MEDIPAL HOLDINGS CORPORATION

News Release

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Translation

MEDIPAL HOLDINGS CORPORATION
JCR Pharmaceuticals Co., Ltd.

MEDIPAL HOLDINGS CORPORATION and JCR Pharmaceuticals Announce Initiation of First Dosing in Phase I/II Clinical Trial of JR-446 for Mucopolysaccharidosis Type IIIB in Japan

- The study aims to evaluate the safety, tolerability, and preliminary efficacy of JR-446 for the treatment of individuals with MPS IIIB, for which there is no approved treatment -

Tokyo and Hyogo, Japan – Dec. 3, 2024 – MEDIPAL HOLDINGS CORPORATION (TSE 7459, MEDIPAL) and JCR Pharmaceuticals Co., Ltd. (TSE 4552, JCR) today announced the initiation of the Phase I/II clinical trial of JR-446 in Japan following the dosing of the first individual from the trial. JR-446 is a proprietary blood-brain barrier (BBB)-penetrating α-N-acetylglucosaminidase in development for the treatment of mucopolysaccharidosis type IIIB (Sanfilippo syndrome type B or MPS IIIB).

MPS IIIB affects an estimated 500 to 1,000 individuals worldwide[1], causing severe central nervous system (CNS) symptoms. Despite the dire need, there are currently no approved treatments available for this condition. JR-446, developed using JCR's proprietary J-Brain Cargo® technology, has shown promising non-clinical results in addressing the symptoms of this challenging disorder.

This Phase I/II clinical trial is an open-label, single-arm, multi-center study that includes individuals under 18 years of age who are diagnosed with MPS IIIB. The study aims to evaluate the safety, tolerability, and exploratory efficacy of JR-446, while also assessing the optimal dosage through the administration of multiple doses. For more details on the trial, visit the Clinical Research Submission and Disclosure System (JR-446-101, jRCT2071240043)

"We are pleased to be advancing a long-awaited treatment option for MPS IIIB, a condition for which there are no approved therapies," said Dr. Motomichi Kosuga, Medical Director of the Division of Medical Genetics, National Center for Child Health and Development, and the Medical Expert of the study. "In Japan, MPS IIIB is one of the more frequently observed forms of MPS III, and it primarily affects the CNS, leading to severe symptoms. This trial represents a hopeful step forward in addressing these neurological challenges, and we sincerely hope it will bring meaningful improvements in both the medical outlook and quality of life for patients and their families."

In September 2023, MEDIPAL and JCR entered into a licensing agreement in which MEDIPAL will commercialize JR-446 outside of Japan. In addition, MEDIPAL will support JCR in the clinical development of JR-446 in Japan, including the distribution of investigational drugs, disease awareness, and clinical trial advancement[2].
This collaboration highlights the commitment of MEDIPAL and JCR to pioneer treatments for ultra-rare diseases. By advancing therapies like JR-446, we aim to bring hope to patients and their families, while enhancing corporate value and contributing to a society where everyone can live with physical and mental well-being.

About Mucopolysaccharidosis Type IIIB (Sanfilippo Syndrome Type B)
Mucopolysaccharidosis type IIIB, or Sanfilippo syndrome type B, is an autosomal recessive disease caused by pathogenic mutations in the *NAGLU* gene, encoding a lysosomal enzyme involved in the degradation of heparan sulfate. With the accumulation of heparan sulfate in the central nervous system in the brain, individuals with this condition present rapid neurological decline, including sleep disorders, loss of speech, and behavioral changes, which may significantly affect the quality of life of patients and their families.

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 MEDIPAL HOLDINGS CORPORATION
MEDIPAL is a holding company which controls, administers and supports the operating activities of companies in which it holds shares in the Prescription Pharmaceutical Wholesale Business; the Cosmetics, Daily Necessities and OTC Pharmaceutical Wholesale Business; and the Animal Health Products and Food Processing Raw Materials Wholesale and Related Business, and conducts business development for the MEDIPAL Group. For more information, visit https://www.medipal.co.jp/english/.

About JCR Pharmaceuticals Co., Ltd.
JCR is a global specialty pharmaceuticals company dedicated to advancing treatments for rare and genetic diseases. With nearly 50 years of expertise in Japan, we are expanding to the US, Europe, and Latin America. Our innovative therapies address conditions like growth disorder, MPS II, Fabry disease, acute graft-versus-host disease, and renal anemia. We are also developing treatments for rare diseases like MPS I, MPS II, MPS IIIA and B, and more. Our core values of reliability, confidence, and persistence drive our mission to enhance global medical progress. For more information, 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. Based on data from the Ministry of Health, Labour and Welfare's public research and JCR's own investigations.
2. Reference: Press release on the licensing agreement for JR-446 between MEDIPAL and JCR (September 28, 2023).

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