FY2019 Results Briefing Session
- Research and Development Highlights -

May 18, 2020

JCR Pharmaceuticals Co., Ltd.

【Securities code】 4552, 1st Sec. TSE

FORWARD-LOOKING STATEMENT

This presentation contains 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 mentioned in this document 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 mentioned in this document includes data not yet published in peer-reviewed academic journals or not yet presented at academic conferences. We will 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.
The progress of clinical development may be affected by the pandemic of novel coronavirus infection (COVID-19) in the future .

Development Pipeline

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

As of May 18, 2020

Code	Indication	Preclinical	Clinical trials	Filed	Approved	Remarks
JR-141	MPS type II (Hunter Syndrome)	**Phase 3** / **Phase 2**				• ERT • J-Brain Cargo®
JR-162	Pompe disease	**Preclinical**				• ERT • J-Brain Cargo®
JR-171	MPS type I (Hurler Syndrome etc.)	**Preclinical**				• ERT • J-Brain Cargo® • J-MIG System®
JR-441	MPS type III A (Sanfilippo A Syndrome)	**Preclinical**				• ERT • J-Brain Cargo®
JR-443 *NEW*	MPS type VII (Sly Syndrome)	**Preclinical**				• ERT • J-Brain Cargo®
JR-446 *NEW*	MPS type III B (Sanfilippo B Syndrome)	**Preclinical**				• ERT • J-Brain Cargo®
JR-401X	SHOX deficiency	**Phase 3**				• Expanded indication of GROWJECT®
JR-041	Infertility	**Phase 1/2**				• Out-licensed to ASKA Pharmaceutical Co., Ltd.
JR-142	Pediatric growth hormone deficiency	**Phase 1**				• 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

Development Progress

① Progress of JR-141

② Progress of Other Compounds

(JR-171, 441, 142, 401X, 031HIE, JTR-161/JR-161)

Research Progress (JR-443, 446, 441, 162)

Development Progress

① Progress of JR-141

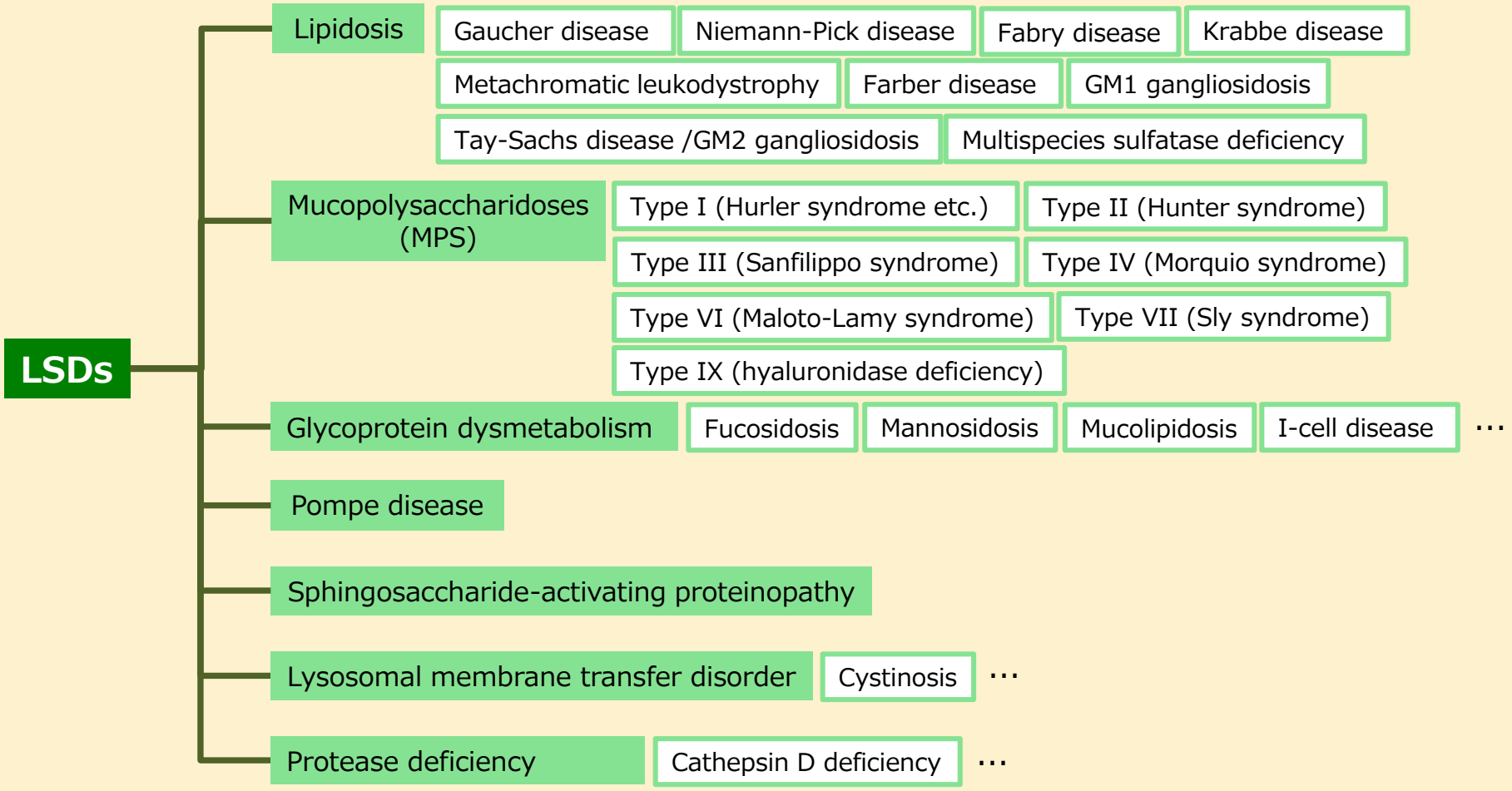
② Progress of Other Compounds

(JR-171, 441, 142, 401X, 031HIE, JTR-161/JR-161)

Research Progress (JR-443, 446, 441, 162)

Lysosomal Storage disorders（LSDs）

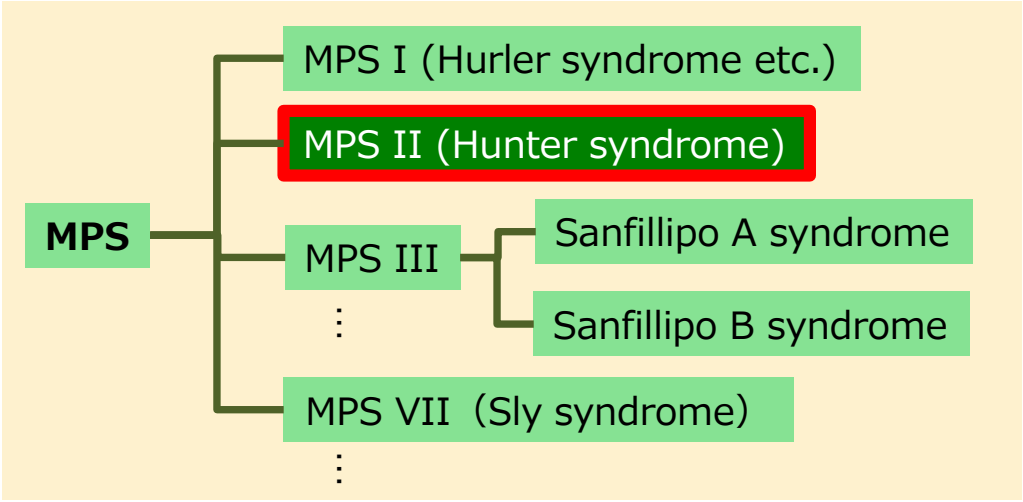
LSD is a group of rare inherited disorders in which one of enzymes in the lysosomes is congenitally missing or functionally deficient, resulting in the accumulation of metabolic wastes which fail to dissolve.
Their symptoms vary depending on the affected enzymes and the accumulating substrates.
They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



Progress of JR-141

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

BBB : Blood Brain Barrier

Indication	**MPS type II (Hunter syndrome)** 
Patient population*1	250 (Japan) , 7,800 (WW) est.
Market size*2	7.6 billion JPY est. (2019 Japan), 87 billion JPY est. (2019 WW)
Disease overview	A X-linked recessive disease caused by a deficiency of the enzyme iduronate-2-sulfatase that metabolizes mucopolysaccharides within the body. Symptoms are systemic and multiple; **central nervous system (CNS) disorders** is notable in particular..

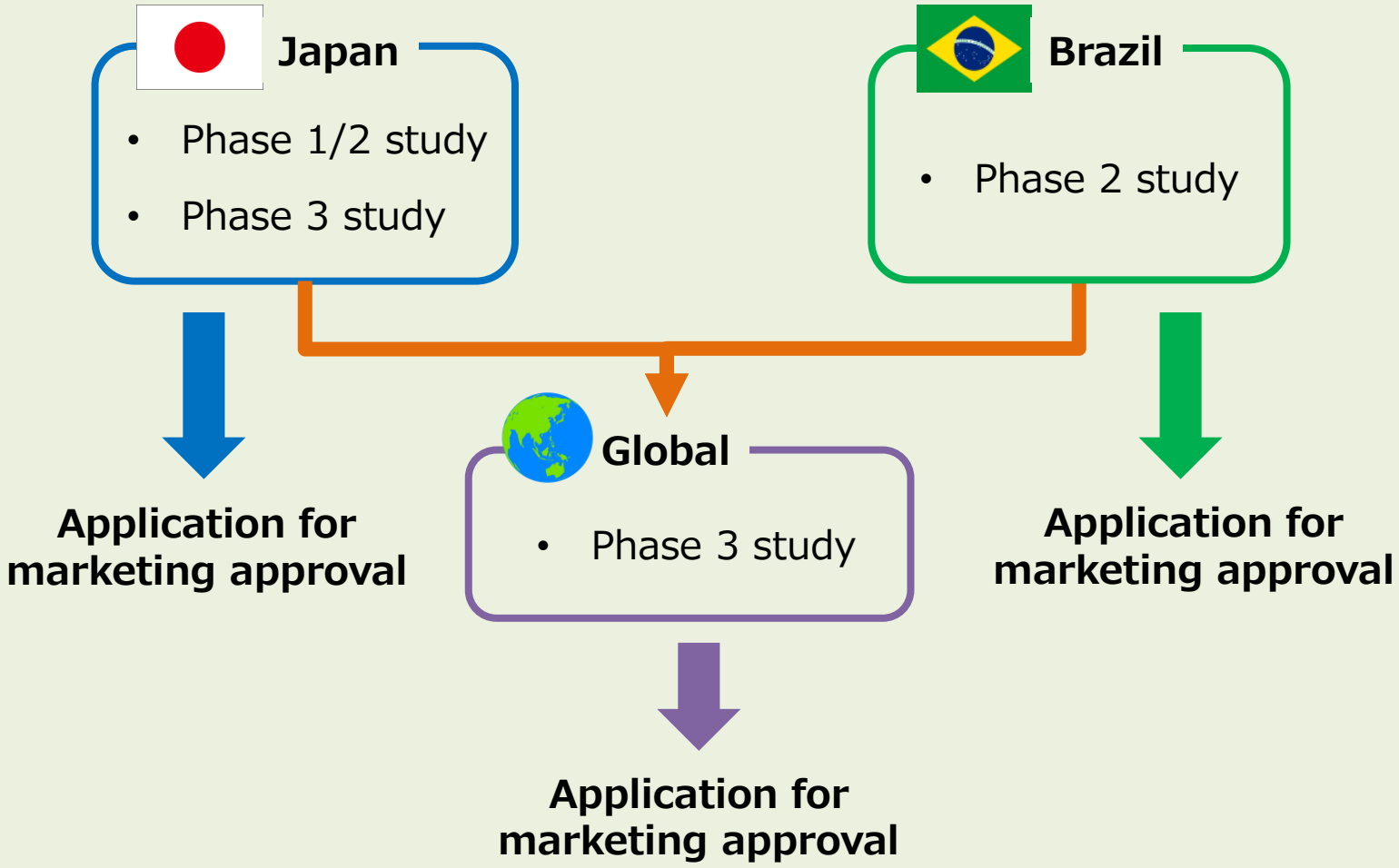
*1 Calculated internally based on the date from MHLW *2 Actual sales of existing ERT and data from Evaluate Pharma and IQVIA

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

Progress of JR-141

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

JR-141 Study Design



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

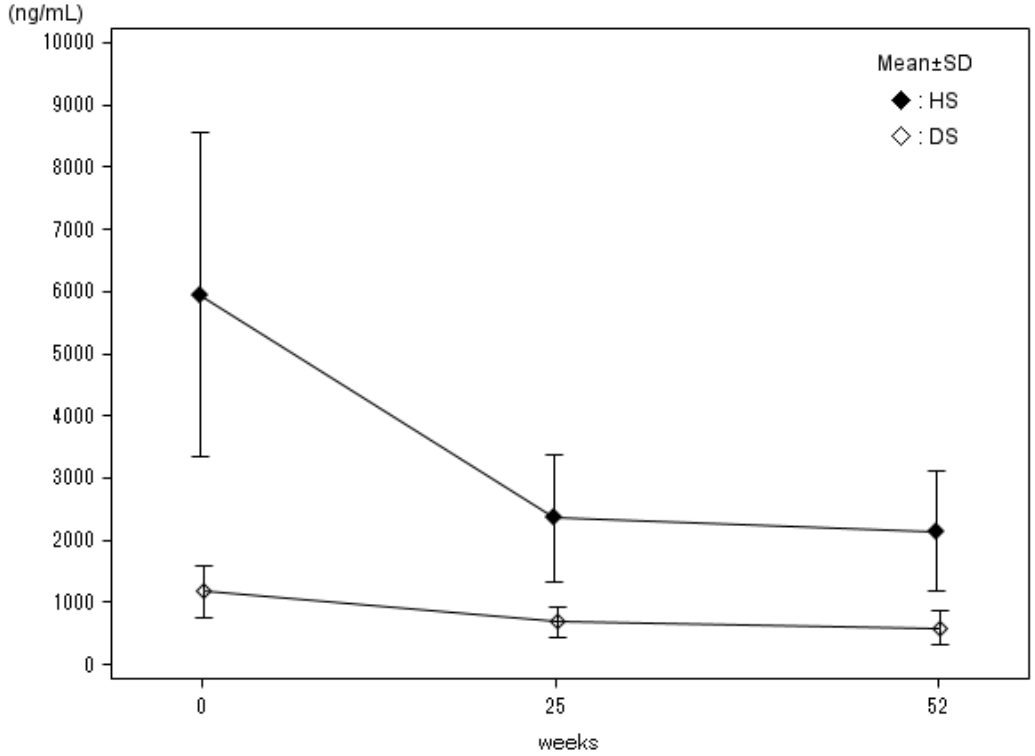
Phase 3 study (JR-141-301): Study design

Primary Endpoint	Change of Heparan Sulfate (HS) in Cerebrospinal Fluid (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 Subjects	28

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

Phase 3 study（JR-141-301): Results（52 weeks)

<Concentrations of HS and Dermatan Sulfate (DS) in CNS>



HS and DS concentrations in CSF decreased in all subjects
→HS concentrations in CSF decreased significantly（-61.3%±12.1%, p<0.001）
52 weeks average: 2124±882.6 ng/mL

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

Phase 3 study（JR-141-301): Results（52 weeks)

<New Kyoto Scale Developmental Assessment of Age Equivalence (AE) : after 52 weeks>

Classification of Disease phenotype	Number of subjects	Slope
Attenuated	8	0.9543
Severe: Initial phase	2	0.6705
Severe: Middle phase	11	-0.0802
Severe: Late phase	5	-0.0904

Initial phase ：
Age < 3y and developmental index > 80
Middle phase :
Age 8y or younger, or developmental index of > 20
Late phase ：
Age > 8y or developmental index < 20

Interpretation of the data

- Attenuated : AE developed almost normally（normal development = slope 1）
- Severe（<3y） : AE improved（neurodegeneration suppressed）
- Severe（>3y） : AE stabilized（deteriorations of neurodegeneration suppressed）

Therapeutic implications

- Early intervention maintains CSF substrate concentrations in low level and maintains AE development.
- JR-141 maintains AE by suppressing deteriorations of neurodegeneration even in severe subjects.

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

Phase 3 study（JR-141-301): Results（52 weeks)

<Behavioral improvements in severe subjects（52 weeks）*>

- Gradual increase in vocabulary
- Willingness to communicate
- Understood what the parents said
- Speech of short sentences increased
- Often in better mood than before
- Increase in utterance
- Understood words and moved as instructed
- Facial expressions livelier
- No obvious delays or symptoms compared with the brother of the same genotype at the same age

*Based on the questionnaire from the investigators

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

Phase 3 study（JR-141-301): Results（52 weeks)

- **All subjects completed the final observation ⇒ participated in the extension study**
- **Efficacy for CNS symptoms**
  - ✓ HS and DS concentrations in CSF decreased in all subjects ⇒ Primary endpoint achieved
  - ✓ AE of severe subjects : Increasing in younger subjects
    Being maintained in older subjects
- **Systemic/peripheral efficacy: similar to that of the existing enzyme replacement therapy**
  - ✓ Substrate concentrations in blood and urine : maintained in switched patients
    decreased in new treatment patients
  - ✓ Liver and Spleen Volumes : maintained in switched patients
    decreased in new treatment patients
  - ✓ 6-minute walk, others : maintained in switched patients
- **Safety**
  - ✓ No severe adverse events related to JR-141 reported
  - ✓ Infusions of 2.0mg/kg/week JR-141: well-tolerated for a total of 52 weeks

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

- Feb.2019:
  Orphan Drug Designation

- Mar. 2018: Designated under **"SAKIGAKE Designation System"**
- **Administration in all subjects completed** in Phase 3
- The extension study ongoing

- Oct.2018:
  Orphan Drug Designation

Application for marketing approval planned
in the end of Sep. 2020
(materials have been submitted in accordance with the prior evaluation system under the **SAKIGAKE Designation System)**

Application for marketing approval planned
in the end of Nov. 2020

Phase 3 global study planned in 2020

- Locations (TBD) : USA, Brazil, EU (Germany, France, UK)
- Study design: under discussion with FDA / EMA
  (to be fixed around the summer 2020)

- **Administration in all subjects completed** in Phase 2
- The extension study ongoing

Development Progress

① Progress of JR-141

② Progress of Other Compounds

(JR-171, 441, 142, 401X, 031HIE, JTR-161/JR-161)

Research Progress (JR-443, 446, 441, 162)

Progress of Other Compounds

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

Indication	**MPS type I (Hurler syndrome, Hurler-Scheie syndrome, Scheie syndrome)**
Patient population*1	60 (Japan), 3,600 (WW) est.
Market size*2	1.6 billion JPY est.（2019 Japan）, 28 billion JPY est.（2019 WW）
Disease overview	An autosomal recessive disease caused by a deficiency of the enzyme α-L-iduronidase that metabolizes mucopolysaccharides within the body. Symptoms are systemic and multiple; **CNS disorders** is notable in particular.

*1 Calculated internally based on the date from MHLW *2 Actual sales of existing ERT and data from Evaluate Pharma and IQVIA

- Phase 1/2 study: Study design（planned）
  - Number of subjects : 19
  - Country : Japan, USA, Brazil
  - Administration period : 12 weeks
  - Primary Endpoint : Safety
  - Secondary Endpoint : effects for CNS symptoms and Systemic symptoms
    Plasma pharmacokinetics

▶ Phase 1/2 study is planned in 2020

Progress of Other Compounds

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

Indication	**MPS type III A (Sanfilippo A syndrome)**
Patient population*1	60 (Japan) , 6,900 (WW) est.
Market size*2	No existing drug
Disease overview	An autosomal recessive disease caused by a deficiency of the enzyme heparan-N-sulfatase that metabolizes mucopolysaccharides within the body. Notably, rapid progression of **CNS disorders** affects neurocognitive development, with a peak at 2 or 3 years of age. Type III A is relatively severe. Hematopoietic stem cell transplantation can be a treatment option, but its effectiveness remains to be established.

*1 Calculated internally based on the date from MHLW (Total of Type A&B) *2 Actual sales of existing ERT and data from Evaluate Pharma and IQVIA

- Feb. 2020: New guidance about developing drugs for treatment of MPSIII issued from the FDA

Overall JR-441 development strategy to be reviewed accordingly

Phase 1/2 study is planned in FY 2022

Progress of Other Compounds

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

Indication	**Pediatric growth hormone deficiency**
Note	JCR's proprietary half-life extension technology, based on a novel modified albumin, allows significant increase in the half-life of various biotherapeutics (Patent filed)

- Phase 1 study :
  - -Pharmacokinetics and pharmacological effects confirmed in healthy adult males
  - -No serious safety issues related to JR-142 being observed

▶ Phase 2 study is estimated to start in 2021

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

Indication	**Short stature homeobox-containing gene (SHOX) deficiency**
Prevalence* (Japan)	450-500 est. per year *Internal analysis

- Phase 3 study : Administration ongoing

▶ Application for marketing approval is planned in 2022

Progress of Other Compounds

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

Indication	**Neonatal Hypoxic Ischemic Encephalopathy**
Prevalence* (WW)	2.5 of 1,000 live births *Internal analysis (Target: 150-200 patients per year with moderate-severe disease indicated for therapeutic hypothermia as standard of care)

- Phase 1/2 study : Administration started; ongoing
  - Application for marketing approval is planned in 2023

JTR-161/JR-161 Human dental pulp stem cells (DPCs)

Indication	**Acute cerebral infarction**
Prevalence* (Japan)	300,000 est. per year. *Internal analysis
Note	Jul. 2017 : Co-development and license agreement with **Teijin Limited** (Indication : Acute cerebral infarction)

- Phase 1/2 study : Ongoing
  - Completion of phase 1/2 study is planned in July 2021

Development Progress

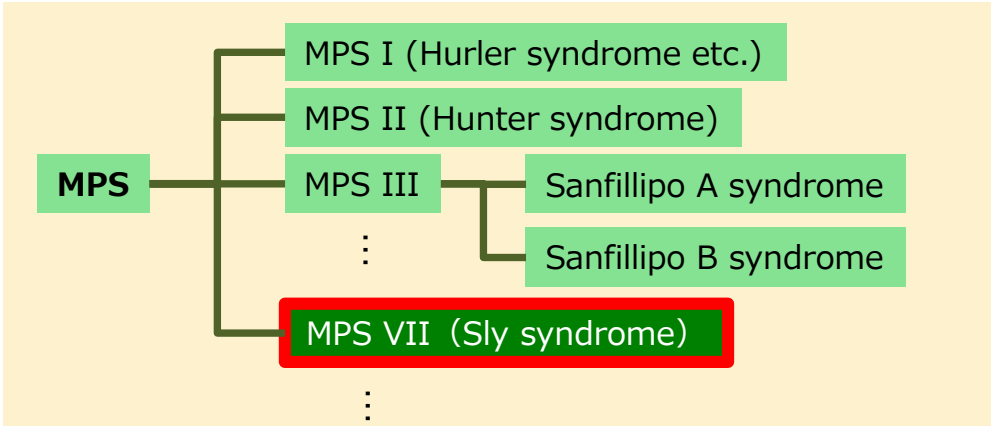
① Progress of JR-141

② Progress of Other Compounds

(JR-171, 441, 142, 401X, 031HIE, JTR-161/JR-161)

Research Progress (JR-443, 446, 441, 162)

JR-443 BBB-penetrating β-glucuronidase (rDNA origin)

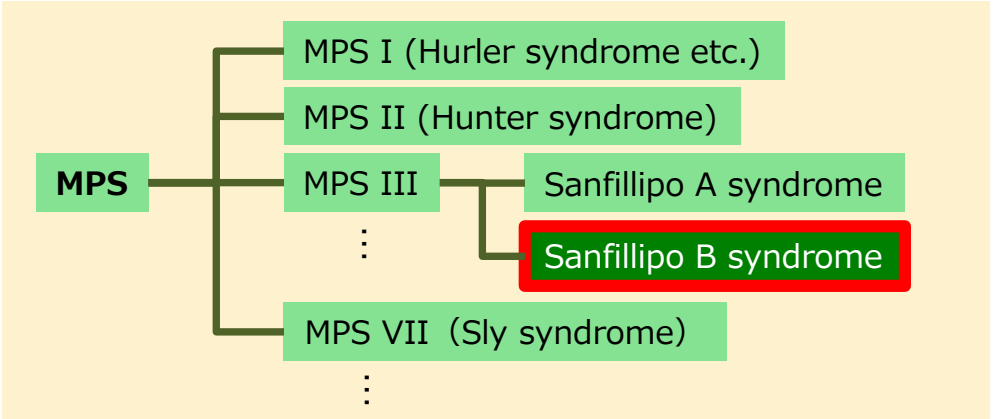
Indication	**MPS type VII (Sly syndrome)** 
Patient population*1	several (Japan) , 200 (WW) est.
Market size*2	1.4 billion JPY est. (2019 WW)
Disease overview	An autosomal recessive disease caused by deficiency of an enzyme, β-glucuronidase, that metabolizes mucopolysaccharides within the body, leading to accumulations of heparan sulfate and dermatan sulfate. Symptoms include bone deformation, joint contraction, as well as **CNS disorders** in severe cases. Hematopoietic stem cell transplantation and enzyme replacement therapy are treatment options, but their effectiveness, including that for CNS disorders remains to be established.

*1 Calculated internally based on the date from MHLW*2 Actual sales of existing ERT and data from Evaluate Pharma and IQVIA

- Drug delivery into the brain in mice and monkeys confirmed
- Reductions in the mucopolysaccharides accumulations in the mouse brain confirmed

▶ Clinical study to start within 3 years

JR-446 BBB-penetrating α-N-acetylglucosaminidase (rDNA origin)

Indication	**MPS type III B (Sanfillipo B syndrome)** 
Patient population*1	60 (Japan) , 6,900 (WW) est.
Market size*2	No existing drug
Disease overview	An autosomal recessive disease caused by a deficiency of the enzyme α-N-acetylglucosaminidase that metabolize mucopolysaccharides within the body. Symptoms include accumulation of heparan sulfate 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. Hematopoietic stem cell transplantation can be a treatment option, but its effectiveness remains to be established.

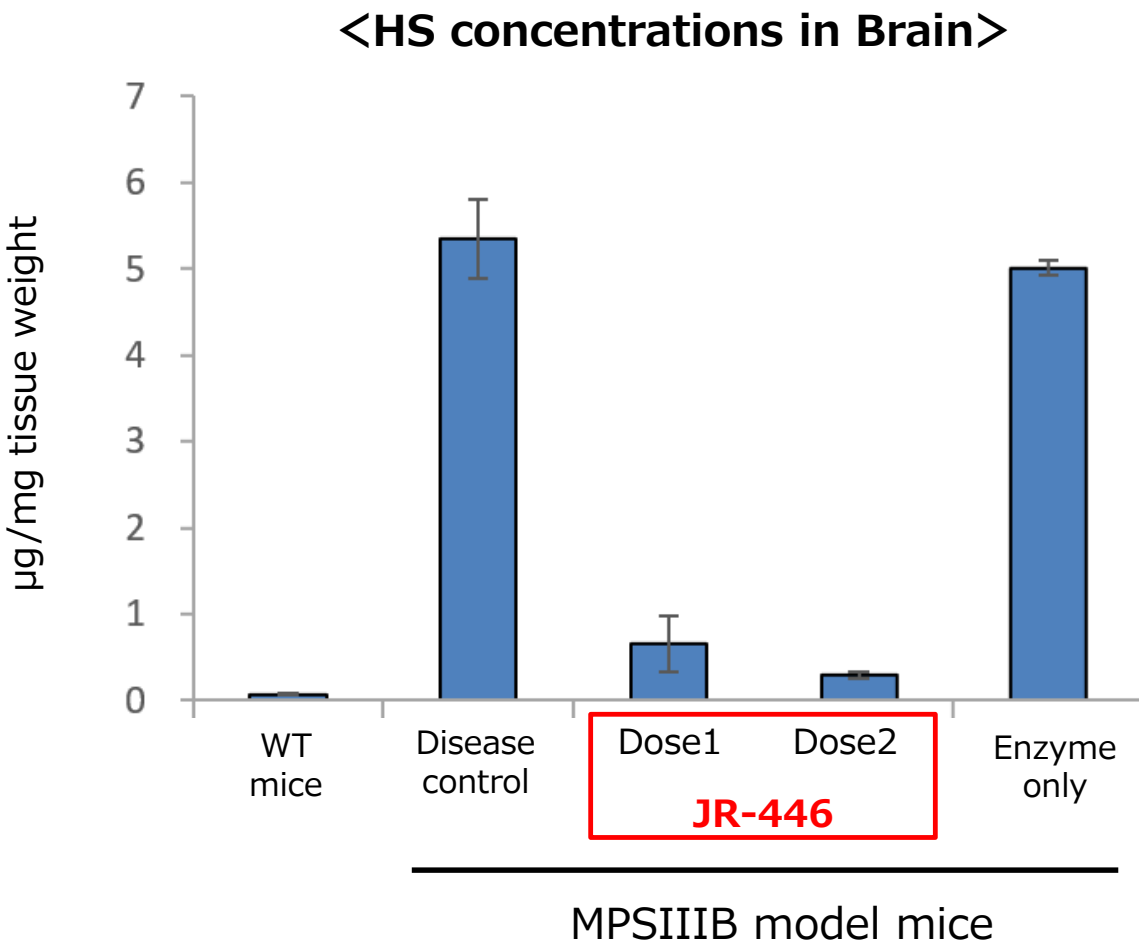
*1 Calculated internally based on the date from MHLW (Total of Type A&B) *2 Actual sales of existing ERT and data from Evaluate Pharma and IQVIA

- Drug delivery into the brain in mice and monkeys confirmed
- Reductions in the mucopolysaccharides accumulations in the mouse brain confirmed

▶ Clinical study to start within 3 years

JR-446 BBB-penetrating α-N-acetylglucosaminidase (rDNA origin)

■ The results of drug efficacy study in MPSIIIB model mice



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

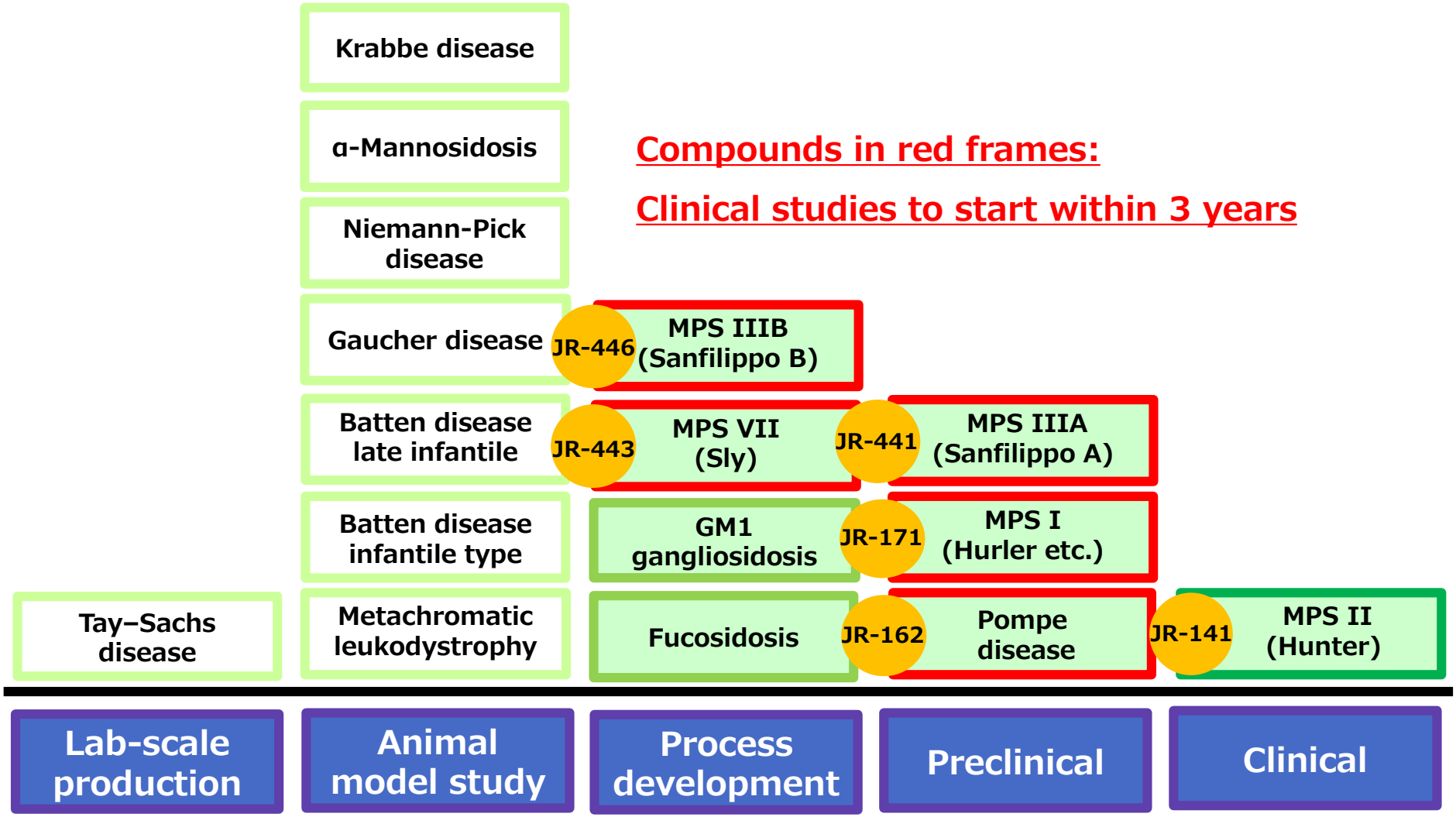
Indication	**Pompe disease**
Patient population*1	80 (Japan), 10,600 (WW) est.
Market size*2	3 billion JPY est. (2019 Japan), 110 billion JPY est. (2019 WW)
Disease overview	An autosomal recessive disease caused by a deficiency of the enzyme acid α-glucosidase that causes an **accumulation of Glycogen in muscle cells and nerve cells.** The infantile onset manifests as suckling and muscle force lowering in postnatal 2 months. Natural history suggests a life expectancy of less than 18 months due to cardiac dysfunction and respiratory failure. Delayed onset cases present muscle weakness that involves respiratory muscles. Symptoms are multiple and systemic, including **CNS disorders**.

*1 Calculated internally based on the date from MHLW *2 Actual sales of existing ERT and data from Evaluate Pharma and IQVIA

- Summary of Non-clinical study results :
  (from the presentation at the 16th Annual WORLD*Symposium*™2020)
  - JR-162 has potentials to exert therapeutic effects on muscle weakness and respiratory dysfunctions caused by both myogenic as well as neurogenic myopathies

Phase 1/2 study is planned in 2023

Developmental stages of the LSD therapeutics by JCR



R&D Target Timeline

	2020	2021	2022	2023
JR-141	**Application for marketing approval** (Japan) **Application for marketing approval** (Brazil) **Global study initiated**			
JR-171	**Phase 1/2 initiated**			
JR-142	Phase 1	**Phase 2 initiated**		
JTR-161 /JR-161	Phase 1/2	**Phase 1/2 completed**		
JR-441	Preclinical		**Phase 1/2 initiated**	
JR-401X	Phase 3		**Application for marketing approval**	
JR-031HIE	Phase 1/2			**Application for marketing approval**
JR-162	Preclinical			**Phase 1/2 initiated**
JR-443	Preclinical			**Phase 1/2 initiated**
JR-446	Preclinical			**Phase 1/2 initiated**

変革

REVOLUTION
into the Future

With all the strengths of "Team JCR“,

we achieve Global specialty pharma

in the rare disease arena

Utilizing three platforms, JCR promotes its objective of
“Realizing medical care for those living with rare diseases”

Recombinant Protein Therapeutics

Cell Therapy Regenerative Medicine

Gene Therapies