News Release

April 21, 2020
JCR Pharmaceuticals Co., Ltd.

Translation

JCR to Initiate Development of New Drug Candidates for Sly Syndrome and Sanfilippo Syndrome Type B Using J-Brain Cargo®

JCR Pharmaceuticals Co., Ltd. (TSE 4552; Chairman and President: Shin Ashida; "JCR") announced today its decision to develop new drug candidates, JR-443, a blood-brain barrier (BBB)-penetrating β-glucuronidase for the treatment of patients with Sly syndrome, and JR-446, a BBB-penetrating α-N-acetylglucosaminidase for the treatment of patients with Sanfilippo syndrome type B, to both of which J-Brain Cargo®, JCR's proprietary BBB penetration technology, is applied.

JCR has initiated new development to treat Sly syndrome (MPS VII), which, in the same way as Hunter syndrome, is classified into as mucopolysaccharidosis (MPS), a type of lysosomal storage disorders (LSDs). It is caused by deficiency of an enzyme, β-glucuronidase, that brings about accumulations of heparan sulfate, dermatan sulfate, and chondroitin sulfate in tissues throughout the body, thus gives rise to bone deformation and joint contraction, as well as central nervous system (CNS) disorders in severe cases,.
Sanfilippo syndrome type B (MPS IIIB) is also a type of MPS, caused by deficiency of an enzyme, α-N-acetylglucosaminidase, bringing about heparan sulfate accumulation in tissues throughout the body. Notably, it leads to rapid progression of CNS disorders, whereby neurocognitive development, with its peak around 2 or 3 years of age, deteriorates thereafter.
In Japan, there is no approved therapeutics for enzyme replacement therapy for either disease, thus development of a new treatment option has long been awaited.

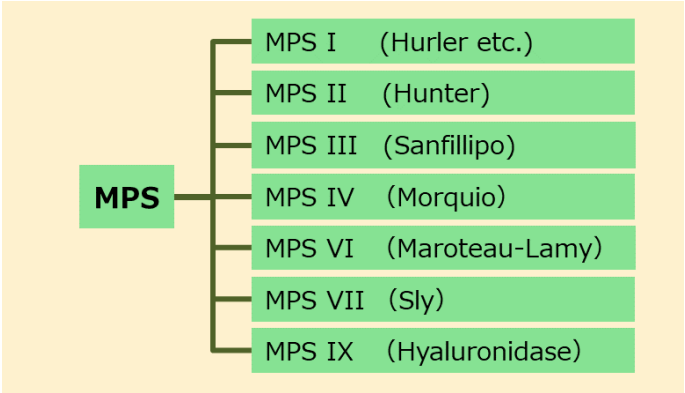
Animal studies with intravenously administered JR-443 and JR-446 demonstrated delivery of these compounds to the brain, along with reductions in intracerebral mucopolysaccharide accumulations. JCR is moving forward to devise developmental plans aiming to initiate clinical trials within three years.

JCR has conducted a series of development of therapeutic enzymes for LSDs that harness J-Brain Cargo® technology. As a specialty pharma devoted to the development of pharmaceutical products for rare diseases, JCR will accelerate its research and development activities to contribute to treatment for a broader patient population.

This new drug development is expected to have a minor impact on JCR's consolidated financial results for the year ending March 31, 2021.

Lysosomal storage disorders (LSDs)
LSDs are designated as intractable diseases by the Ministry of Health, Labour and Welfare. They are also classified as chronic pediatric diseases of specific categories. LSDs are diseases in which genetic defects or mutations in hydrolytic enzymes, membrane proteins that serve as oxygen transporters and other proteins within lysosomes, which are organelles found in cells, result in the accumulation of substrates that cannot be decomposed within the lysosomes. This condition causes disorders in cells and tissues. There is a wide range of clinical symptoms that can appear depending on the specific substrates that accumulate. CNS disorders are present in many cases of LSDs.

Mucopolysaccharidosis (MPS)
MPS is a type of LSDs. It is caused by a deficiency or decreased activity of enzymes needed to decompose mucopolysaccharides named glycosaminoglycans (GAGs), leading to excessive accumulation of GAGs in cells, which causes symptoms to appear in various parts of the body. GAG substrates mainly include dermatan sulfate, heparan sulfate, keratan sulfate, chondroitin sulfate, and hyaluronic acid. As the accumulating substrate varies depending on which enzyme is affected, they are classified into seven disease types based on the accumulated substrates and clinical symptoms.



Sly syndrome (MPS VII)
Sly syndrome is an autosomal recessive disease caused by a deficiency of the enzyme β-glucuronidase that metabolizes mucopolysaccharides within the body, leading to accumulations of heparan sulfate, dermatan sulfate, and chondroitin sulfate. Its symptoms include bone deformation, joint contraction, hepatomegaly, corneal clouding, valvular heart disease, and CNS disorders. Symptomatic and causal treatments are available, the latter including hematopoietic stem cell transplantation, which, however, cannot prevent the disease progression completely.

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, rapid progression of CNS disorders affects neurocognitive development, with a peak at 2 or 3 years of age, before subsequent deterioration leading to a complete loss of speech by the age of 7 or 8. Progression gives rise to symptoms such as sleep disorders, hepatosplenomegaly, and seizures. Hematopoietic stem cell transplantation can be a treatment option, but its effectiveness remains to be established.

[About JCR Pharmaceuticals]
JCR is a specialty pharma company engaged in the research, development, manufacturing and marketing of biopharmaceuticals and regenerative medicine with a focus on rare diseases. Its

philosophy, “Contributing towards people’s healthcare through pharmaceutical products” drives JCR to create innovative pharmaceutical products as value-added treatment options for the under-served patient populations.

[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 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.

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