FY2020 Results Briefing Session
- Research and Development Highlights -

May 17, 2021

JCR Pharmaceuticals Co., Ltd.

【Securities code】4552, 1st Sec. TSE

Development Pipeline

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

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

Contents

Research & Development News (Nov.-Mar.)

2020

- Oct. : **First Patient Dosed** in Phase 1/2 Global Clinical Trial of JR-171
- Dec. : Completion of Phase 2 Clinical Trial Notification of JR-142
- Dec. : **JCR Files for Marketing Approval of JR-141 in Brazil**
- Dec. : **JCR** Signs Provisional Production Master Service Agreement with **AstraZeneca Regarding Domestic Production of COVID 19 Vaccine Bulk Product**

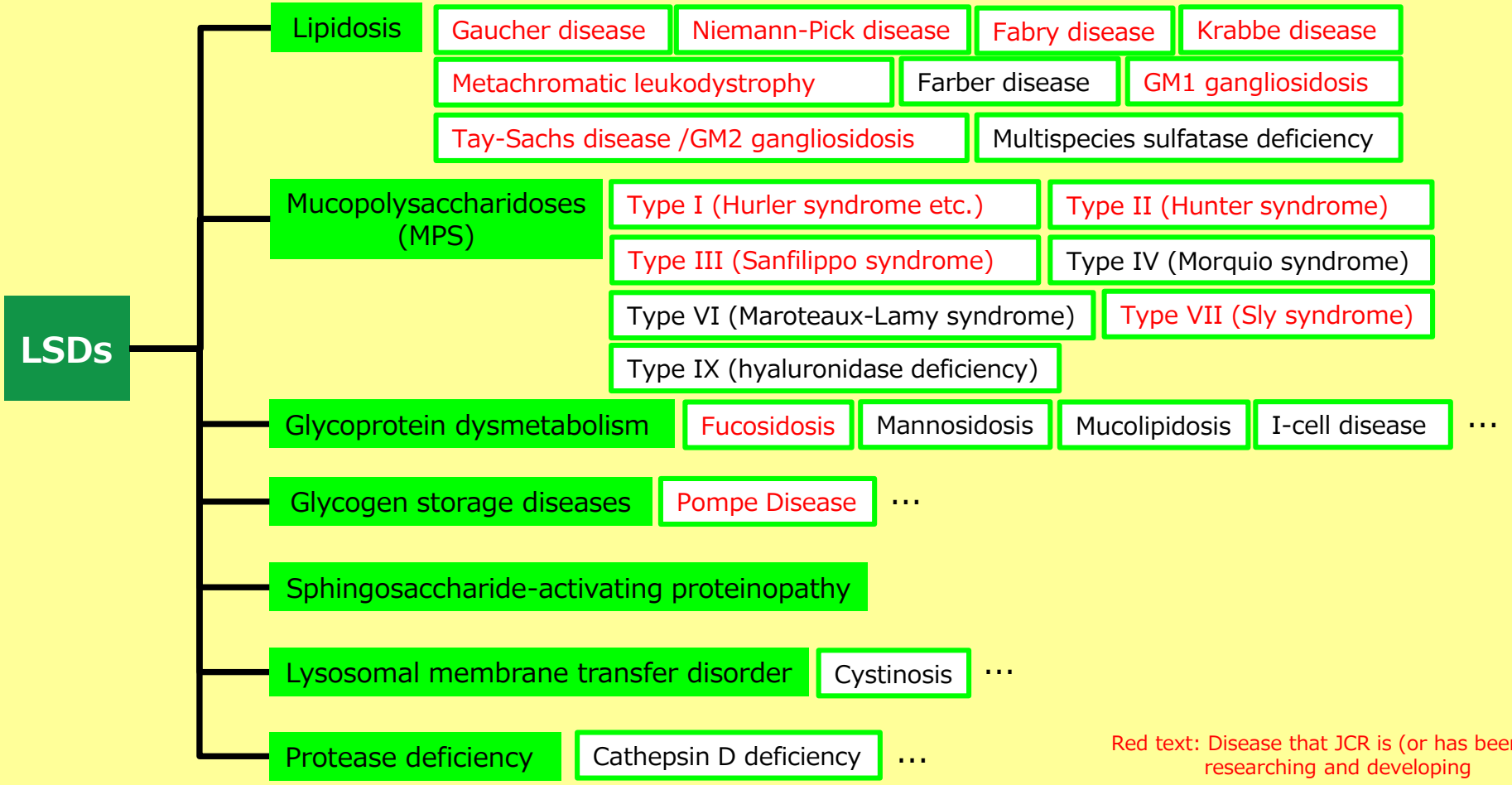
2021

- Jan. : JCR Initiates Operation of "**Bio Research Center**"
- Feb. : **JCR Receives** IND Clearance to **Initiate Global P3 Clinical Trial of JR-141 from FDA**
- Feb. : **JCR Receives** FDA **Fast Track Designation to JR-141**
- Feb. : JCR Receives FDA **Orphan Drug Designation to JR-171**
- Mar. : JCR Announces Discontinuation of Development of JR-031EB,Expanded Indication of TEMCELL® HS Inj. for Epidermolysis Bullosa
- Mar. : **Approval of IZCARGO® (Pabinafusp Alfa) for Treatment of MPS II (Hunter Syndrome) in Japan**
- Mar. : JCR Receives EMA **Orphan Drug Designation to JR-171**

Contents

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 waste which fails to dissolve.
Symptoms vary depending on the affected enzymes and the accumulated substrates.
They are designated by MHLW as intractable disease as well as specific pediatric chronic disease.



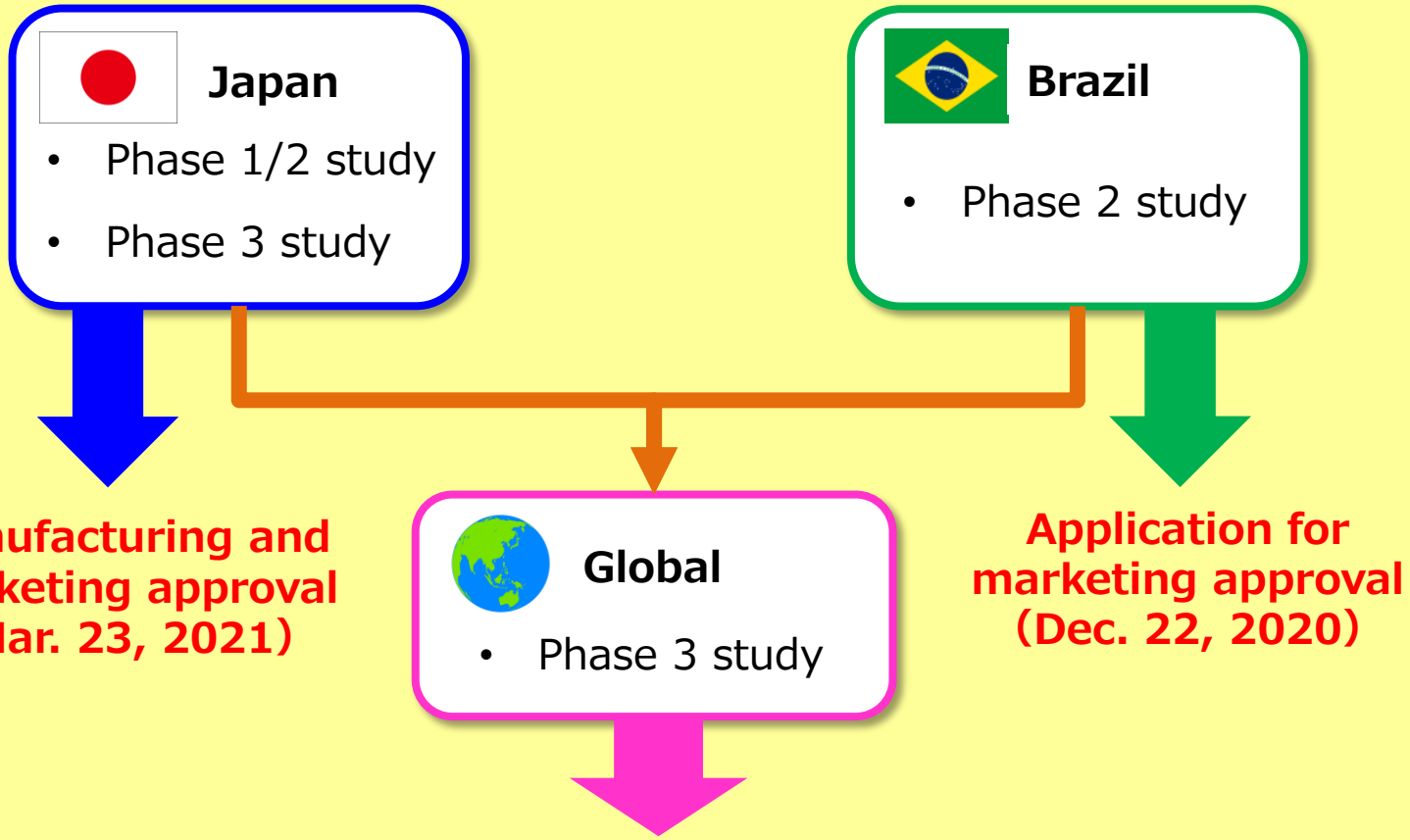
Red text: Disease that JCR is (or has been) researching and developing

Progress of JR-141

JR-141

IZCARGO® (Product name in Japan)
Pabinafusp alfa (BBB-penetrating iduronate-2-sulfatase, rDNA origin)

JR-141 Study Design

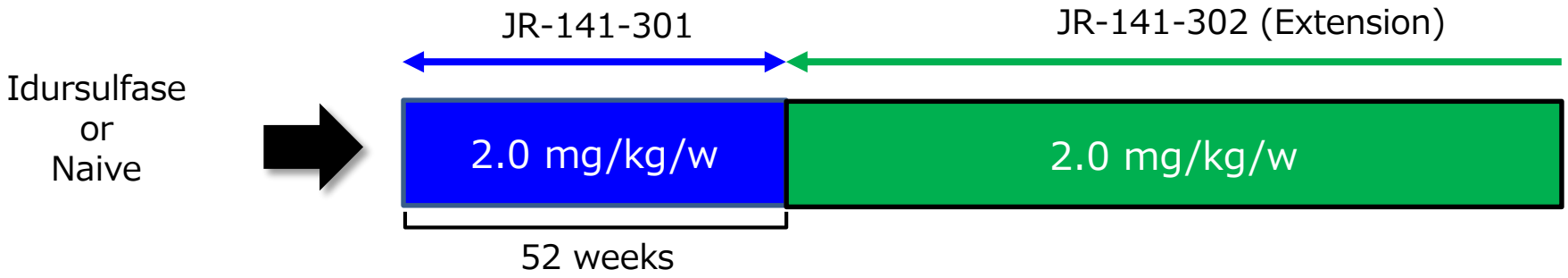


Progress of JR-141

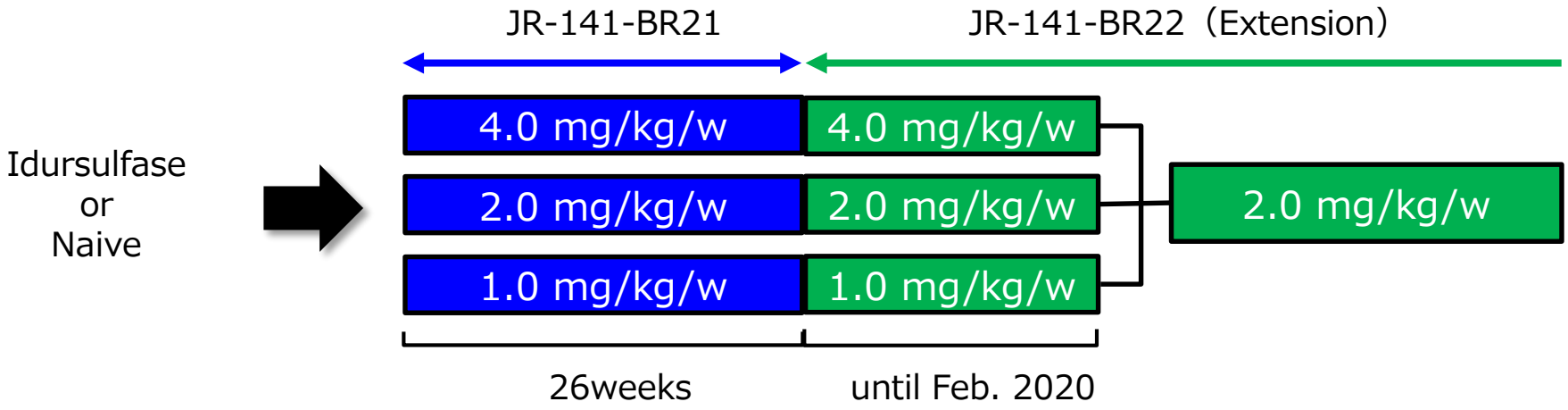
JR-141

IZCARGO® (Product name in Japan)
Pabinafusp alfa (BBB-penetrating iduronate-2-sulfatase, rDNA origin)

JR-141-301(phase II/III) and JR-141-302(Extension) Study in Japan



JR-141-BR21(phase II) and JR-141-BR22(Extension) Study in Brazil

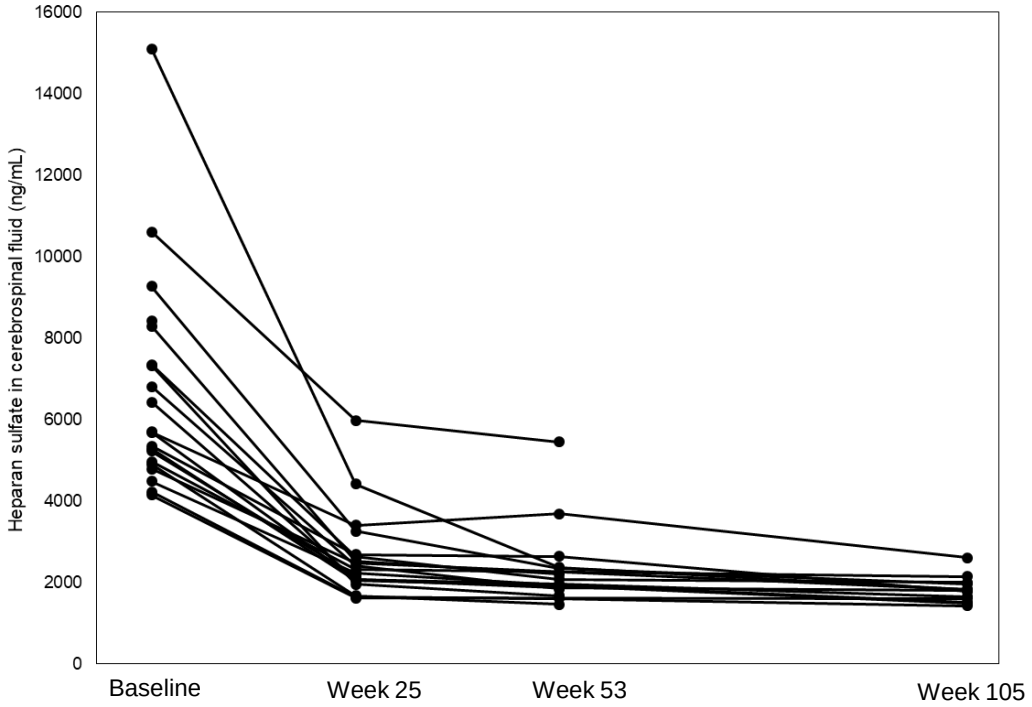


JR-141

IZCARGO® (Product name in Japan)
Pabinafusp alfa (BBB-penetrating iduronate-2-sulfatase, rDNA origin)

Phase 3 trial・Extension study(JR-141-301/302) : Results

- **Time course of Heparan Sulfate (HS) in CSF (severe)**



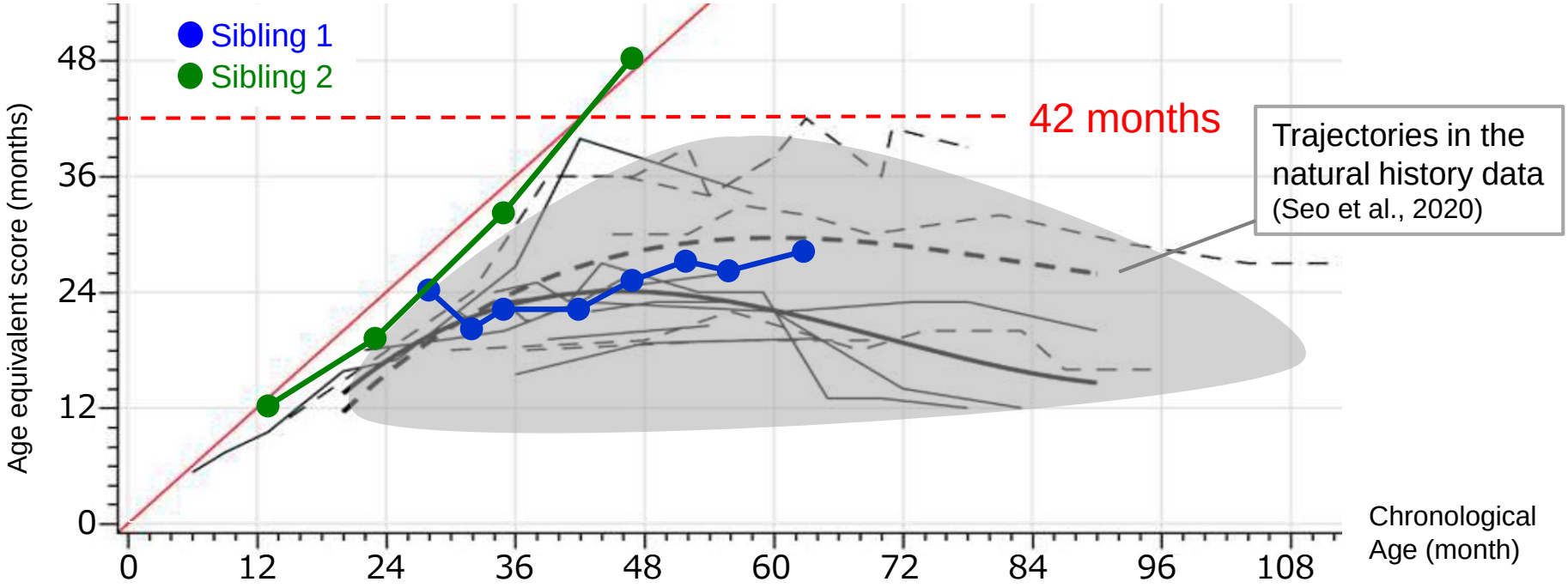
- The concentration of substrates in CSF decreased in all subjects after 53 or 105 weeks of JR-141 administration, confirming that JR-141 passes through the blood-brain barrier(BBB) and has a long-term substrate degrading effect in the central nervous system

JR-141

IZCARGO® (Product name in Japan)
Pabinafusp alfa (BBB-penetrating iduronate-2-sulfatase, rDNA origin)

Phase 3 trial･Extension study (JR-141-301/302) : Results

➢ **Developmental Trajectories of the siblings**



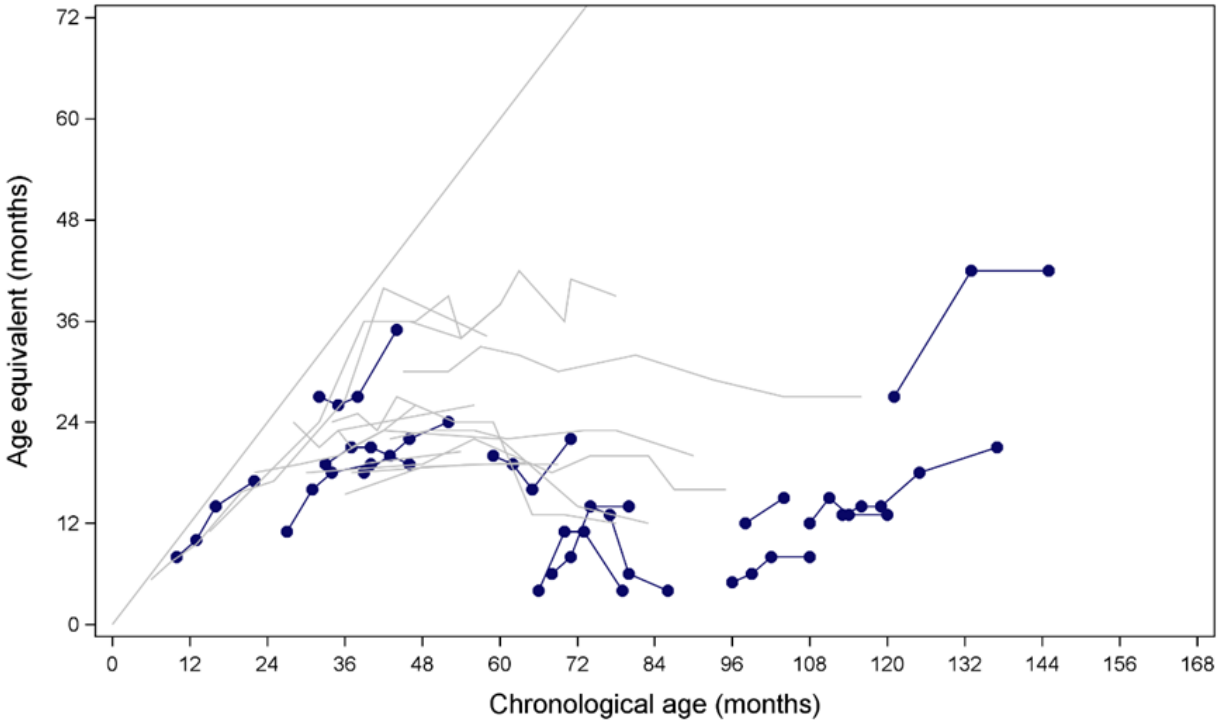
➢ Demonstrating the importance of early diagnosis and early treatment in MPS type II and suggesting the effectiveness of enzyme replacement therapy for BBB transit type

JR-141

IZCARGO® (Product name in Japan)
Pabinafusp alfa (BBB-penetrating iduronate-2-sulfatase, rDNA origin)

Phase 2 trial (JR-141-BR21/BR22) : Results

- **developmental assessment （BSID-III）**



- Developmental assessment was stabilized or improved, suggesting that JR-141 may improve central nervous system symptoms in MPS type II

JR-141

IZCARGO® (Product name in Japan)
Pabinafusp alfa (BBB-penetrating iduronate-2-sulfatase, rDNA origin)

Global Phase 3 trial (JR-141-GS31) : Brief Summary

Countries : USA, Brazil, EU (Germany, France, UK)

Objective : To show efficacy on CNS and systemic symptoms.

Design :

- **2 cohorts, standard of care controlled, parallel-group trail**
- Target number of patients : 50 (Male)

	Subjects	Standard of Care	JR-141	Duration
CohortA	• **Neuronopathic patients** • 36-71 months old, IQ=55-75 • 30-35 months old, mutation in the IDS gene, judged the severe phenotype	**15**	**15**	105 weeks
CohortB	• **Attenuated patients** • >6 years old, IQ≧70	**10**	**10**	53 weeks

Endpoints :

- HS in CSF, CNS symptoms (cognitive)
- Physical symptoms (liver volume, 6-minute walk)

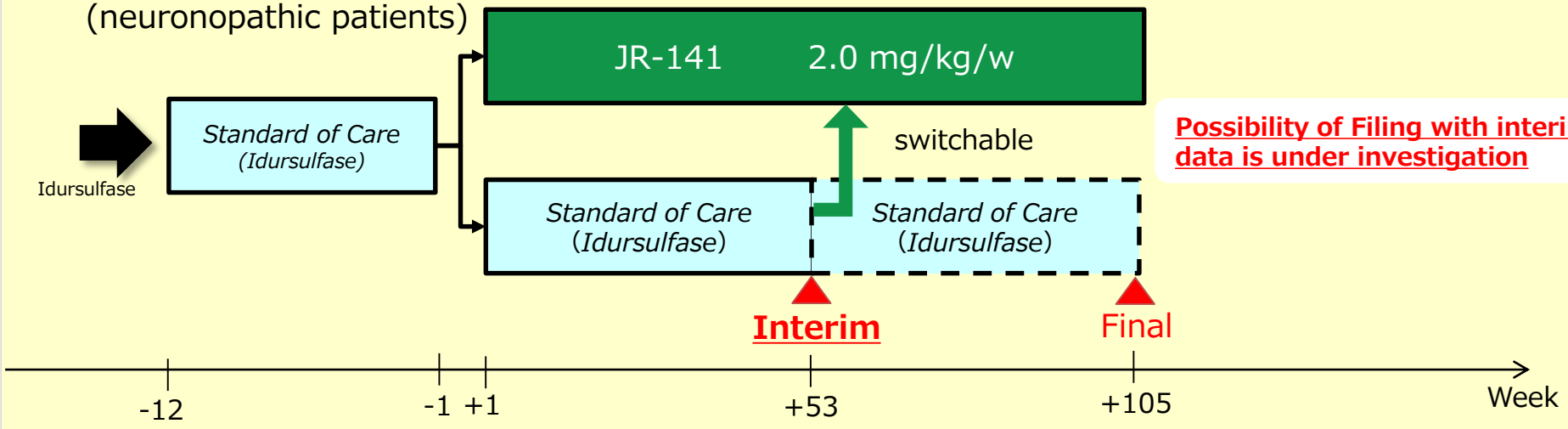
ClinicalTrials.gov : Identifier : NCT04573023

JR-141

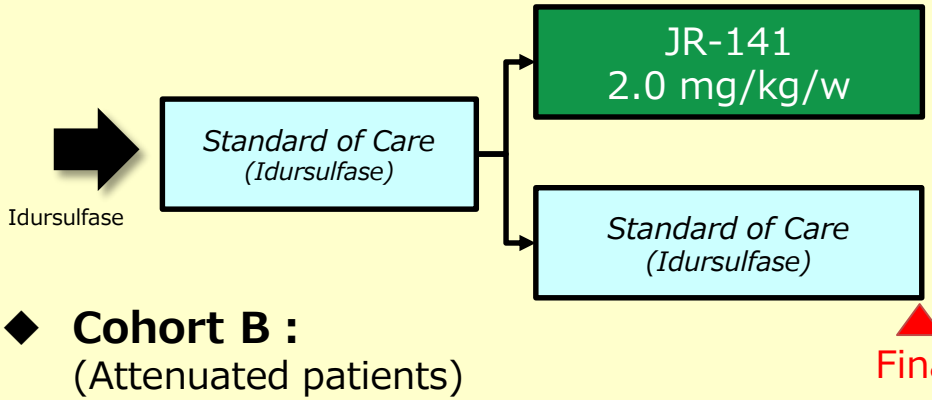
IZCARGO® (Product name in Japan)
Pabinafusp alfa (BBB-penetrating iduronate-2-sulfatase, rDNA origin)

Global Phase 3 trial (JR-141-GS31) : Brief Summary

◆ **Cohort A :**
(neuronopathic patients)



Possibility of Filing with interim data is under investigation



◆ **Cohort B :**
(Attenuated patients)

Progress of JR-141

JR-141

IZCARGO® (Product name in Japan)
Pabinafusp alfa (BBB-penetrating iduronate-2-sulfatase, rDNA origin)

- Feb.2019:
  Orphan Drug Designation

- Mar. 2018: Designated under
  "SAKIGAKE Designation System"
- **Mar. 2021: Approval**
- **NHI price listing may occur in May, 2021**

- Oct.2018:
  Orphan Drug Designation
- Feb. 2021:
  Fast Track Designation

- **Dec. 2020:**
  Application for marketing approval

Phase 3 global study planned to start in FY2021

Contents

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.

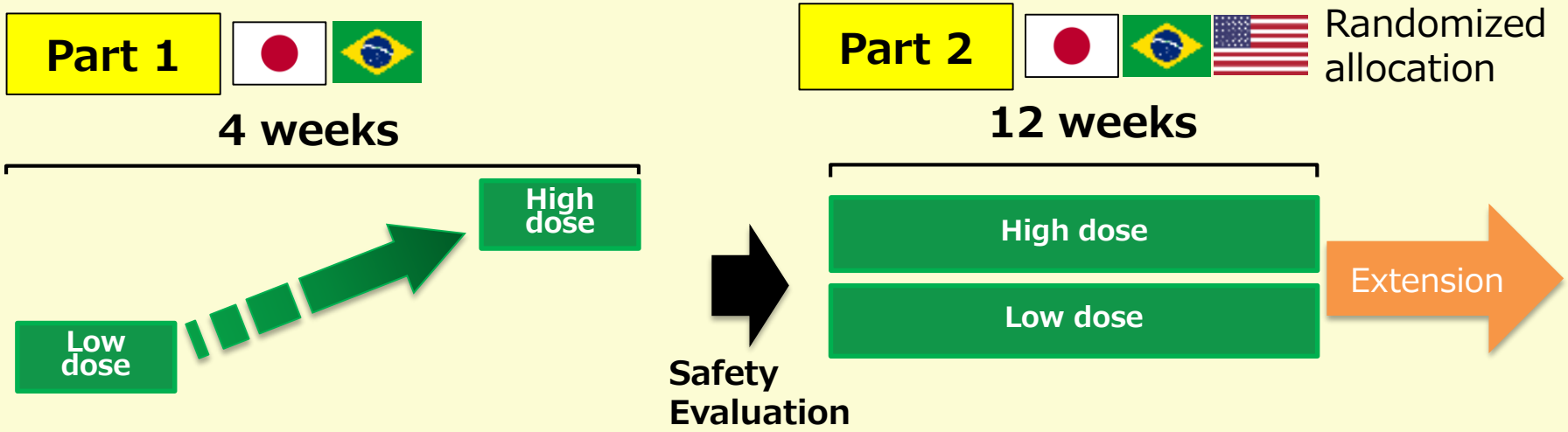
*1 Calculated internally based on the date from MHLW *2 Actual sales of existing ERT and data from Evaluate Pharma and IQVIA

JR-171 Global development

- 2020
  - Jul. : **Completion of Phase 1/2 Clinical Trial Notification** of JR-171 as a Global Clinical Trial in Japan
  - Oct. : **First Patient Dosed** in Phase 1/2 Global Clinical Trial of JR-171
- 2021
  - Feb. 12 : FDA grants **Orphan Drug Designation** to JR-171
  - Mar. 30 : EMA grants **Orphan Drug Designation** to JR-171

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

Phase 1/2 Global Clinical Trial（JR-171-101）: Brief Summary

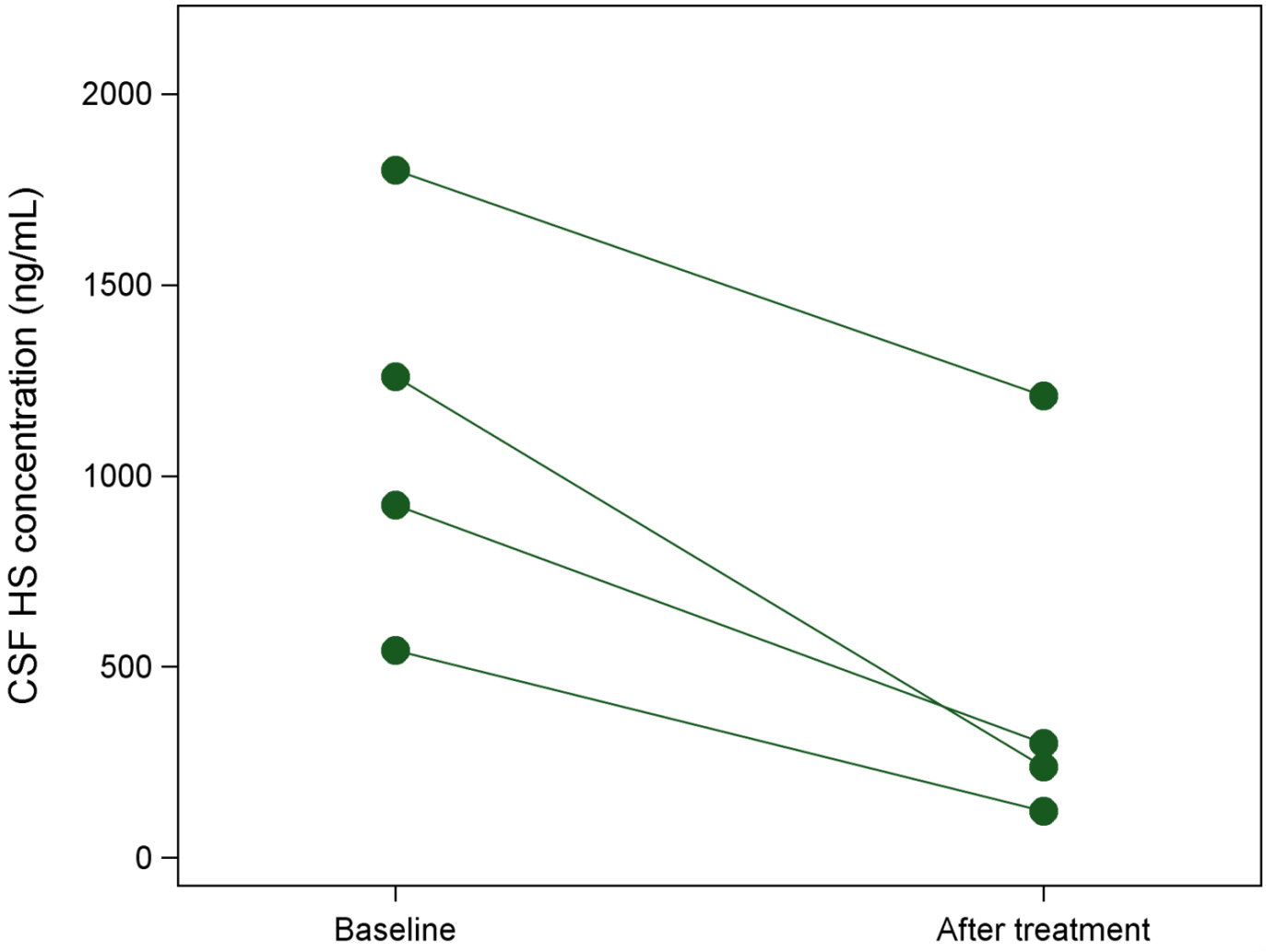


	Part1	Part2
Primary endpoint	Safety	
Secondary and exploratory endpoints	• Plasma drug concentrations and pharmacokinetic parameters • Exploratory Efficacy for Central Nervous System Symptoms and Systemic Symptoms	
Number of subjects	19	
Allocation	Japan・Brazil	Japan・Brazil・USA
clinicaltrials.gov	Identifier : NCT04227600	

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

Phase 1/2 Global Clinical Trial（JR-171-101）: Results

Part 1(N=4)



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Progress of JR-142

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

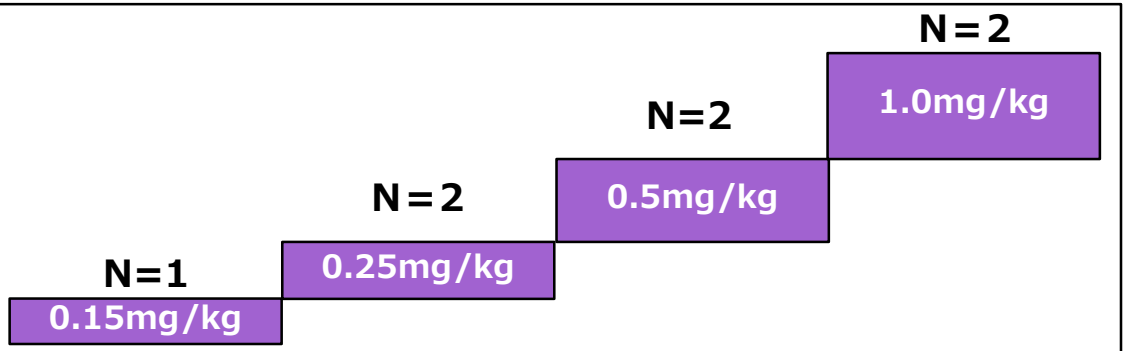
Indication : **Pediatric growth hormone deficiency**

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 Clinical Trial (JR-142-101) : Brief Summary

First period

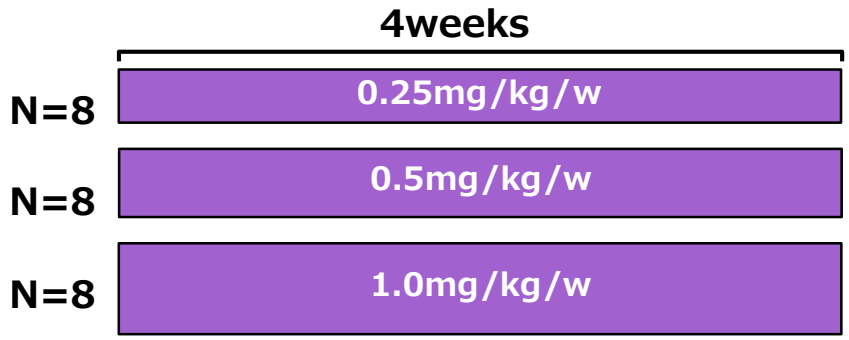
Subjects	Healthy adult males(N=7)
Endpoints	• Safety (single dose) • Assessment of PK/PD profile
study drug	JR-142



Safety Evaluation

Second period

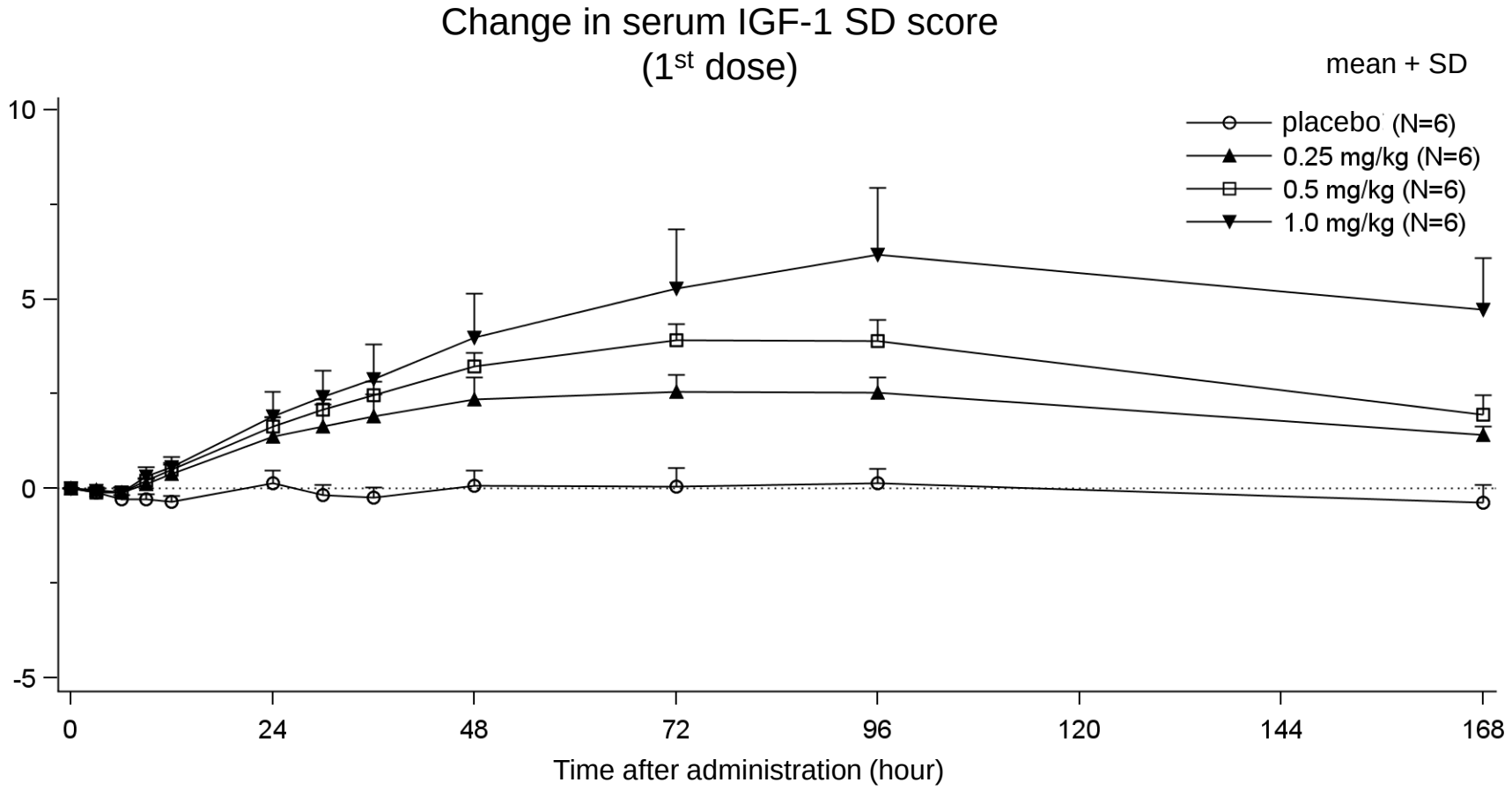
Subjects	Healthy adult males(N=24) Each Group N=8 (JR-142: N=6 Placebo:N=2)
Endpoints	• Safety (multiple dose) • Assessment of PK/PD profile
study drug	JR-142



*Observation : 3weeks

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

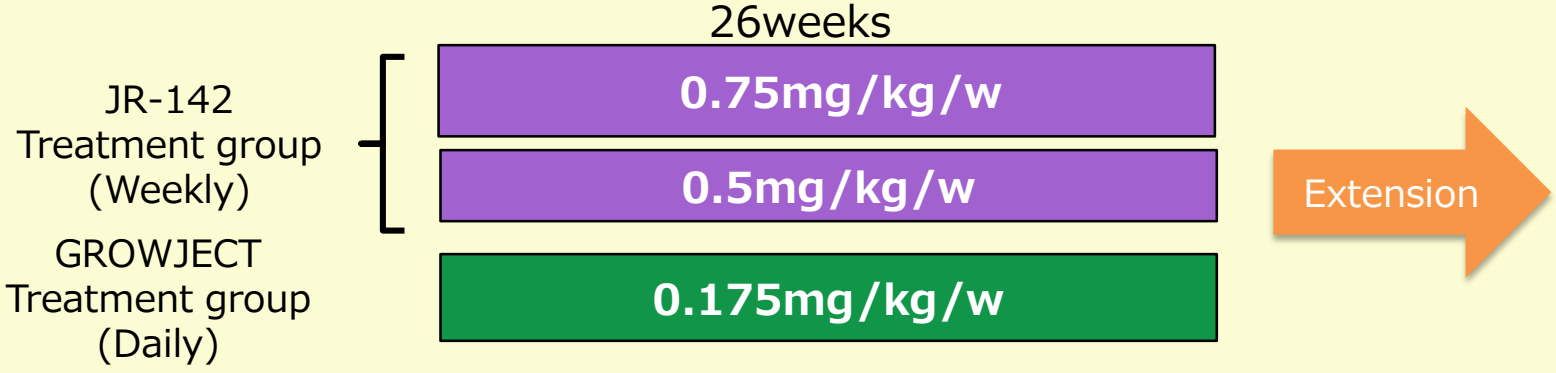
Phase 1 Clinical Trial (JR-142-101): Results



- Dose-dependent increases in PK parameters and pharmacodynamic markers were observed.
- No safety concerns were observed.

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

Phase 2 Clinical Trial（JR-142-201）: Brief Summary



First patient dosing in Phase 2 clinical trial scheduled for May 2021

Subjects	Pediatric Growth Hormone Deficiency (Pediatric GHD)
Endpoints	• Assessment of PK/PD profile • Growth rate (after 26 weeks) • Safety etc.
Number of Subjects	24subjects
study drug	JR-142 / GROWJECT
Details	jRCT(Identifier : jRCT2031200372)

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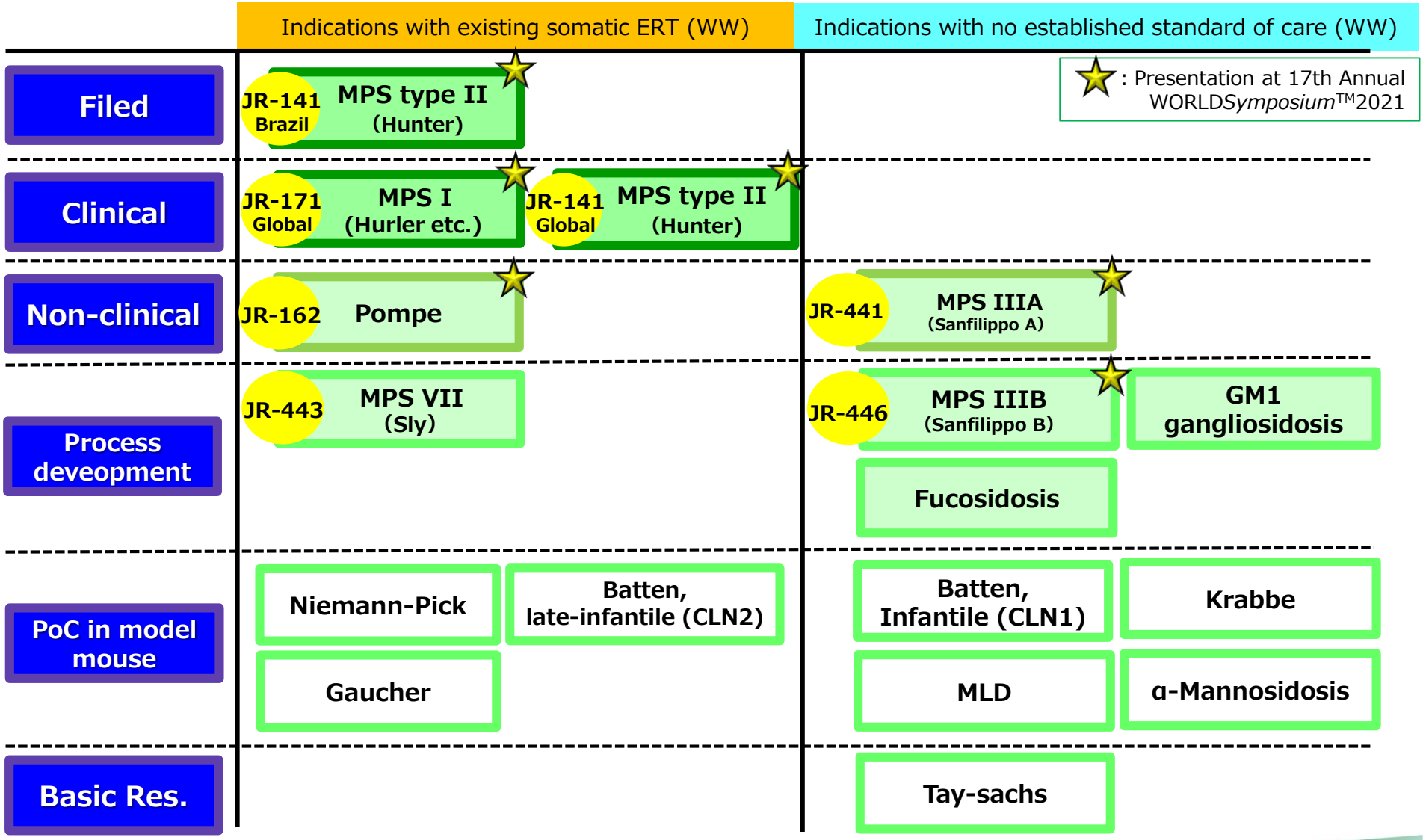
JCR's pipeline for Lysosome diseases



Expected timeline (Lysosome diseases)

	2021	2022	2023	2024
JR-141 pabinafusp alfa (MPS II)	**Japan : Approval** Brazil : To be approved Global : Initiation of Phase 3 trial			
JR-171 (MPS I)	**Global : Phase 1/2 trial (ongoing)**			Initiation of Phase 3 trial
JR-441 (MPS IIIA)	**Non-clinical (ongoing)**	Initiation of Phase 1/2 trial		
JR-162 (Pompe)	**Non-clinical (ongoing)**			Initiation of Phase 1/2 trial
JR-443 (MPS VII)	**Non-clinical (ongoing)**			Initiation of Phase 1/2 trial
JR-446 (MPS IIIB)	**Non-clinical (ongoing)**			Initiation of Phase 1/2 trial

Note: Information after 2022 is a plan at this stage and is subject to change

Other pipeline (GH and regenerative medicine area)

Expected timeline (GH area)

	2021年	2022年	2023年	2024年
JR-142 (Pediatric short stature, GHD)	**Initiation of Phase 2 trial**		Initiation of Phase 3 trial	
JR-401X (Pediatric short stature, SHOX abnormalities)	**Phase 3 (ongoing)**		To be filed	

Note: Information after 2022 is a plan at this stage and is subject to change

Other pipeline (regenerative medicine)

	2021年	2022年	2023年	2024年
JTR-161/JR-161 (Acute cerebral infarction)	**Phase 1/2 (Complete)**		Initiation of Phase 3 trial	
JR-031HIE (Hypoxic ischemic encephalopathy)	**Phase 1/2 (ongoing)**		To be filed	

Note: Information after 2022 is a plan at this stage and is subject to change

変革

REVOLUTION
into the Future

With all the strengths of "Team JCR“, we propel to the forefront as a Global specialty pharma in the rare disease arena

Leveraging the three platforms, JCR is committed to its objective of
“Realizing medical care for those living with rare diseases”

- **Recombinant Protein Therapeutics**
- **Cell Therapy Regenerative Medicine**
- **Gene Therapies**

Appendix

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

Indication :	**MPS type III A (Sanfilippo A syndrome)**
Patient population*1 :	30 (Japan : Total of Type A&B) , 4,000 (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.

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 and own research *2 Actual sales of existing ERT and data from Evaluate Pharma and IQVIA

Progress of Other Compounds

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.

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

Indication :	**MPS type III B (Sanfillipo B syndrome)**
Patient population*1 :	30 (Japan : Total of Type A&B) , 1,900 (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 and own research *2 Actual sales of existing ERT and data from Evaluate Pharma and IQVIA

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)

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

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

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 (Target: 150-200 patients per year with moderate-severe disease indicated for therapeutic hypothermia as standard of care)

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

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

TEIJIN

JCR Pharmaceuticals

*Internal analysis

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 do not guarantee future results, nor do they guarantee the efficacy or effects of products under development.
This document is not intended to guarantee or advertise the efficacy of the product under development.
The clinical development data mentioned in this document include data not yet published in peer-reviewed academic journals or not yet presented at academic conferences. We will make them 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 .