Takeda to Commercialize Next-Generation Hunter Syndrome Therapy Through Collaboration with JCR Pharmaceuticals

- ***JR-141 is a potentially transformative therapy designed to deliver proteins to the brain and peripheral tissues to treat neuronopathic features along with somatic symptoms of Hunter syndrome via intravenous administration***
- ***Takeda to exclusively commercialize JR-141 outside the U.S. (except Japan and certain other Asia-Pacific countries) upon regulatory approval***
- ***Takeda receives a separate option to obtain an exclusive license to commercialize in the U.S. after completion of the global Phase 3 program***

Osaka and Hyogo, Japan, September 30, 2021 – Takeda Pharmaceutical Company Limited (TSE:4502/NYSE:TAK) ("Takeda") and JCR Pharmaceuticals Co., Ltd. (TSE:4552) ("JCR") announced today a geographically-focused exclusive collaboration and license agreement to commercialize JR-141 (INN: pabinafusp alfa), an investigational, next-generation recombinant fusion protein of an antibody against the human transferrin receptor and iduronate-2-sulfatase (IDS) enzyme for the treatment of Hunter syndrome (also known as Mucopolysaccharidosis type II or MPS II). Hunter syndrome is caused by a deficiency of IDS and manifests in different forms. JR-141, applied with J-Brain Cargo®, JCR's proprietary blood-brain barrier (BBB) technology, is engineered to transport the therapeutic enzyme across the BBB to directly reach the brain and address both the somatic and neuronopathic manifestations of the disease, which can lead to progressive cognitive decline.

Under the terms of the exclusive collaboration and license agreement, Takeda will exclusively commercialize JR-141 outside of the United States, including Canada, Europe, and other regions (excluding Japan and certain other Asia-Pacific countries). JCR will receive an upfront payment for such ex-U.S. license, and is eligible to receive additional development and commercial milestones as well as tiered royalties on potential sales. The two companies will collaborate to bring this therapy to patients as quickly as possible upon completion of the global Phase 3 program, which will be conducted by JCR.

Takeda receives an option under a separate option agreement, which allows Takeda to acquire an exclusive license to commercialize JR-141 in the U.S. upon completion of the Phase 3 program.

"Takeda is committed to continuously improving the way Hunter syndrome is treated. JR-141 introduces a new way to deliver proteins across the blood-brain barrier, overcoming our current challenges to treat the underlying neuronopathic manifestations of Hunter syndrome and help maintain or improve cognitive function in these patients," said Dan Curran, M.D., Head, Rare Genetics & Hematology Therapeutic Area Unit at Takeda. "We will work closely with JCR to apply our expertise in enzyme replacement therapies with the hope of bringing this potentially transformative therapy to patients as quickly as possible."

"JCR is pleased to have reached an agreement with Takeda who is well placed to achieve our common goal of maximizing the impact of JR-141," said Shin Ashida, President, Chairman of JCR. "Our mission is to provide transformative treatment options as soon as possible to patients with lysosomal storage disorders (LSDs) with central nervous system symptoms, such as Hunter syndrome. JR-141 is the first-ever approved biopharmaceutical in Japan that penetrates the blood-brain barrier. I expect that we will be able to achieve this mission through our partnership with Takeda to deliver a new treatment option to Hunter patients around the world as swiftly as possible."

JR-141 met its primary endpoint in an open-label Phase 2/3 clinical trial in Japan demonstrating significant reductions in heparan sulfate (HS) in the cerebrospinal fluid, a biomarker for assessing the drug's effectiveness in reducing disease-causing substrate in the central nervous system, in all subjects for whom measurements were available after 52 weeks of treatment. Somatic disease control was maintained in patients who switched from standard enzyme replacement therapy (ERT). The study also demonstrated an improvement in somatic symptoms in participants who had not previously received standard ERT prior to the start of the trial. Additionally, a neurocognitive development assessment demonstrated maintenance or improvement of age-equivalent function in 21 of the 25 patients at one year. There were no reports of serious treatment-related adverse events in the trial.[1]

About JR-141

JR-141 is a recombinant fusion protein of an antibody against the human transferrin receptor and iduronate-2-sulfatase, the enzyme that is missing or malfunctioning in subjects with Hunter syndrome. It is expected to be effective against the neuronopathic manifestations of the disease by crossing the BBB through transferrin receptor mediated transcytosis using J-Brain Cargo®, JCR's proprietary BBB technology. Uptake into cells is mediated through the transferrin receptor and mannose-6-phosphate receptor. JCR has advanced development activities by establishing the necessary evidence from the molecular design stage to the nonclinical and clinical trial phases. In non-clinical trials, JCR has confirmed both high affinity binding of JR-141 to transferrin receptors, and passage across the BBB into neuronal cells as evidenced by electron microscopy.

In addition, JCR has confirmed that using J-Brain Cargo® technology, enzymes are taken up into various brain tissues. A decrease in substrate accumulation has also been confirmed in an animal model of Hunter syndrome.[2,3,4]

In several clinical trials with JR-141, JCR obtained evidence of reduction of heparan sulfate concentrations in the CSF, a biomarker for assessing the drug's effectiveness in reducing disease-causing substrate in the central nervous system, consistent with the results obtained from non-clinical studies. JCR also obtained clinical results that demonstrate positive effects of JR-141 on neurocognition.[5,6,7,8]

JR-141 was approved by the Ministry of Health, Labour and Welfare and marketed since May 2021 under the brand name "IZCARGO® I.V. Infusion 10mg."

About Hunter Syndrome

Hunter syndrome is a severely debilitating, rare lysosomal disease caused by a deficiency of iduronate-2-sulfatase, an enzyme that is needed to break down substances in the body called glycosaminoglycans (GAGs).[9] Without this enzyme, GAGs can build up, causing a range of disease-related signs and symptoms.[9,10] Roughly two of every three patients with Hunter syndrome are also affected with progressive cognitive decline.[11] Hunter syndrome affects 1 in 162,000 total live births, and almost exclusively males.[12]

About Takeda Pharmaceutical Company Limited

Takeda Pharmaceutical Company Limited (TSE: 4502/NYSE: TAK) is a global, values-based, R&D-driven biopharmaceutical leader headquartered in Japan, committed to discover and deliver life-transforming treatments, guided by our commitment to patients, our people and the planet. Takeda focuses its R&D efforts on four therapeutic areas: Oncology, Rare Genetics and Hematology, Neuroscience, and Gastroenterology (GI). We also make targeted R&D investments in Plasma-Derived Therapies and Vaccines. We are focusing on developing highly innovative medicines that contribute to making a difference in people's lives by advancing the frontier of new treatment options and leveraging our enhanced collaborative R&D engine and capabilities to create a robust, modality-diverse pipeline. Our employees are committed to improving quality of life for patients and to working with our partners in health care in approximately 80 countries and regions. For more information, visit https://www.takeda.com.

About JCR Pharmaceuticals Co., Ltd.

JCR Pharmaceuticals Co., Ltd. (TSE 4552) is a global specialty pharmaceuticals company that is redefining expectations and expanding possibilities for people with rare and genetic diseases worldwide. We continue to build upon our 46-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, 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 (Hunter syndrome), Pompe disease, 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. Together we soar. For more information, please visit https://www.jcrpharm.co.jp/en/site/en/.

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The companies in which Takeda directly and indirectly owns investments are separate entities. In this press release, "Takeda" is sometimes used for convenience where references are made to Takeda and its subsidiaries in general. Likewise, the words "we", "us" and "our" are also used to refer to subsidiaries in general or to those who work for them. These expressions are also used where no useful purpose is served by identifying the particular company or companies.

Forward-Looking Statements

This press release and any materials distributed in connection with this press release may contain forward-looking statements, beliefs or opinions regarding Takeda's future business, future position and results of operations, including estimates, forecasts, targets and plans for Takeda. Without limitation, forward-looking statements often include words such as "targets", "plans", "believes", "hopes", "continues", "expects", "aims", "intends", "ensures", "will", "may", "should", "would", "could" "anticipates", "estimates", "projects" or similar expressions or the negative thereof. These forward-looking statements are based on assumptions about many important factors, including the following, which could cause actual results to differ materially from those expressed or implied by the forward-looking statements: the economic circumstances surrounding Takeda's global business, including general economic conditions in Japan and the United States; competitive pressures and developments; changes to applicable laws and regulations, including global health care reforms; challenges inherent in new product development, including uncertainty of clinical success and decisions of regulatory authorities and the timing thereof; uncertainty of commercial success for new and existing products; manufacturing difficulties or delays; fluctuations in interest and currency exchange rates; claims or concerns regarding the safety or efficacy of marketed products or product candidates; the impact of health crises, like the novel coronavirus pandemic, on Takeda and its customers and suppliers, including foreign governments in countries in which Takeda operates, or on other facets of its business; the timing and impact of post-merger integration efforts with acquired companies; the ability to divest assets that are not core to Takeda's operations and the timing of any such divestment(s); and other factors identified in Takeda's most recent Annual Report on Form 20-F and Takeda's other reports filed with the U.S. Securities and Exchange Commission, available on Takeda's website at: https://www.takeda.com/investors/sec-filings/ or at www.sec.gov. Takeda does not undertake to update any of the forward-looking statements contained in this press release or any other forward-looking statements it may make, except as required by law or stock exchange rule. Past performance is not an indicator of future results and the results or statements of Takeda in this press release may not be indicative of, and are not an estimate, forecast, guarantee or projection of Takeda's future results.

JCR Pharmaceuticals 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.

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