfa on disease burden in hunter syndrome: a 4-year follow-up of patient-reported outcomes*
Date/Time: *February 6, 2025, 15:30-17:30 PST*
Presenter: *Ana Maria Martins, M.D., Ph.D. (Federal University of São Paulo)*
Poster Number: *222*

The first presentation will spotlight JR-479, an investigational BBB-penetrating β-Hexosaminidase A (rDNA origin) enzyme replacement therapy (ERT) that JCR is developing for the treatment of people with GM2 gangliosidoses.

The second presentation 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 people 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 a rare lysosomal storage disorder.

WORLD*Symposi*um™ attendees who would like to receive more information about JCR Pharmaceuticals can visit JCR's on-site conference booth (#307).

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 21st Annual WORLD*Symposium*™, please visit https://worldsymposia.org/.

About the J-Brain Cargo® Platform Technology
JCR Pharmaceuticals has developed a proprietary BBB-penetrating technology J-Brain Cargo® to bring biotherapeutics into the central nervous system. The first drug developed based on this technology and approved in Japan for a rare lysosomal storage disorder.

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.[3] Clinical studies have also demonstrated the positive effects of pabinafusp alfa on CNS symptoms.[4,5,6]

Pabinafusp alfa was approved in Japan by the Ministry of Health, Labour and Welfare and marketed since May 2021 under the brand name "IZCARGO® I.V. Infusion 10mg" for the treatment of people with a rare lysosomal storage disorder.

About JR-479
JR-479 is a recombinant fusion protein of β-Hexosaminidase A and J-Brain Cargo®, JCR's proprietary blood-brain barrier (BBB)-penetrating technology. This product is being developed for the treatment of GM2 gangliosidoses (Tay-Sachs disease and Sandhoff disease), currently in the pre-clinical stage.

About Mucopolysaccharidosis Type II (Hunter Syndrome)
Mucopolysaccharidosis type II (MPS II, or Hunter syndrome) is an X-linked recessive lysosomal storage disorder 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 2,000-3,000 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 enzyme replacement therapy. Central nervous system symptoms related to MPS II have been unmet medical needs so far.

About GM2 Gangliosidoses
GM2 gangliosidoses are an autosomal recessive, lysosomal storage disorders caused by deficiency of β-Hexosaminidase A (Hex A), an enzyme consisting of α and β subunits. Depending on whether the α- or β- subunit is deficient, GM2 gangliosidoses are classified as Tay-Sachs or Sandhoff disease, respectively. Deficiency of Hex A results in the progressive accumulation of GM2 gangliosides and other glycolipids, which leads to severe neurodegeneration. The development of a therapeutic agent is desirable since there are currently no approved treatments available for this condition.

About JCR Pharmaceuticals Co., Ltd.

JCR Pharmaceuticals Co., Ltd. (TSE 4552) is a global specialty pharmaceuticals company that is expanding possibilities for people with rare and genetic diseases worldwide. We continue to build upon our 49-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, MPS II (Hunter syndrome), 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, MPS IIIA and B (Sanfilippo syndrome 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 belief – benefit all our stakeholders, including patients, partners, and employees. 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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