

ABSTRACT SUMMARY

WORLDSymposium 2021

JCR Pharmaceuticals Co., Ltd. is a global specialty pharmaceuticals company that is redefining expectations and expanding possibilities for people with rare and genetic diseases worldwide.

Please note that the therapies mentioned within these abstracts are investigational therapies, and are not approved for commercial use. Any information on the investigational therapies contained herein is not intended to provide medical advice, nor should it be used as a substitute for the advice provided by your physician or other healthcare provider. Please visit the JCR Pharmaceuticals website for more information.

At WORLDSymposium 2021, JCR Pharmaceuticals is pleased to present a total of nine abstracts focusing on investigational therapies intended to treat LSDs.

Abstracts for JR-141 (pabinafusp alfa, for the treatment of patients with MPS II)

Abstract 84:

Exploration of the efficacy of pabinafusp alfa (JR-141) on neurocognitive development in Hunter syndrome (MPS-II): 52-week data from clinical trials in Japan and Brazil (Giugliani et al.)

Weekly treatment with JR-141 led to stabilization or improvement of neurocognition in 47 patients across the two trials (2.0 mg/kg for 52 weeks in Japan; 1.0, 2.0, and 4.0 mg/kg for 25 weeks in Brazil, followed by extension studies). Both studies found stabilization or improvement in developmental scores and positive changes in behavior, suggesting that JR-141 may ameliorate the neurological disease burden of MPS II, in addition to the somatic signs and symptoms of the disease.

Abstract 242:

Therapy for mucopolysaccharidosis type II with an intravenous blood-brain barrier-crossing enzyme (JR-141): Phase III global clinical trial design (So et al.)

Investigators present the design for a randomized, active-controlled, assessor-blinded global Phase III multinational trial to assess the efficacy and safety of JR-141 (2 mg/kg/week), compared to standard-of-care idursulfase, in patients with MPS II. JCR is planning to initiate a Phase 3 trial for JR-141 in the US, UK, Brazil, Germany, and France in the second quarter of 2021.

For more information:

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Abstract 176:

Drug delivery across the blood-brain barrier and resultant heparan sulfate in the cerebrospinal fluid in patients with Hunter syndrome (MPS-II): an integrated analysis of 25-week Japanese and Brazilian data on pabinafusp alfa (JR-141) (Okuyama et al.)

In the two studies described above, HS concentrations in the CSF – the studies' primary endpoint – were reduced significantly after treatment with JR-141. As the potential neurocognitive effects of JR-141 are thought to result from substrate reduction in the CNS, HS levels in the CSF may serve as both a valid surrogate endpoint and as a clinically informative indicator of treatment response and prognosis.

Abstract LB-50:

A comparison of developmental trajectories in sibling cases with neuropathic MPS-II receiving conventional and novel enzyme replacement therapies (Tomita et al.)

This case report focuses on two siblings with MPS II: Sibling 1 was diagnosed at 2 years of age and started conventional ERT soon thereafter; Sibling 2 was diagnosed prenatally, received conventional ERT from 1 month to nearly 2 years of age, and then switched to JR-141. Compared to Sibling 1, Sibling 2 exhibited notable preservation of neurocognitive development, as well as a significant decline in CSF HS levels. The marked difference in the developmental trajectories in these siblings highlights the importance of early diagnosis and treatment in MPS II, along with potential benefits of brain-penetrating ERT.

Abstract 163:

Reduction of heparan sulfate in the brain by pabinafusp alfa results in prevention of neurodegeneration and neurocognitive impairment in a mouse model of mucopolysaccharidosis II (Morimoto et al.)

A 36-week course of JR-141 (2 mg/kg once weekly or 4 mg/kg biweekly) reduced HS deposition in the brain in a mouse model of MPS II. The reduced HS deposition in the brain correlated with reduction of the substrate in the CSF and retention of spatial learning ability in the MPS II mice. The data further suggest that CSF HS levels may serve as a valuable surrogate biomarker for the effectiveness of JR-141 in addressing the neurological disease burden in MPS II.

Abstracts for JR-171 (for the treatment of patients with MPS I)

Abstract 99:

Phase I/II clinical trial design for a novel therapy for mucopolysaccharidosis type I with an intravenously administered blood-brain barrier-crossing enzyme (JR-171) (Higurashi et al.)

Investigators present the design for a global, first-in-human, open-label, multicenter Phase I/II trial assessing the safety, plasma pharmacokinetics, and efficacy of once-weekly intravenous infusions of JR-171 in patients with MPS I.

Abstracts for additional investigational therapies, for the treatment of patients with Pompe disease, MPS IIIA - Sanfilippo A, and MPS IIIB - Sanfilippo B

Abstract 94:

Usefulness of hexose tetrasaccharide as a biomarker for monitoring glycogen accumulation in peripheral tissues and brain in Pompe disease (Hashimoto et al.)

Intravenous administration of JR-162, a BBB-penetrating fusion protein consisting of a Fab consisting of an anti-hTfR antibody and acid α -glucosidase (GAA, the gene implicated in Pompe disease), markedly reduced glycogen accumulation in peripheral tissues and the brain in a mouse model of Pompe disease. JR-162 also reduced hexose tetrasaccharide (Hex4) concentrations in the urine and CSF, correlating highly with glycogen concentrations in peripheral tissues and the brain, respectively. The results validate urinary Hex4 as a biomarker for monitoring glycogen accumulation and demonstrate the utility of Hex4 in the CSF as a predictor of glycogen concentrations in the brain.

Abstract 252:

Non-clinical evaluation of a blood-brain barrier-penetrable N-sulfoglucosamine sulfohydrolase in a mouse model of Mucopolysaccharidosis IIIA (Tanaka et al.)

JR-441, a fusion protein consisting of a Fab fragment of an anti-hTfR antibody and N-sulfoglucosamine sulfohydrolase (SGSH, the gene implicated in MPS IIIA), penetrates the brain by crossing the BBB and reduces the accumulated substrate when administered intravenously in a mouse model of MPS IIIA (Sanfilippo syndrome type A). The data suggest that JR-441 has the potential to exert a therapeutic benefit on the CNS sequelae of MPS IIIA.

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Abstract 103:

Non-clinical evaluation of a blood-brain barrier-penetrable α -N-acetylglucosaminidase in a mouse model of mucopolysaccharidosis IIIB (Imakiire et al.)

JR-446, a fusion protein consisting of a Fab fragment of an anti-hTfR antibody and α -N-acetylglucosaminidase (NAGLU, the gene implicated in MPS IIIB), distributes to the brain by crossing the BBB and reduces the accumulated substrate when administered intravenously in a mouse model of MPS IIIB (Sanfilippo syndrome type B). The data suggest that JR-446 has the potential to exert therapeutic effects on the CNS signs and symptoms of MPS IIIB.

We continue to make progress with our investigational therapy JR-141 for the treatment of patients with MPS II (Hunter syndrome). In December 2020, we filed an application for marketing approval of JR-141 in Brazil, which, when accepted, will mark our first approved therapy outside of Japan. JCR is planning to initiate a Phase 3 trial for JR-141 in the US, UK, Brazil, Germany, and France in the second half of 2021.

Additionally, we continue to move forward with our investigational therapy JR-171 for the treatment of patients with MPS I (Hurler Syndrome, etc.). The first patient was dosed in a global Phase 1/2 clinical trial of JR-171 in October 2020. We are also developing therapies for patients with LSDs including Pompe disease, MPS IIIA (Sanfilippo A), and MPS IIIB (Sanfilippo B).

Our first-in-class proprietary technology, J-Brain Cargo[®], enables us to develop therapies that cross the BBB and penetrate the CNS. With J-Brain Cargo[®], we seek to address the unresolved clinical challenges of LSDs by delivering the enzyme to both the body and the brain. We strive to expand the possibilities for patients while accelerating medical advancement at a global level.

LSD: Lysosomal storage disorders

MPS: Mucopolysaccharidosis

ERT: Enzyme replacement therapy

CNS: Central nervous system

BBB: Blood-brain barrier

Fab: Antigen-binding fragment

hTfR: Human transferrin receptor

HS: Heparan sulfate

CSF: Cerebrospinal fluid



Together we soar.

At JCR, we continue to build upon our **45-year legacy** in Japan while expanding our global footprint with clinical trials in the **US, Europe, and Latin America.**

We are applying our scientific expertise and unique technologies to research, develop, and deliver next-generation therapies to patients with LSDs.

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