News Release

September 5, 2024
JCR Pharmaceuticals Co., Ltd.

JCR Pharmaceuticals' Data Presentations at SSIEM Annual Symposium 2024 Highlight Investigational Treatments for Lysosomal Storage Disorders

- Presentations Explain Potential Benefits of J-Brain Cargo® Technology in Delivering Biotherapeutics Across the Blood-Brain Barrier -

Hyogo, Japan, September 5, 2024 – JCR Pharmaceuticals Co., Ltd. (TSE: 4552) made significant contributions at the Society for the Study of Inborn Errors of Metabolism (SSIEM) Annual Symposium 2024, held in Porto, Portugal from September 3-6, 2024. We highlighted our proprietary J-Brain Cargo® technology through two key presentations focused on advanced therapies for lysosomal storage disorders, demonstrating our pioneering role in medical innovation.

"In treating lysosomal storage disorders, it's critical to address the neurological symptoms that often accompany these conditions." said Shin Ashida, Chairman and President of JCR "Our focus is on developing therapies that meet these unmet medical needs. Clinical data for JR-171 shows its potential to be an effective treatment for both the somatic and neurological symptoms associated with Mucopolysaccharidosis I (MPS I). Additionally, our preclinical trials in GM1 gangliosidosis AAV gene therapy development program have demonstrated the potential of combining our J-Brain Cargo® technology with gene therapy. We will continue to update on the progress of these programs."

JCR showcased the following two presentations:

JR-171: Mucopolysaccharidosis Type I (MPS I) Poster

The following poster presentation provides a case report for four individuals with MPS I who were treated with JR-171:

Neurobehavioural and somatic improvements observed in MPS I patients treated with lepunafusp alfa (JR-171): report of four cases (PO-238)
Presenter: Ana Maria Martins, M.D., Ph.D. (Federal University of São Paulo, São Paulo, Brazil)

This study reports clinical data from four individuals with MPS I in Brazil who were treated intravenously with JR-171 (2 mg/kg weekly, n=2; 4 mg/kg weekly, n=2), focusing on neurobehavioral changes. These individuals with MPS I experienced marked neurobehavioral and somatic improvements, which resulted in tangible, positive changes in their quality of life.
These cases illustrate the positive neuropsychiatric and behavioral changes observed during the Phase 1/2 study of JR-171, as well as the drug's somatic efficacy, and demonstrate its potential as an effective treatment for the somatic symptoms and neuronopathy found in individuals with MPS I. Further neurocognitive and developmental evaluation is required to consolidate and establish the efficacy of JR-171 for neuronopathic symptoms.

GM1 Gangliosidosis Poster

This poster presentation was selected as one of the highest-ranked posters. It highlights preclinical data from an adeno-associated virus (AAV) gene therapy in a mice model of GM1 gangliosidosis:

Gene therapy for GM1 gangliosidosis mediated by AAV vector carrying BBB-penetrable enzyme (PO-211)
Presenter: Saki Matsushima, Ph.D. (Division of Gene Therapy, Research Center for Medical Sciences, The Jikei University School of Medicine, Tokyo, Japan)

This study reports preclinical data that demonstrated efficacy of AAV that expresses anti-transferrin receptor-antibody (anti-TfR antibody) fused β-galactosidase (TβGal). AAV was administered intravenously to the GM1-gangliosidosis mouse models. TβGal expressed in the liver was secreted into the blood and efficiently penetrated the CNS as well as peripheral organs. Substrates in the CNS decreased in a dose-dependent manner. The data also demonstrated efficacy of TβGal in survival, histology, and behavioral evaluations. This therapeutic approach, which is the combination of AAV and anti-TfR antibody fused biotherapeutics, is expected to be applied for the treatment of several hereditary neurological diseases with CNS involvement. Further evaluation is required.

About the Society for the Study of Inborn Errors of Metabolism (SSIEM)
Established in 1963, the aim of the society is to foster the study of inherited metabolic disorders and related topics. An international annual symposium is held to promote exchange of ideas between professional leaders in different disciplines who are interested in inborn errors of metabolism. Learn more about SSIEM: https://www.ssiem.org/.

About the J-Brain Cargo® Platform Technology
JCR Pharmaceuticals has developed a proprietary blood-brain barrier-penetrating technology J-Brain Cargo®, to bring biotherapeutics into the central nervous system. The first drug developed based on this technology is IZCARGO® (INN: pabinafusp alfa) and was approved in Japan for the treatment of a lysosomal storage disorder.

About Mucopolysaccharidosis I (Hurler, Hurler-Scheie, Scheie syndrome)
Mucopolysaccharidosis I ("MPS I") is an autosomal recessive lysosomal storage disorders ("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 3,000-4,000 (according to JCR internal 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 for the severe form of the disease. Significant unmet medical need persists in all forms of MPS I.

About GM1 Gangliosidosis
GM1 gangliosidosis is an autosomal recessive disease caused by pathogenic mutations in the *GLB1* gene which results in dysfunction or lack of production of lysosomal enzyme, β-galactosidase, responsible for the breakdown of GM1 gangliosides and other glycolipids. Accumulation of GM1 gangliosides in multiple tissues including the brain leads to severe neurodegeneration and systemic disease manifestations resulting in premature mortality. GM1 gangliosidosis is classified into three forms (Type I to III) based on the age of onset of clinical symptoms.

About JR-171
JR-171 is a recombinant fusion protein of an antibody against the human transferrin receptor and α-L-

iduronidase, the enzyme that is missing or malfunctioning in patients with MPS I. By crossing the blood brain-barrier ("BBB") through transferrin receptor mediated transcytosis it is expected to be effective against central nervous system ("CNS") signs and symptoms of the disease thereby addressing a significant unmet need for the treatment of MPS I. JR-171 previously was granted Fast Track designation by the US Food and Drug Administration ("FDA").

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 persistence – benefit all our stakeholders, including employees, partners, and patients. 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.

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

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