FY2019 First-Half Results Briefing Session
- Research and Development Highlights -

November 6, 2019

JCR Pharmaceuticals Co., Ltd.

【Securities code】 4552, 1st Sec. TSE

FORWARD-LOOKING STATEMENT

This presentation contains, and answers given to questions that may be asked today may constitute, forward-looking statements that are subject to a number of risks and uncertainties, many of which are outside our control. All forward-looking statements regarding our plans, outlook, strategy and future performance are based on judgments derived from the information available to us at this time.

All forward-looking statements speak only as of the date of this presentation.
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.

FORWARD-LOOKING STATEMENT

The clinical development data published in this document is the result at the time of the interim analysis. It does not guarantee future results, nor does it guarantee the efficacy or effects of products under development. This document is not intended to guarantee and advertise the efficacy of the product under development.

The clinical development data published in this document includes data not yet published in academic journals that have been presented at academic conferences or peer-reviewed. We will try to make it public in the future.

In accordance with the Fair Disclosure Rules, data other than those listed in this document will not be disclosed in questions and answers. We appreciate your understanding.

R&D News Release Highlights
(from May to October, 2019)

R&D for Lysosomal Storage Disorders（LSDs）

① Report on Clinical Study of JR-141

② Progress of Other LSDs Pipeline

Progress of Other R&D Pipeline

Development Pipeline

■ Lysosomal Storage Disorders (LSDs) ■ Other Recombinant Protein Therapeutics
■ Regenerative Medical Product

As of Nov. 6, 2019

Code	Indication	Preclinical	Clinical trials	Filed	Approved	Remarks
JR-141	Hunter syndrome	Phase 3 / Phase 2				• ERT • J-Brain Cargo®
JR-162	Pompe disease	Preclinical				• ERT • J-Brain Cargo® • J-MIG System®
JR-171	Hurler syndrome Hurler-Scheie syndrome Scheie syndrome	Preclinical				• ERT • J-Brain Cargo® • J-MIG System®
JR-441	Sanfilippo syndrome type A	Preclinical				• ERT • J-Brain Cargo® • J-MIG System®
Darbepoetin Alfa BS Inj. [JCR] (JR-131)	Renal anemia	Approved				• Co-developed with Kissei Pharmaceutical Co., Ltd. • Biosimilar
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JR-041	Infertility	Phase 1/2				• Out-licensed to ASKA Pharmaceutical Co., Ltd.
JR-142	pediatric growth hormone deficiency	Phase 1				• Long-acting human growth hormone product • J-MIG System®
JR-031EB	Epidermolysis bullosa	Suspended (Application withdrawn)				• Expanded indication of TEMCELL®HS Inj.
JR-031HIE	Hypoxic ischemic encephalopathy in neonates	Phase 1/2				• Expanded indication of TEMCELL®HS Inj.
JTR-161/ JR-161	Acute cerebral infarction	Phase 1/2				• Co-developed with Teijin Limited

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Progress of Other R&D Pipeline

May 21 JR-142 : Initiation of Phase 1 study

JR-142 Long-acting growth hormone (rDNA origin)

Indication **Pediatric growth hormone deficiency**

JCR's proprietary half-life extension technology based on a novel modified albumin allows various biotherapeutic products to increase drug half-life significantly

Patent filed

- **May 2019 : Phase 1 study Started**

Phase 1 study design

- Subjects : 31 healthy adult males
- Endpoint : safety and pharmacokinetics

▶ Administration completed and under follow-up

Jun. 10 JR-031HIE : Initiation of Phase 1/2 study

JR-031HIE Human mesenchymal stem cells
(Expanded indication of TEMCELL®HS Inj.)

Indication **Hypoxic ischemic encephalopathy in neonates**

- Cause : an insufficient supply of oxygen to the brain of a newborn due to reduced cerebral blood flow either in the womb or during delivery
- Disease condition : delayed acquisition of motor skills or neurodevelopment, and cerebral palsy
- Prevalence* : **2.5 of 1,000 live births** *Internal analysis
- Treatment : Hypothermia therapy (cannot be effective in around half of cases)

➡ More effective therapies are needed

- **Jul. 2019 : Phase 1/2 study Started**

▶ Administration started; ongoing

Sep. 19 JR-031EB : Withdrawal of Application for Additional Marketing Approval

JR-031EB Human mesenchymal stem cells
(Expanded indication of TEMCELL®HS Inj.)

Indication **Epidermolysis bullosa(EB)**

- Cause : Hereditary disorder of abnormal gene expressed in the cutaneous basement membrane zone
- Disease condition : Slight friction may cause the skin to detach from its basement membrane, producing burn-like blisters and ulcers

News Release (Excerpt)

Following the filing of the application for EB in March 2019, JCR has had extensive discussions with the regulatory agency. However, in the aim to demonstrate the efficacy of TEMCELL for EB with more clarity, JCR decided to withdraw this application for the time being.

JCR will continue discussions with the regulatory agency to pursue the development of JR-031EB.

Sep. 20 JR-131 : Marketing Approval

JR-131

Darbepoetin Alfa (recombinant) [Darbepoetin Alfa Biosimilar 1]

Darbepoetin Alfa BS Injection [JCR]

Indication **Renal anemia**

- Disease overview : a subtype of anemia caused by insufficient production of erythropoietin due to kidney failure

- **Sep. 2013 : Co-development agreement with Kissei Pharmaceutical Co., Ltd.**
  - Phase 3 study : demonstrated equivalence in efficacy and safety compared with darbepoetin alfa

▶ Sep. 20, 2019 : marketing approval

Marketing KISSEI

Manufacturing JCR Pharmaceuticals

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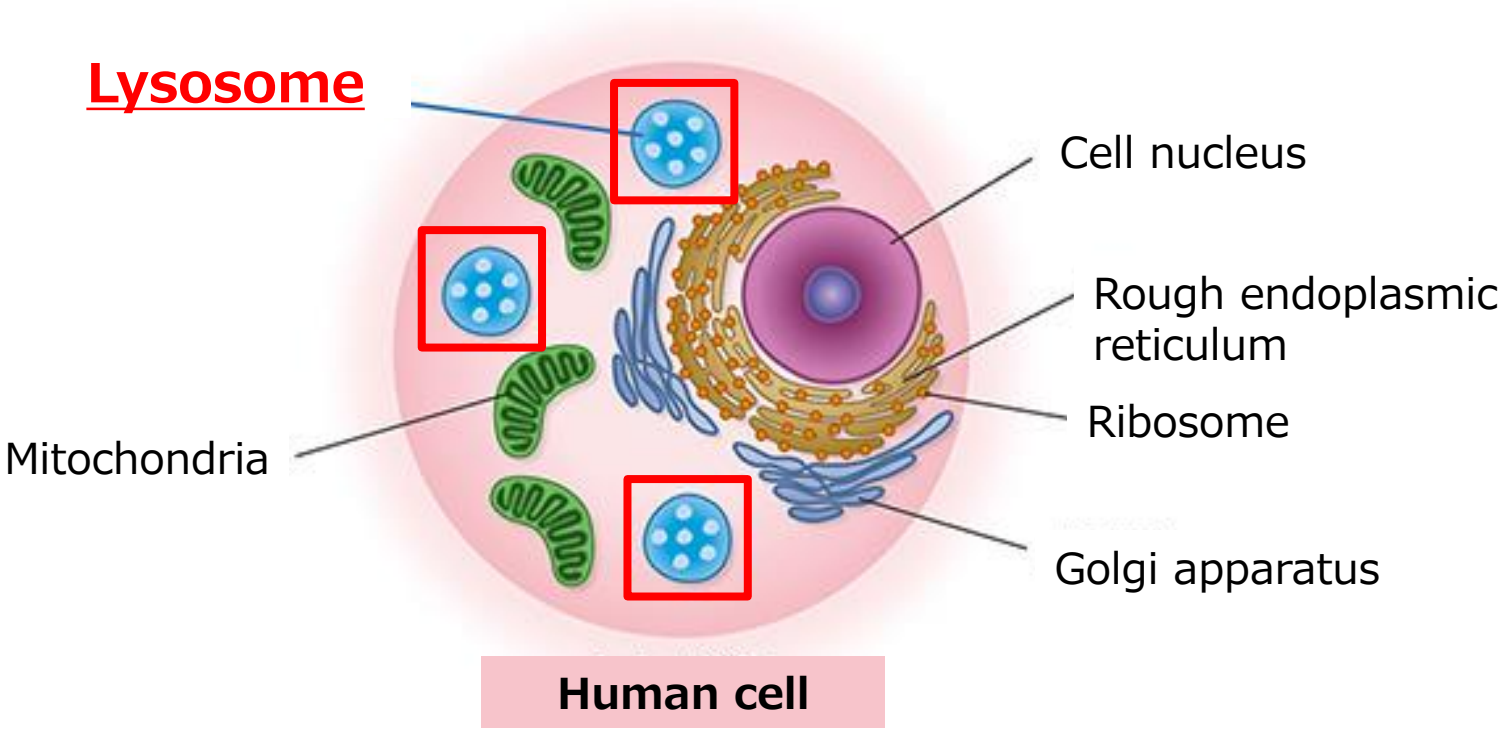
Progress of Other R&D Pipeline

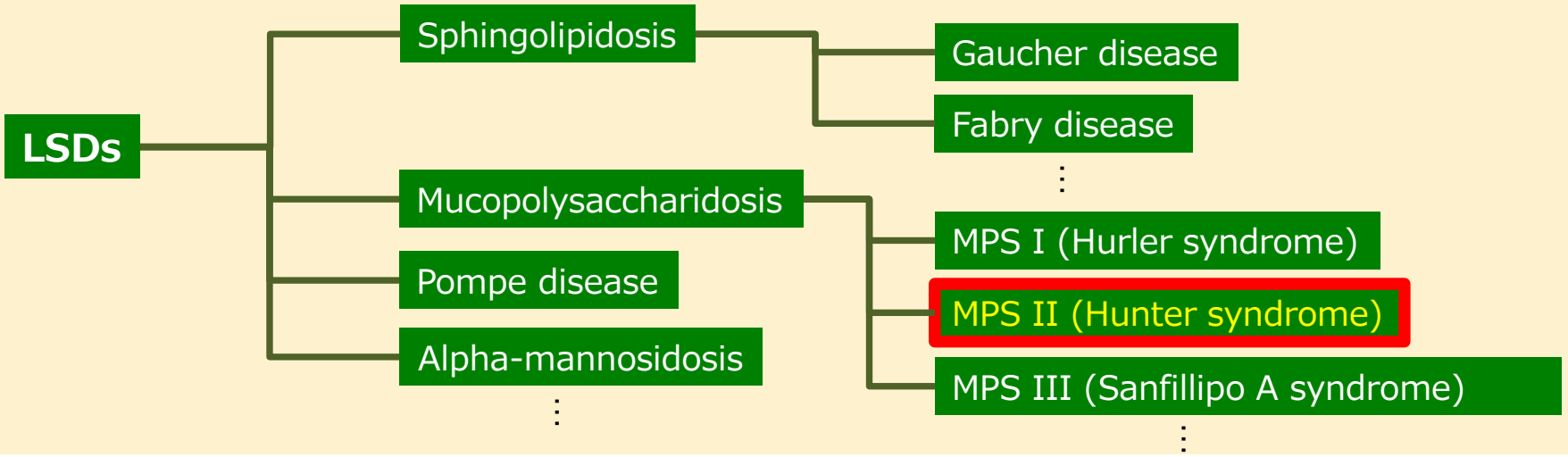
Lysosomal Storage Disorders (LSDs)

LSD is a group of rare inherited disorders in which one of enzymes in the lysosomes is congenitally missing or its function is deficient, resulting in the accumulation of metabolic wastes which fail to dissolve. Its symptoms vary depending on the affected enzymes and the accumulating substrates.
It is designated by MHLW as an intractable disease as well as a specific pediatric chronic disease.



R&D for Lysosomal Storage disorders（LSDs）

hereditary metabolic disorders



JR-141 BBB-penetrating iduronate-2-sulfatase (rDNA origin)

Indication **MPS type II（Hunter syndrome)**

BBB : Blood Brain Barrier

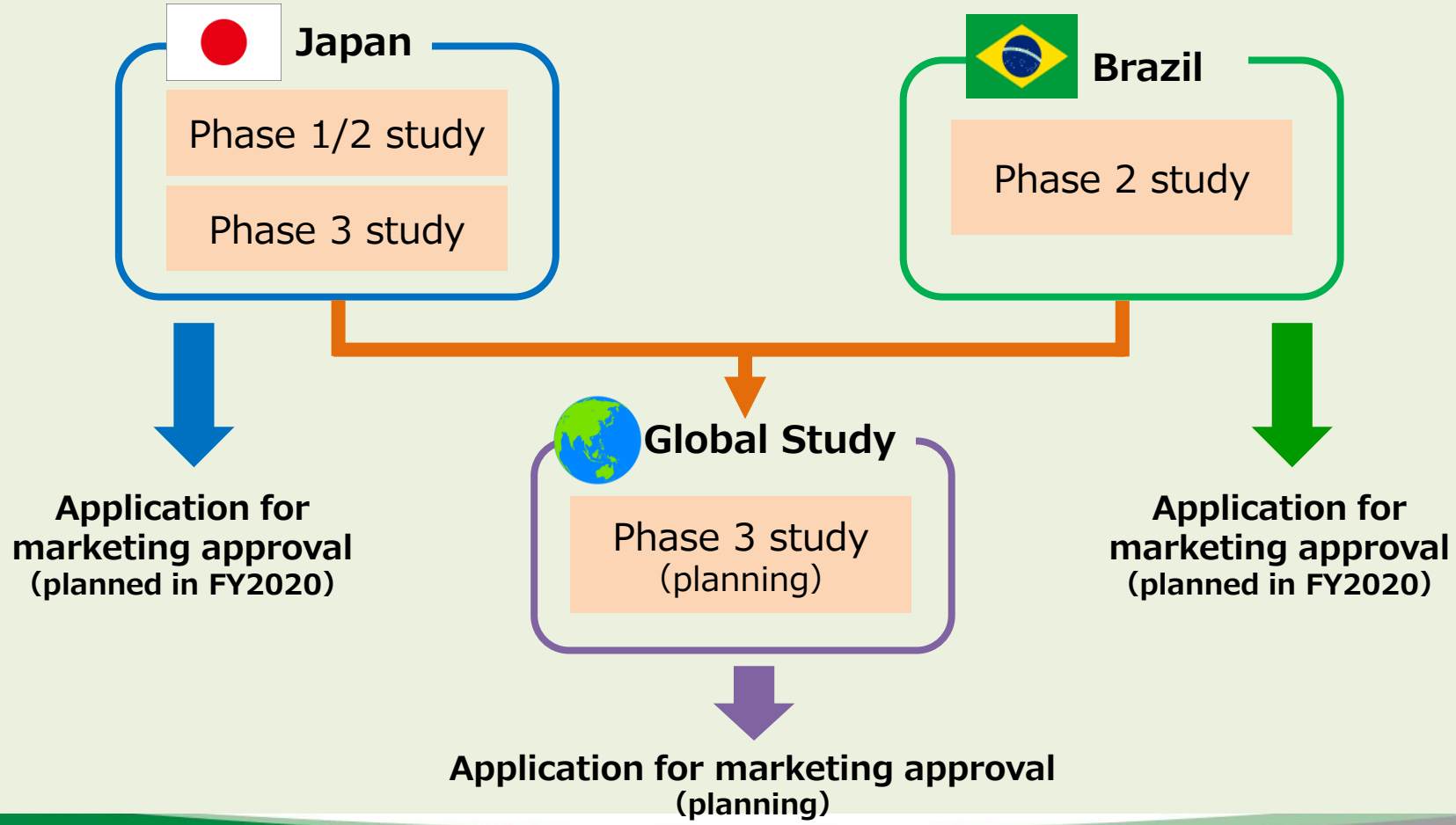
- Patient population*: **250** (Japan) , **7,800** (WW) est. *Internal analysis
- Market size*: **8.4 billion JPY** est. (2018 Japan), **100 billion JPY** est. (2018 WW)
- Disease overview: A deficiency of iduronate-2-sulfatase, causes an accumulation of glycosaminoglycans, leading to multiple systemic and central nervous system (CNS) symptoms.

Existing enzyme replacement therapy **does not show effect on CNS symptoms** due to non-penetration of BBB

JR-141 BBB-penetrating iduronate-2-sulfatase (rDNA origin)

Indication **MPS type II (Hunter syndrome)**

JR-141 Study Design



JR-141 BBB-penetrating iduronate-2-sulfatase (rDNA origin)

Indication **MPS type II (Hunter syndrome)**

Phase 1/2 study (JR-141-101): Study design

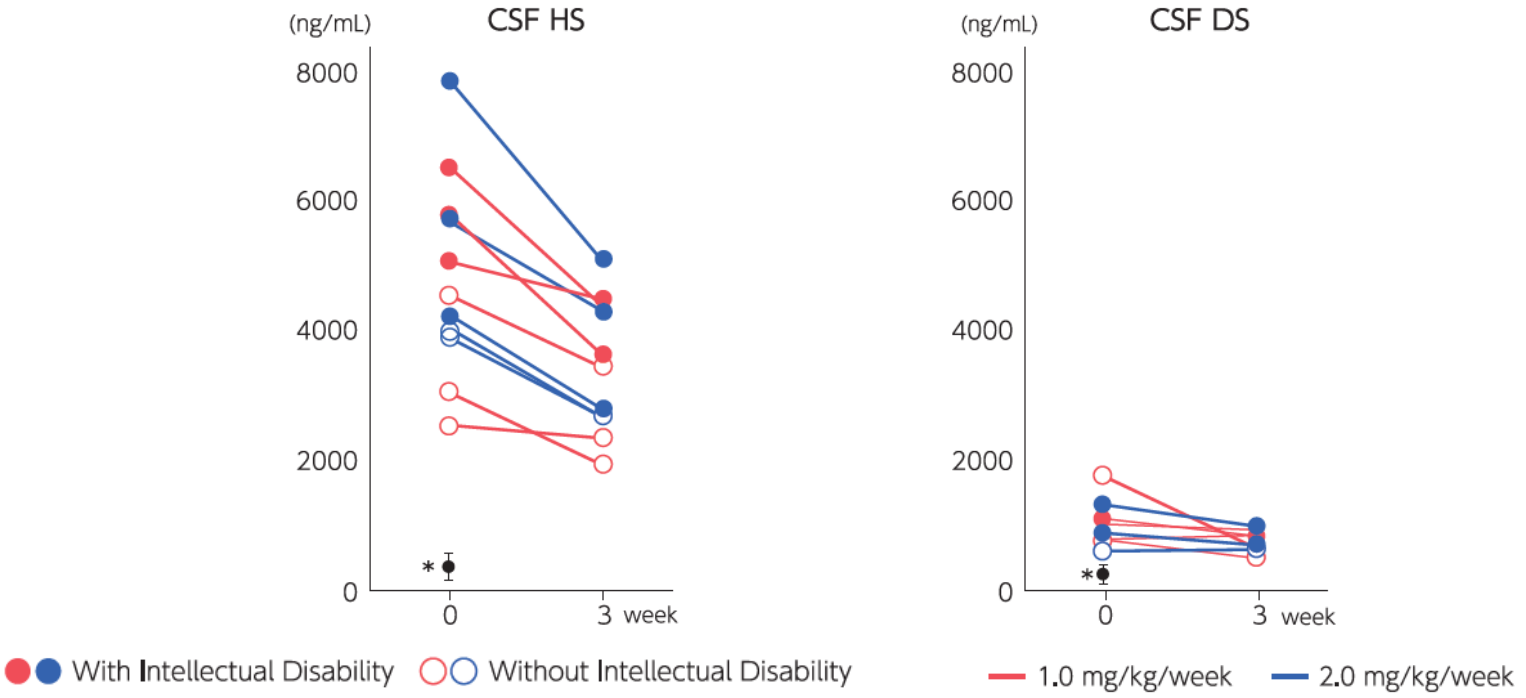
Endpoints	• Adverse Events, efficacy, pharmacokinetics • Change of Heparan Sulfate(HS) and Dermatan sulfate(DS) Levels in Cerebrospinal Fluid(CSF)
Route of administration	Intravenous
Number of Patients	14

Mol. Ther. 27(2), 456-454, 2019.

JR-141 BBB-penetrating iduronate-2-sulfatase (rDNA origin)

Indication **MPS type II (Hunter syndrome)**

Phase 1/2 study (JR-141-101): Part 2 Results



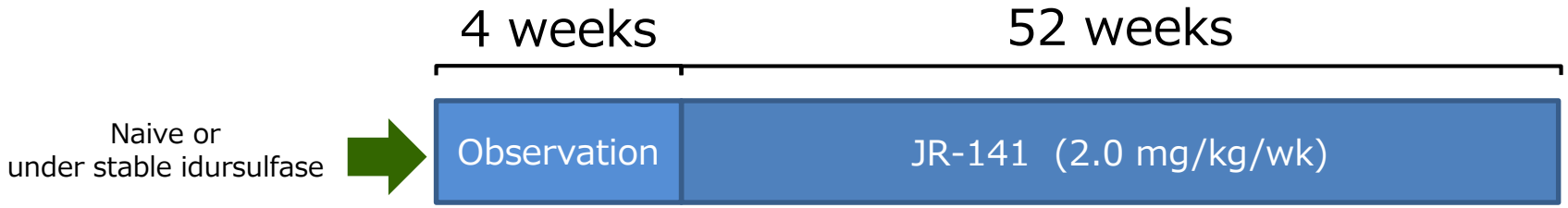
Decrease of HS in CSF indicates BBB-penetration of JR-141
(1.0mg/kg/w: 25.1±12.9% 2.0mg/kg/w: 31.5±3.9%)
These data suggest clinical significance of J-Brain Cargo®

Mol. Ther. 27(2), 456-454, 2019.

JR-141 BBB-penetrating iduronate-2-sulfatase (rDNA origin)

Indication **MPS type II (Hunter syndrome)**

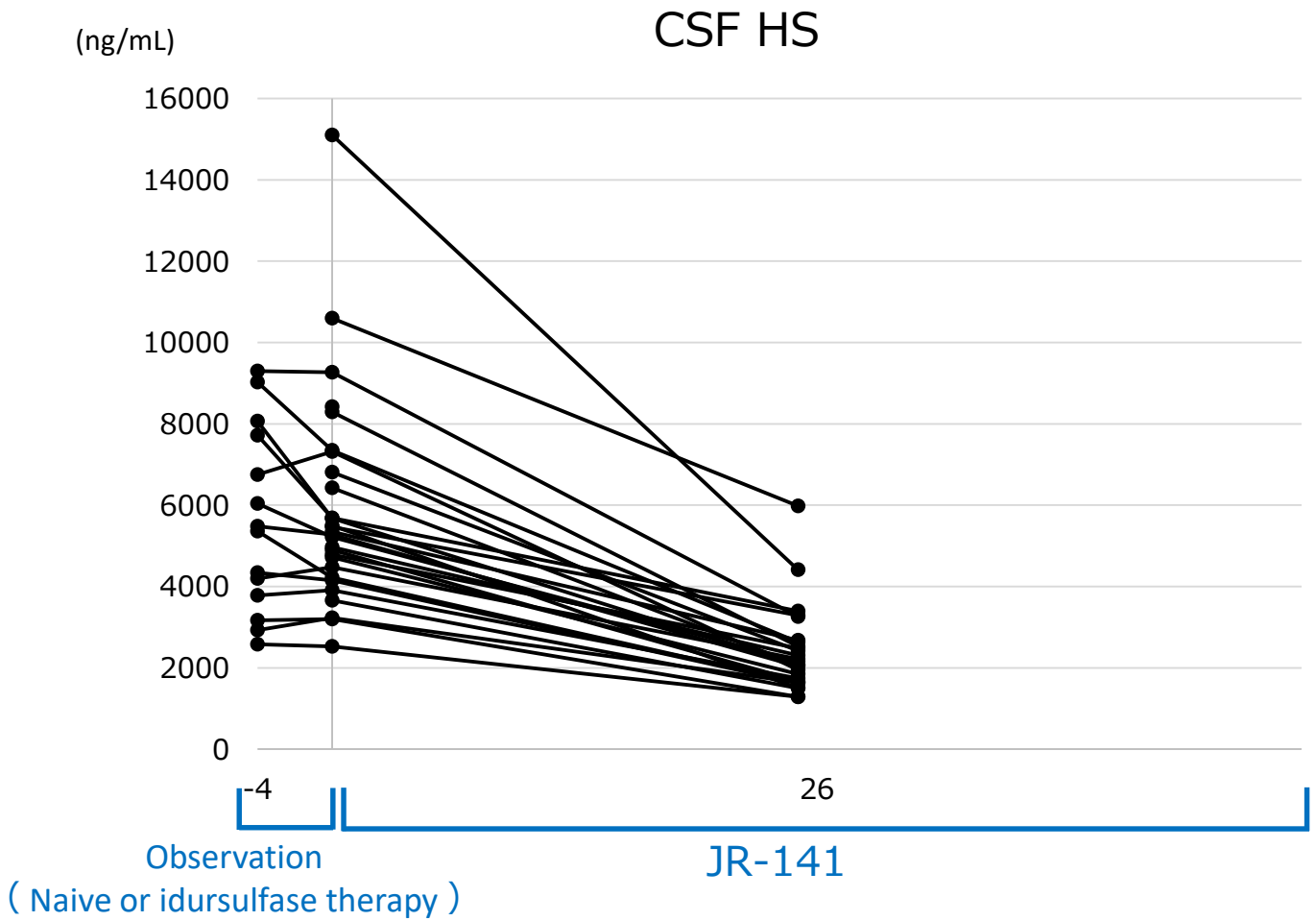
Phase 3 study (JR-141-301): Study design



Primary Endpoint	Change of HS in CSF
Secondary Endpoints	• Neurocognitive test, Adaptive behavioral test • HS and DS in serum and Urine • Liver Volumes, Spleen volumes • 6-minute walk test • Joint range of motion
Number of Patients	28

Interim evaluation to be made at the completion of 26-week infusion

Phase 3 study (JR-141-301): CSF HS concentrations



HS concentrations in CSF decreased in all patients after infusions for 26 weeks（Mean 58.4±9.5%）

Report on Clinical Study of JR-141 -Summary of Ph3 in Japan-

JR-141 BBB-penetrating iduronate-2-sulfatase (rDNA origin)

Indication **MPS type II (Hunter syndrome)**

Phase 3 study (JR-141-301):
Interim evaluation at the completion of 26-week infusion

Enrollment

- 28 patients enrolled from 19 facilities

Efficacy for CNS symptoms

- HS concentrations in CSF decreased in all patients who completed infusions for 26 weeks (Mean 58.4±9.5%)
- Development Age : stabilization or improvement being observed by way of developmental assessment and individual case records

Efficacy for systemic symptoms

- HS and DS concentrations in serum decreased in 3 patients naïve to ERT
- HS and DS concentrations in serum stabilized in 25 patients switched from idursulfase

Safety

- No severe adverse events related to JR-141 reported
- No infusion-associated reaction reported that required study discontinuation

Report on Clinical Study of JR-141 -Total scheme -

JR-141 BBB-penetrating iduronate-2-sulfatase (rDNA origin)

Indication **MPS type II (Hunter syndrome)**

- Feb.2019: Designated under **Orphan Drug Designation**

- Mar. 2018: Designated under **"SAKIGAKE Designation System"**
- Aug. 2018: **Ph3 study initiated**

JCR USA, Inc.

- Oct.2018: Designated under **Orphan Drug Designation**

Brazil

- Jun. 2018: **Ph2 study initiated**

Application for marketing approval planned in FY2020 in Japan and Brazil

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JR-171 BBB-penetrating α-L-iduronidase (rDNA origin)

Indication **MPS type I**
(Hurler syndrome, Hurler-Scheie syndrome, Scheie syndrome)

- Disease overview: A deficiency of **α-L-iduronidase**, causes an accumulation of Mucopolysaccharide, giving rise to multiple systemic and **CNS symptoms**.
- Patient population*: **60** (Japan), **3,600** (WW) est. *Internal analysis
- Market size*: **1.5 billion JPY** est. (2018 Japan) , **24 billion JPY** est. (2018 WW)

- Sep. 2019: Meeting with FDA
  about the design of Phase 1/2 study (JR-171-101)

▶ Phase 1/2 study is planned in 2020

Progress of Other LSDs Pipeline

JR-441 BBB-penetrating heparan N-sulfatase (rDNA origin)

Indication **MPS type III A (Sanfilippo syndrome Type A)**

- Disease overview: A deficiency of **α-L-iduronidase,** causes an accumulation of Mucopolysaccharide, leading to **CNS symptoms** mailny.
- Patient population* : **60** (Japan) , **6,900** (WW) est.

*Total of Type A&B (Internal analysis)

▶ Phase 1/2 study is planned in FY 2020

JR-162 J-Brain Cargo®-applied acid α-glucosidase (rDNA origin)

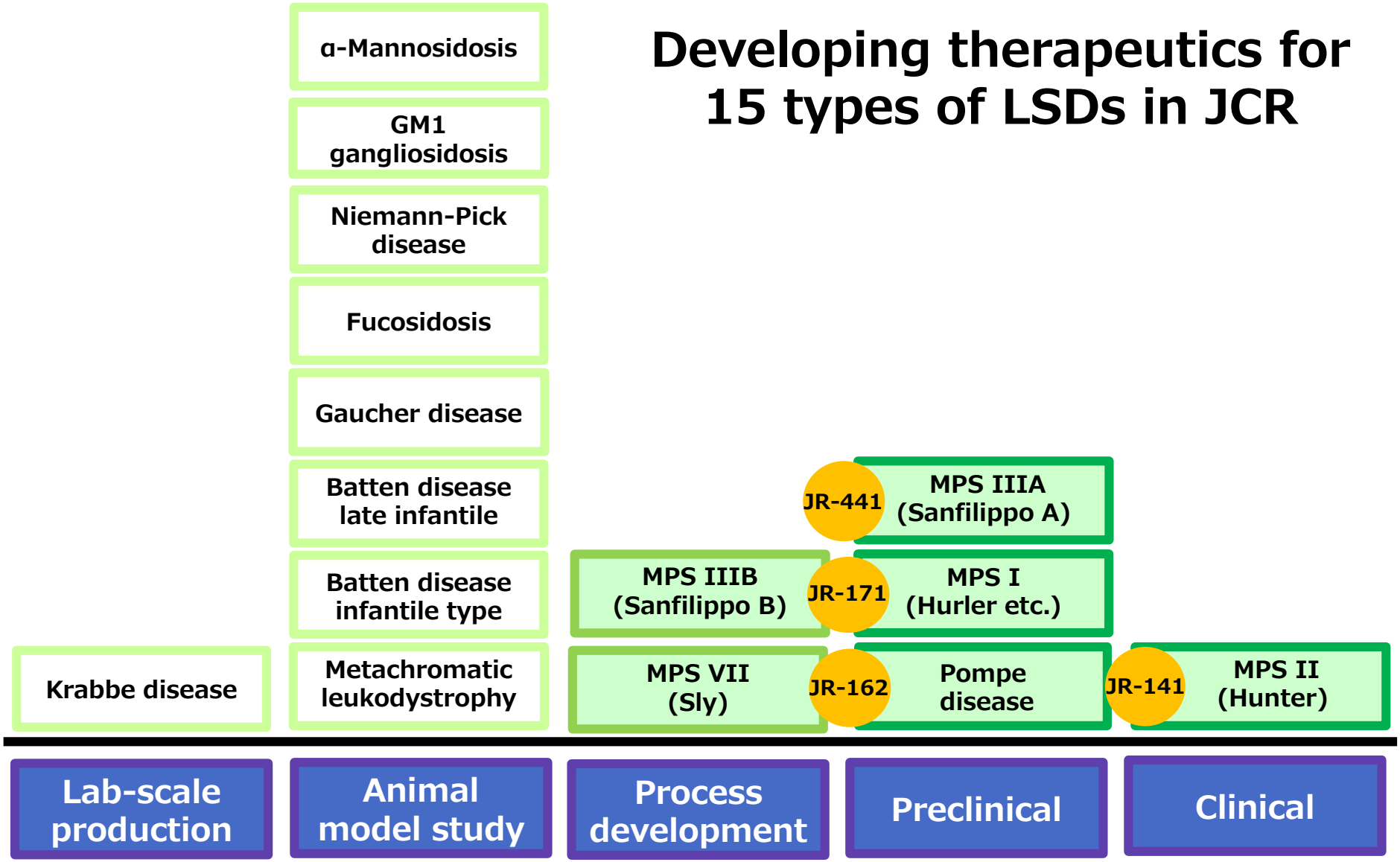
Indication **Pompe disease**

- Disease overview : A deficiency of Glycogen dissolving enzyme (**acid α-glucosidase**), causes an accumulation of Glycogen on sysmtemic cells (especially muscle cells), leading to impairment of **muscles**, respiratory, motor and heart function.
- Patient population*: **80** (Japan) , **10,600** (WW) est.
- Market size*: **3 billion JPY** est. (2018 Japan), **99 billion JPY** est. (2018 WW)

*Internal analysis

▶ JR-162 demonstrated significant proof of concept in the skeletal muscles as well as in CNS that regulates the muscles

Developing therapeutics for 15 types of LSDs in JCR



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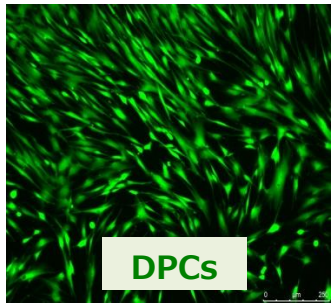
JTR-161/JR-161 Human dental pulpstem cells (DPCs)



Indication **Acute cerebral infarction**

- Cause : hypertension, diabetes mellitus, smoking, obesity, and dyslipidemia
- Prevalence* (Japan) : **300,000** est. per year. *Internal analysis
- Treatment : “thrombolytic therapy” and “endovascular treatment” are performed within several hours of onset, followed by "brain protection therapy", "antiplatelet therapy", and "anticoagulation therapy" are performed

TEIJIN

Jul. 2017 :
Co-development and license agreement with Teijin Limited Indication : Acute cerebral infarction

▶ Jan. 2019 : Administration started for patients in Phase1/2

Progress of Other R&D Pipeline

JR-401X Somatropin (rDNA origin)
(Expanded Indication of GROWJECT®)

Indication **Short stature homeobox-containing gene (SHOX) deficiency**

- Disease overview : a congenital disorder caused by deletions or mutations of a *SHOX* gene (short stature homeobox containing gene) located on the sex chromosomes essential for skeletal growth
- Prevalence* (Japan) : **450-500** est. per year

*Internal analysis

- **Jul. 2018 : Phase 3 study Started**

Phase 3 study design

- Subjects : short stature patients with SHOX deficiency.
- Endpoint : the growth promoting effect and safety of for 12 months / 24 months

▶ Administration started; ongoing

Development Pipeline

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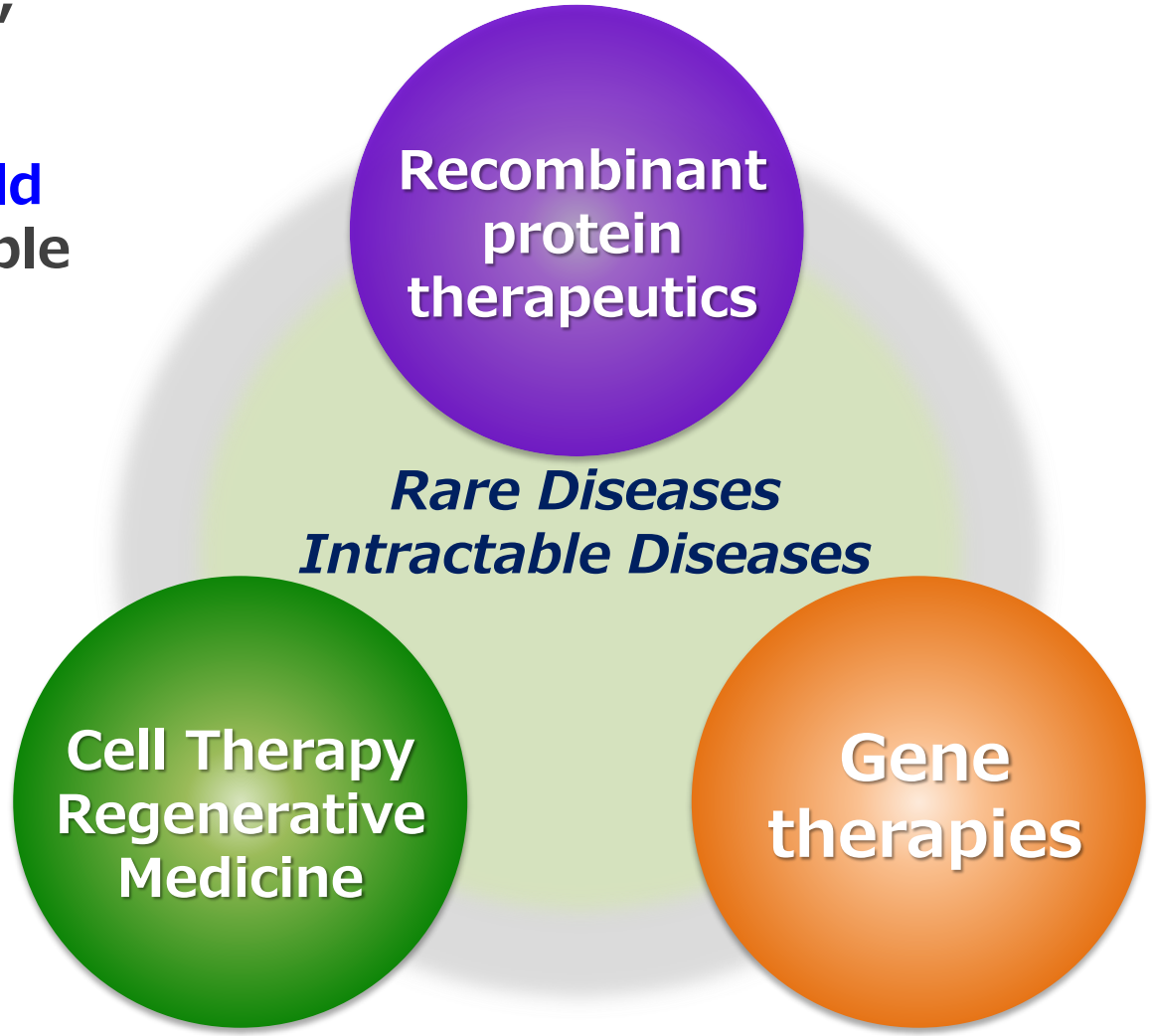
Taking one step ahead,
JCR aims to develop
First-in-class drugs
from Japan to the world
for achieving sustainable
value creation



– JCR Biotech for a New Tomorrow –