FY2022 Results Briefing Session
- Research and Development Highlights -

May 12, 2023

JCR Pharmaceuticals Co., Ltd.

[Securities code]4552, Prime. TSE

Highlights (Oct. 27, 2022- May 11, 2023)

LSD : lysosomal storage disease
MPS : mucopolysaccharidosis

2022

◆Oct.
- JR-471 for Fucosidosis enters Development
- Exclusive Negotiation Rights for Global Commercialization Targeting Four Ultra-Rare Diseases and Conclude a Licensing Contract for the Commercialization of a Fucosidosis Therapeutic concluded with MEDIPAL HOLDINGS

◆Nov.
- Completion of the New API Plant “Kobe Science Park Center”
- JCR Luxembourg S.A., European Packaging and Logistics Hub for a Global Distribution of its Investigational and Commercial Biomedicines against Rare Disease, is Established in Luxembourg

2023

◆Jan.
- FDA Grants Rare Pediatric Disease Designation to JR-141 (pabinafusp alfa)
- JCR Recieved the European Award for Best Practices 2022 by the ESQR

◆Mar.
- Achievement of Preclinical Proof-of-Concept Milestone Using J-Brain Cargo® Technology for LSD in Gene Therapy Collaboration with Takeda
- Research Collaboration, Option and License Agreement Conducted with Alexion, AstraZeneca Rare Disease to Develop a Therapy Using J-Brain Cargo® Technology for Neurodegenerative Disease

◆Apr.
- Entered into Co-Promotion Agreement in Japan for IZCARGO® I.V. Infusion 10 mg, a Recombinant Therapeutic for MPS II

◆May
- Global Collaboration with Angelini Pharma for the Development and Commercialization of Novel Biologic Therapies in Epilepsy

Agenda

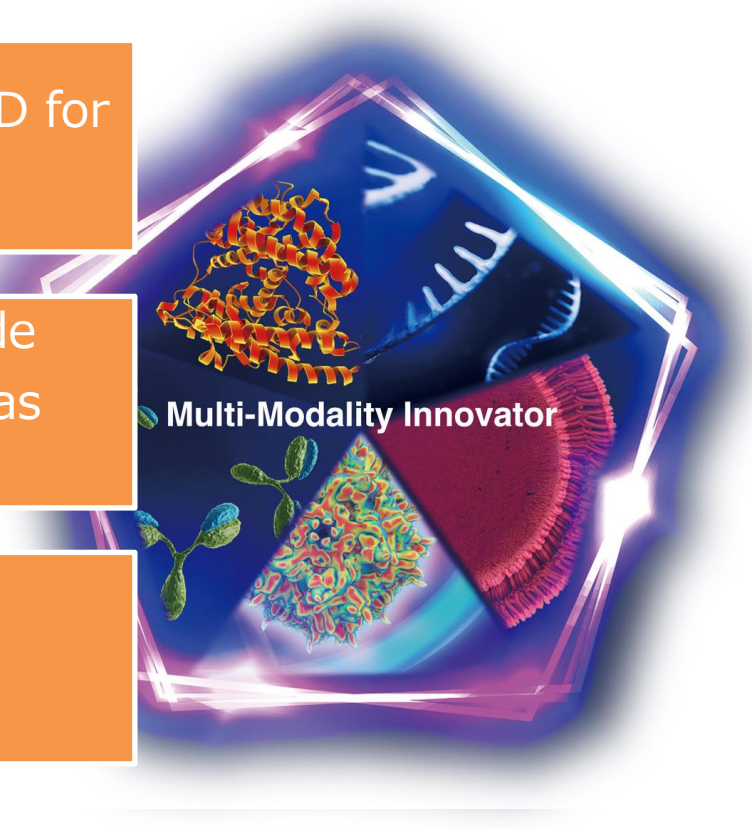
- Progress of Research and Development
- Upcoming Development Schedule

Progress on R&D Products Applying J-Brain Cargo® Technology

JCR Pharmaceuticals

J-Brain Cargo®

- Progress of internal R&D for LSD therapeutics
- Contributing to a wide range of disease areas other than LSDs
- Application to various modalities



Progress on R&D Products Applying J-Brain Cargo® Technology

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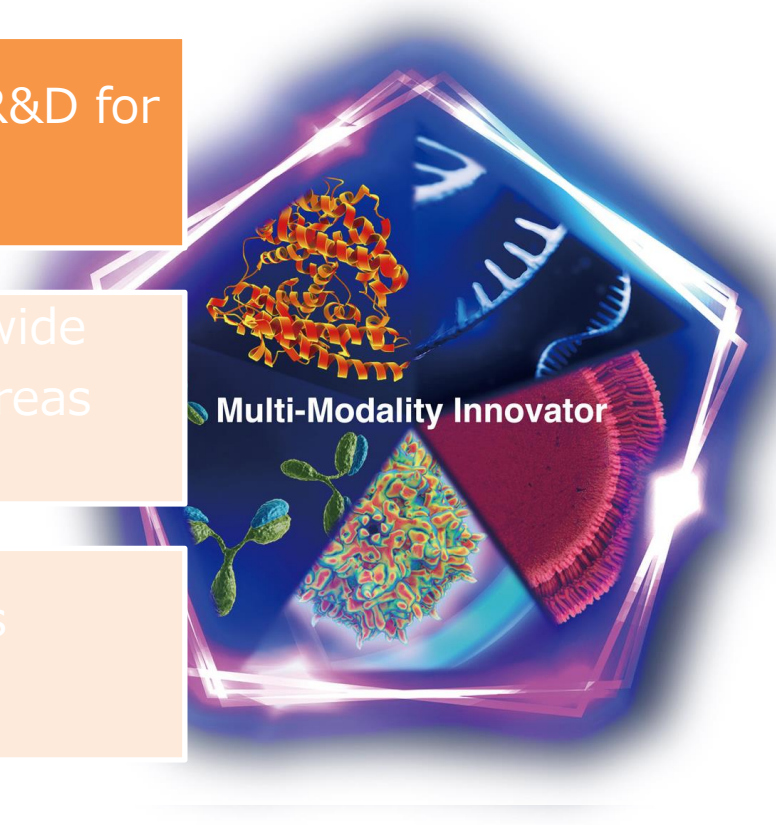


JR-141 Long-term results① (Presented at WORLD*Symposium*™ 2023)

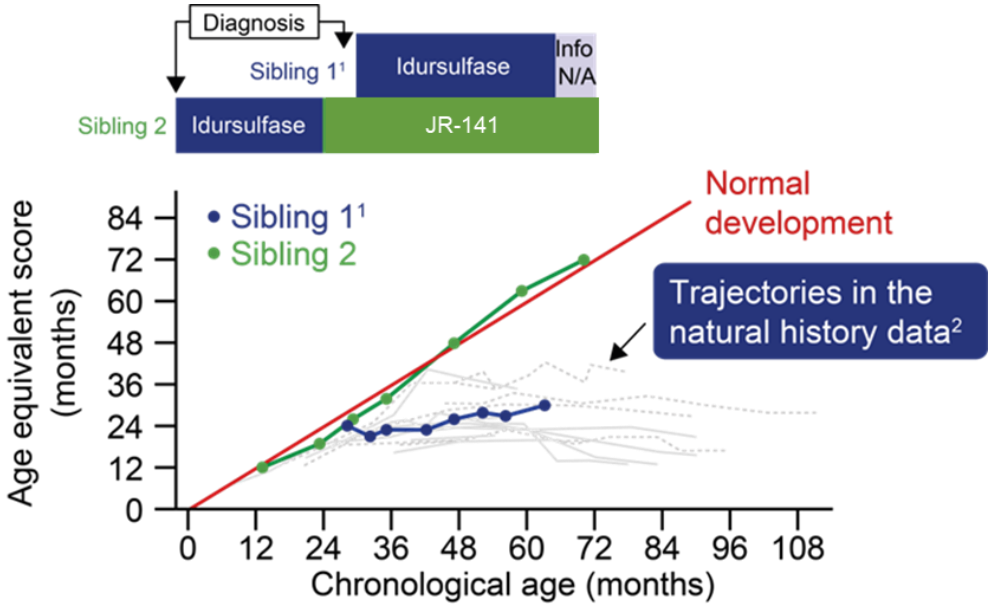
JR-141

IZCARGO® (Brand name in Japan)
pabinafusp alfa: BBB-penetrating iduronate-2-sulfatase (rDNA origin)

Please follow the link provided below
for the content of the WORLD*Symposium*™2023 presentation
giugliani-16-9-poster-05b.pdf

BBB: Blood-brain barrier

- Sibling 1 received idursulfase and had a neurodevelopment course similar to the natural history of severe mucopolysaccharidosis type II.
- Sibling 2 received pabinafusp alfa and continued on a normal neurodevelopment trajectory.
- In patients with neuronopathic mucopolysaccharidosis type II , age-equivalent score typically declines by age 5.



[1]Tomita K et al. JIMD Rep 2021;62:9–14. [2]Seo JH et al. Mol Genet Metab Rep 2020;24:100630.

Sibling case report supports importance of early treatment with BBB-penetrant enzyme replacement therapy for patients with mucopolysaccharidosis type II

JR-141 Long-term results② (Presented at WORLD*Symposium*™ 2023)

JR-141

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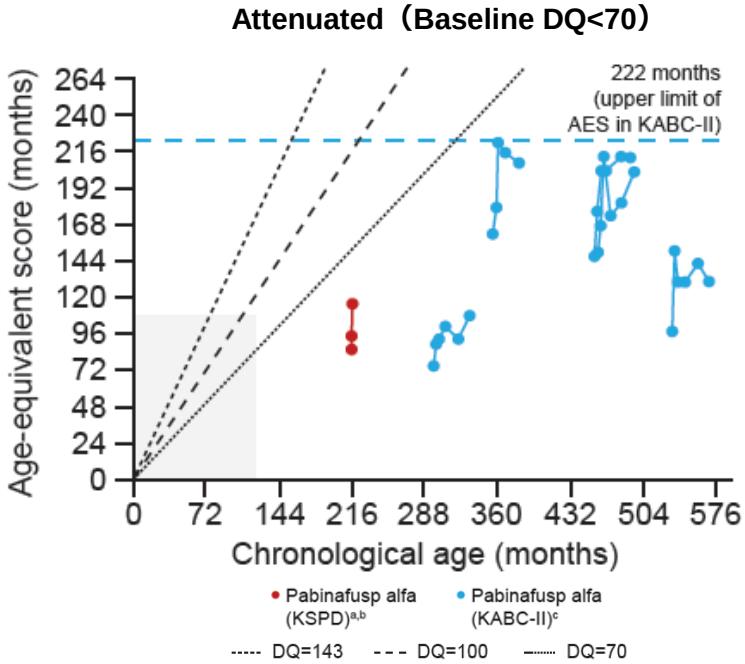
- Some cases classified as attenuated type also have cognitive decline
- These patients with JR-141 showed an increase in age-equivalent scores for cognition over time



Data suggests drug efficacy of JR-141 for CNS symptoms in attenuated patients with cognitive impairment.

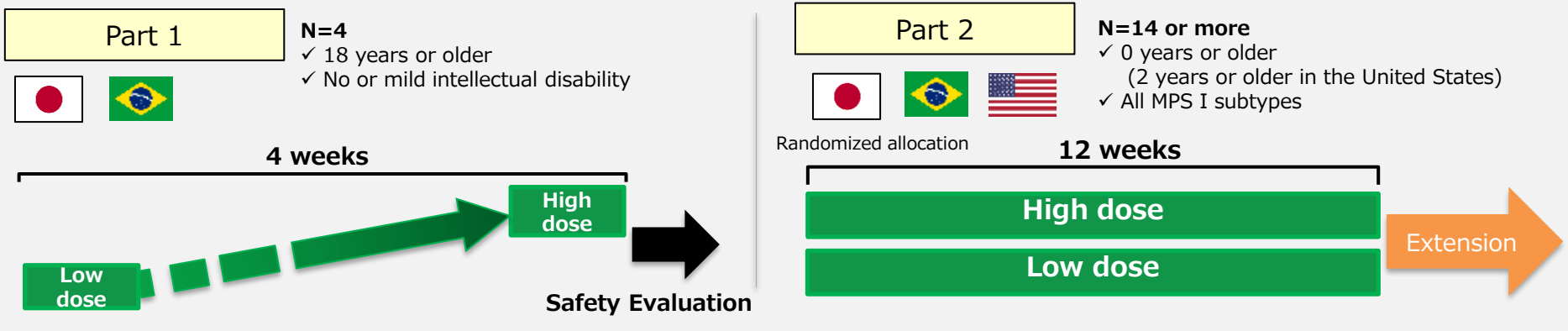
CNS: central nervous system

Progress on JR-171

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

Design of Global Phase 1/2 Clinical Trial (JR-171-101)

◆ **Apr. 2023: Dosing has been completed and data analysis is ongoing**

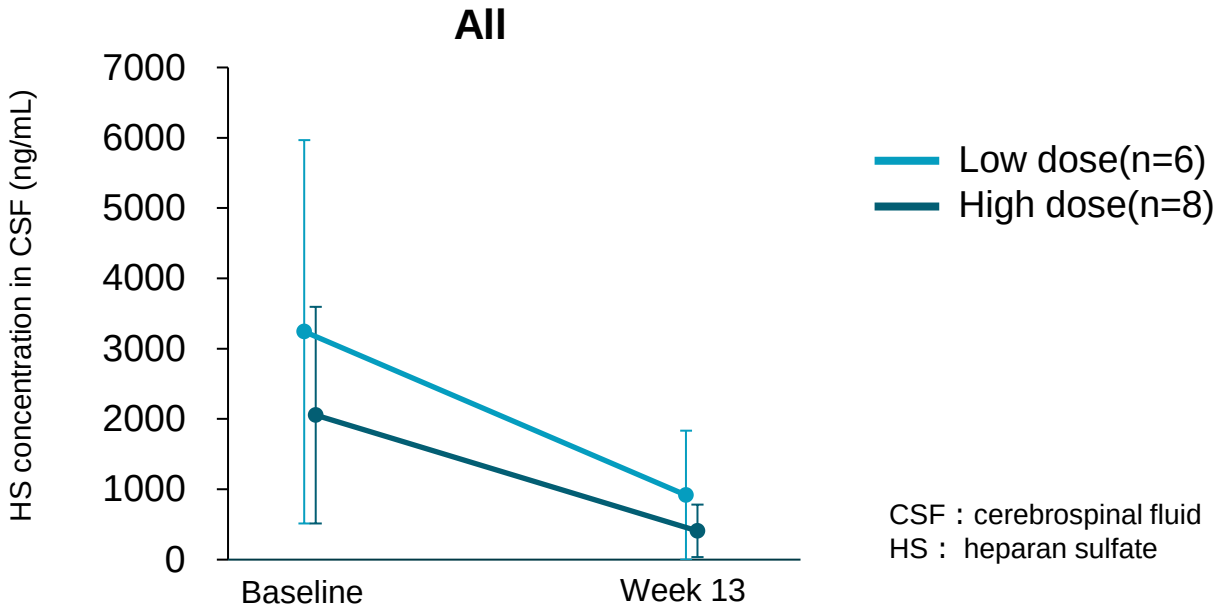


	Part 1	Part 2
Primary endpoint	Safety	
Secondary and exploratory endpoints	・Plasma drug concentration, pharmacokinetic parameters ・Exploratory efficacy on central nervous and systemic signs and symptoms	
Geography	Japan・Brazil	Japan・Brazil・USA
Clinical trials identifier	clinicaltrials.gov NCT04227600	

JR-171 Ph1/2 Clinical trial results① (Presented at WORLD*Symposium*™ 2023)

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

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



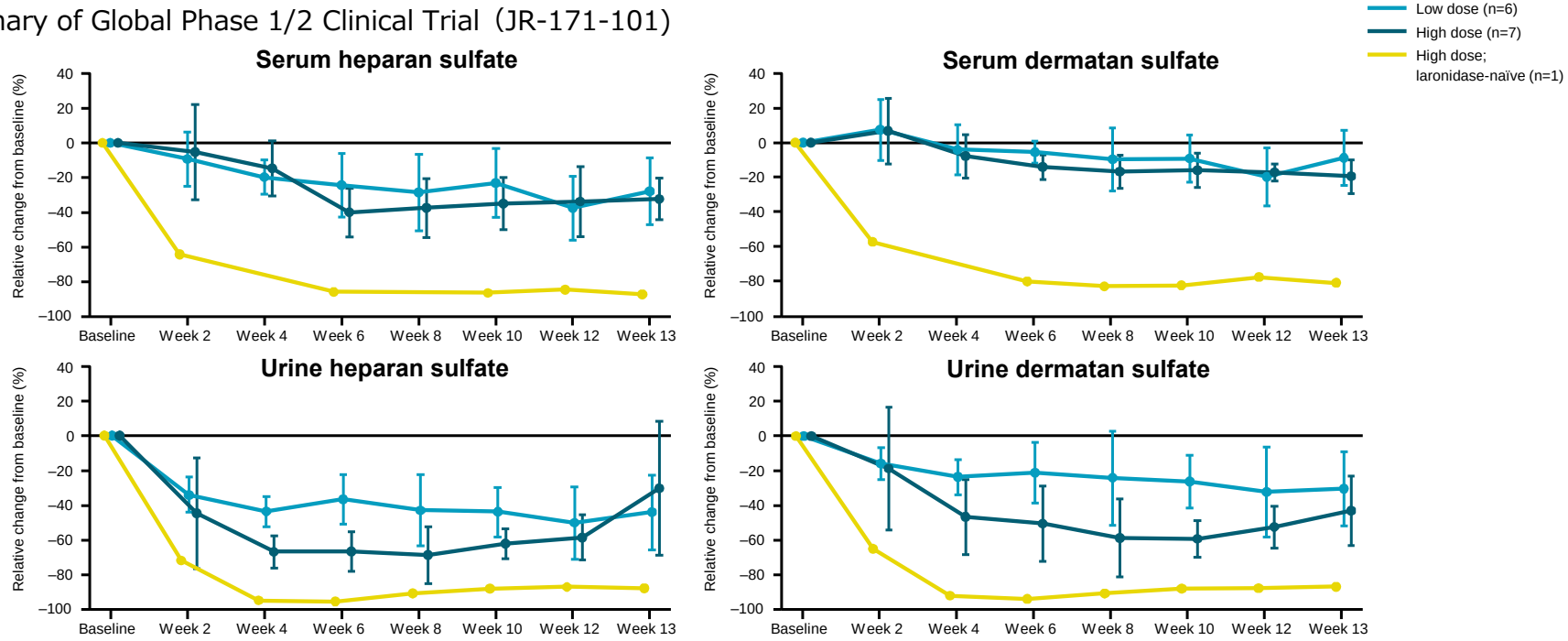
CSF：cerebrospinal fluid
HS： heparan sulfate

» Reduction of CSF biomarker was observed in all patients

JR-171 Ph1/2 Clinical trial results② (Presented at WORLD*Symposium*™ 2023)

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

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



[a]In a laronidase-naive patient, serum and urine baseline data are for reference due to suspicion of heparin contamination

In both laronidase-naïve and treated patients, HS and DS concentrations in urine and serum decreased from baseline to week 13

DS： dermatan sulfate

JR-171 Ph1/2 Clinical trial results③ (Presented at WORLD*Symposium*™ 2023)

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

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

Improvements observed in Phase 1/2

Language

- Expression and communication
- Comprehension
- livelier, longer, and more focused conversations

Motor

- Gait
- Ability to climb stairs
- Shoulder and knee joints
- Limb and finger strength

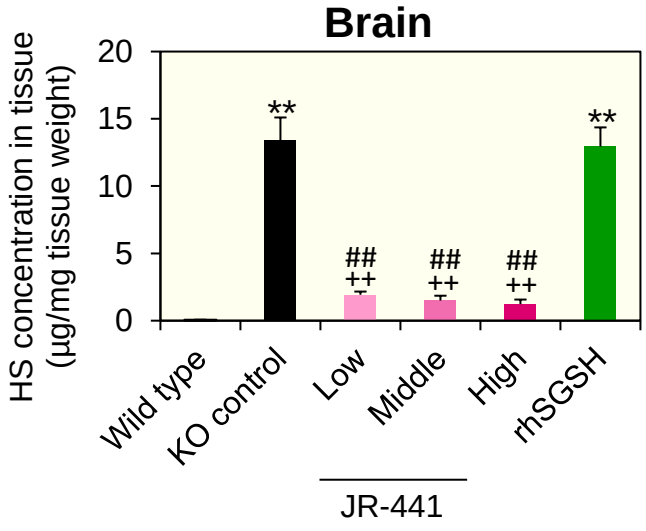
Other domains

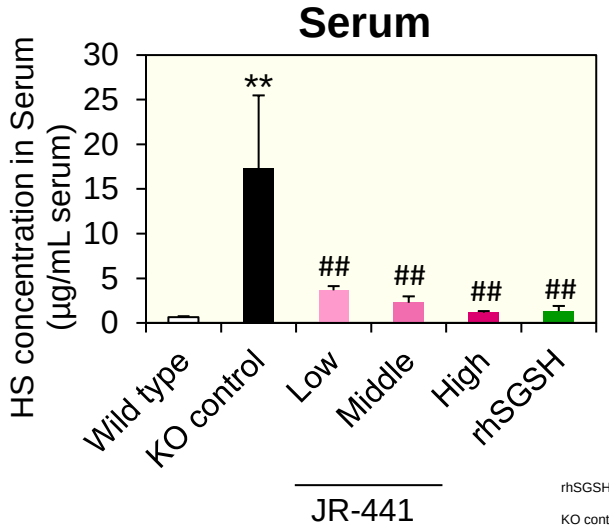
- Obstructive sleep apnea
- Concentration
- Attention to environment
- Mood
- Social interactions

JR-441 Preclinical Validation① (Presented at WORLD*Symposium*™ 2023)

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

- **JR-441 dose-dependently decreased HS concentrations in CSF and brain**
- **Both JR-441 and rhSGSH decreased HS concentrations in serum and peripheral tissues**





N=3-4/group, mean + S.D.
** : p<0.01 (vs Wild type)
: p<0.01 (vs KO control)
++ : p<0.01 (vs rhSGSH), Tukey HSD

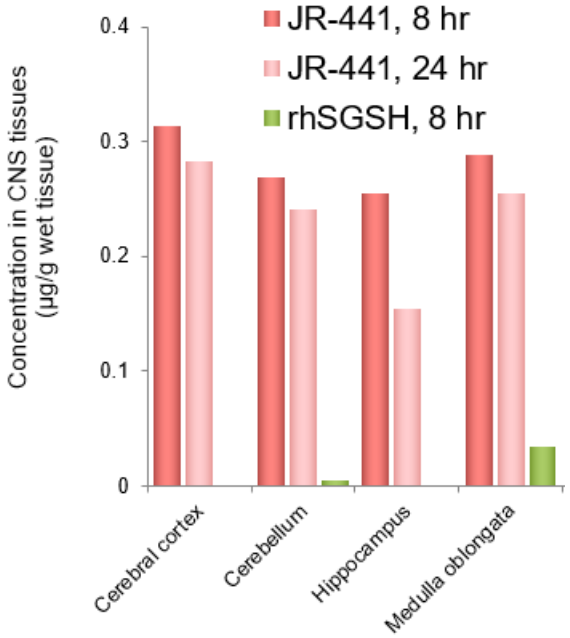
rhSGSH: recombinant human N-sulfoglucosamine sulfohydrolase
KO control: hTfR KI/Sgsh KO

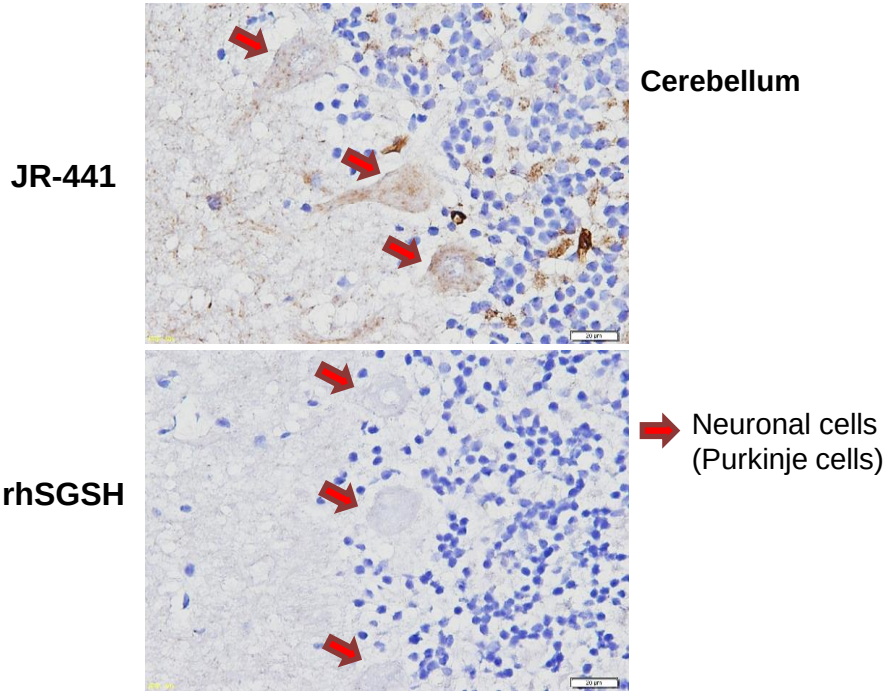
BBB-penetrant enzyme replacement therapy is also important for mucopolysaccharidosis type IIIA (Sanfilippo A Syndrome)

JR-441 Preclinical Validation② (Presented at WORLD*Symposium*™ 2023)

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

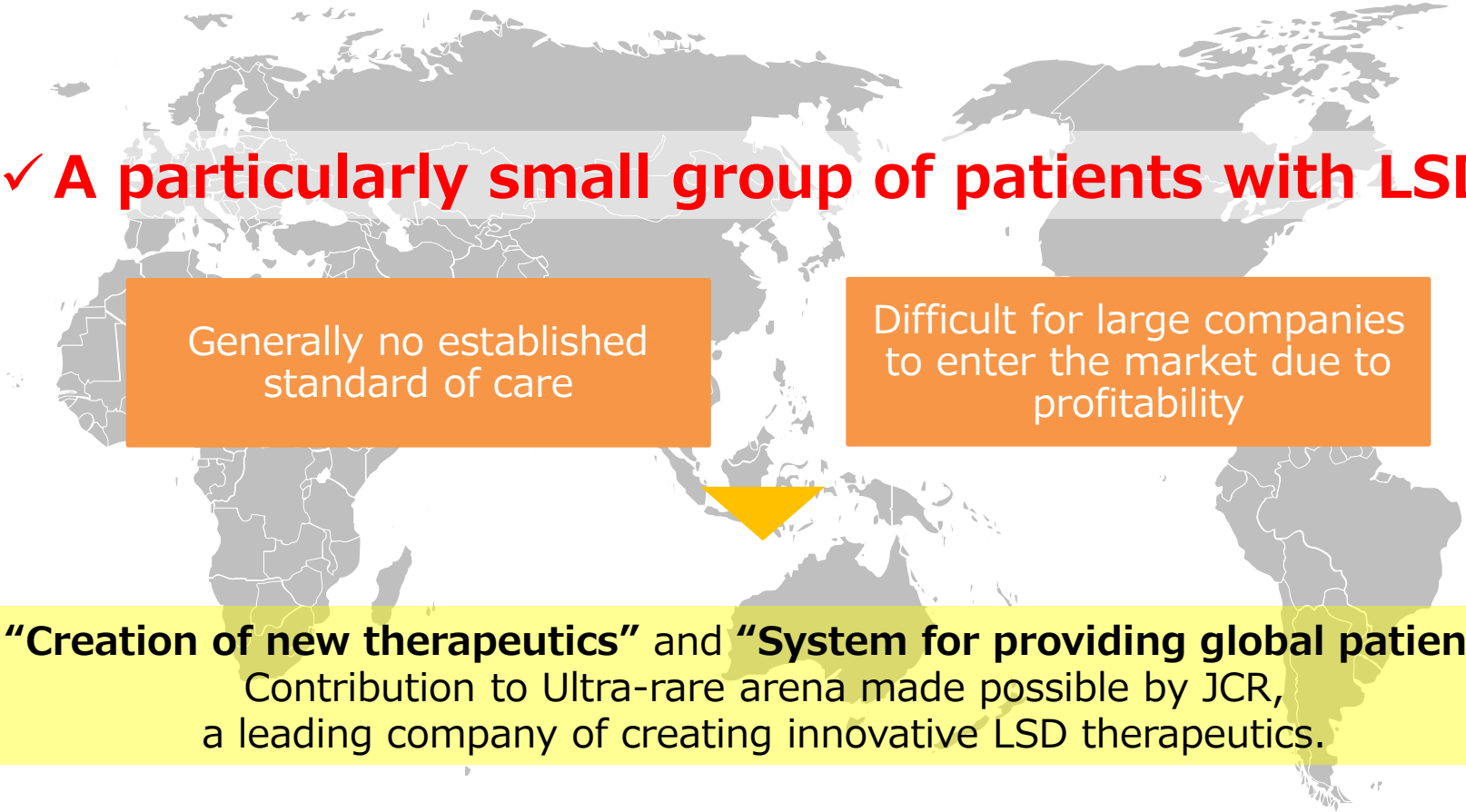
Biodistribution of JR-441 in the CNS of Cynomolgus Monkeys





JR-441 was distributed across various regions of the brain

Our responsibility for Ultra-Rare Diseases



✓A particularly small group of patients with LSDs

Generally no established standard of care

Difficult for large companies to enter the market due to profitability

“Creation of new therapeutics” and **“System for providing global patients”**
Contribution to Ultra-rare arena made possible by JCR,
a leading company of creating innovative LSD therapeutics.

Global Approach to Ultra-Rare Diseases

Oct. 2022 : Signed an agreement with MEDIPAL HOLDINGS for the global commercialization of biotherapeutics ultra-rare diseases

- **Granting of exclusive negotiation rights for the global commercialization of four ultra rare diseases.**
- **Conclusion of licensing agreement for global commercialization of JR-471 (Therapeutics for Fucosidosis)**

MEDIPAL HOLDINGS CORPORATION

- On the distribution of pharmaceuticals Long-standing know-how and knowledge

JCR Pharmaceuticals

- Expertise in biopharmaceuticals
- R&D in the rare disease arena

<u>The two companies have built and maintained a good relationship for many years</u>

- 2016: The two companies developed an Ultra-Low Cold Chain System for the TEMCELL®
- 2017: Strengthen Business and Capital Alliance with MEDIPAL HOLDINGS

Progress on R&D Products Applying J-Brain Cargo® Technology

J-Brain Cargo®

- Progress of internal R&D for LSD therapeutics
- **Contributing to a wide range of disease areas other than LSDs**
- Application to various modalities

Application for CNS Diseases other than LSDs①

Mar. 2023 : Concluded research collaboration, option and license agreement with Alexion to develop the treatment using J-Brain Cargo® for neurodegenerative disease

ALEXION® AstraZeneca Rare Disease

JCR Pharmaceuticals

The first international partnership to apply the J-Brain Cargo® technology for the treatment of a neurodegenerative disease.

Application for CNS Diseases other than LSDs②

May 2023 : Concluded an agreement of global collaboration for the development and commercialization of novel biologic therapies in epilepsy

- ✓ Epilepsy is thought to affect more than 50 million people worldwide*
- ✓ JCR will also be eligible to receive additional payments of **up to US$505.5 million** upon reaching development and commercial milestones, as well as tiered royalties on post-approval net sales.

*WHO, https://bit.ly/3VvsC5E

Progress on R&D Products Applying J-Brain Cargo® Technology

JCR Pharmaceuticals

J-Brain Cargo®

- Progress of internal R&D for LSD therapeutics
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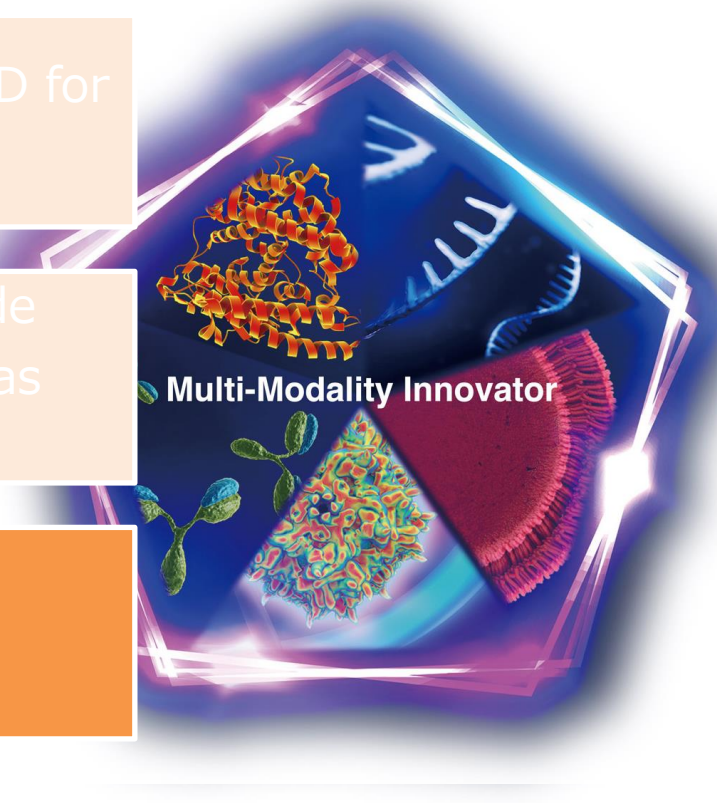
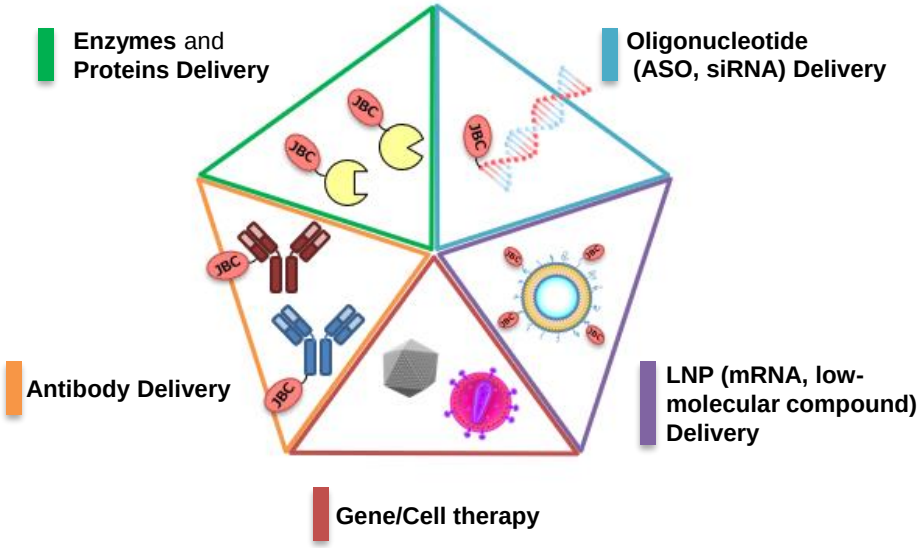


Application to Various Modalities

Mar. 2023 : Achievement of preclinical proof-of-concept milestone using J-Brain Cargo® technology for LSD in gene therapy collaboration with Takeda



Takeda

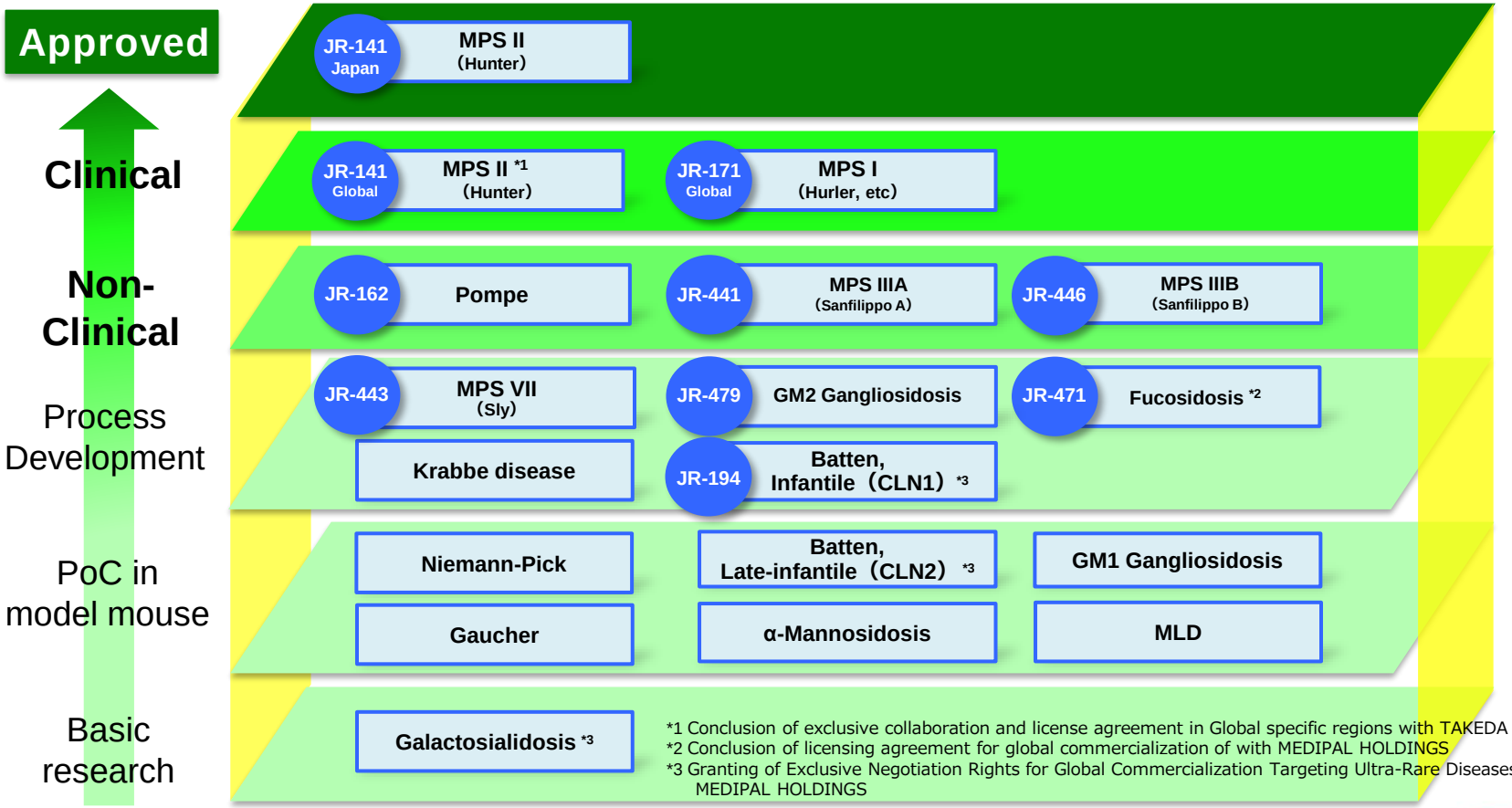
JCR Pharmaceuticals

Applicability of the J-Brain Cargo® technology for gene therapies

Agenda

- Progress of Research and Development
- Upcoming Development Schedule

JCR's LSD Pipeline comprises 17 Programs applied J-Brain Cargo®



*1 Conclusion of exclusive collaboration and license agreement in Global specific regions with TAKEDA
*2 Conclusion of licensing agreement for global commercialization of with MEDIPAL HOLDINGS
*3 Granting of Exclusive Negotiation Rights for Global Commercialization Targeting Ultra-Rare Diseases with MEDIPAL HOLDINGS

Development Portfolio

★Updated

Code	Indication	Status	Next Milestones	Remarks
JR-141	MPS type II (Hunter Syndrome)	Approved	-	• SAKIGAKE/ Orphan Drug
		Phase 3	~FY2027 Approval in US, EU, Brazil	• Conclusion of exclusive collaboration and license agreement in Global specific regions with TAKEDA • US: Orphan Drug/ Fast Track/ RPDD EU: Orphan Drug/ PRIME/
JR-171	MPS type I (Hurler Syndrome etc.)	Phase 1/2 (Under Analysis)	FY2024 Phase 3 ★	• US: Orphan Drug/ Fast Track EU: Orphan Drug
JR-441	MPS type IIIA (Sanfilippo A Syndrome)	Preclinical	FY2023 Phase1/2	• EU: Orphan Drug
JR-446	MPS type IIIB (Sanfilippo B Syndrome)	Preclinical	FY2024 Phase1/2 ★	-
JR-479	GM2 Gangliosidosis (Sandhoff, Tay-Sachs disease)	Preclinical	~FY2025 Phase1	-
JR-471	Fucosidosis	Process Development	-	• Conclusion of a contract on the Granting of Exclusive Negotiation Rights for Global Commercialization with MEDIPAL HOLDINGS
JR-162	Pompe disease	Preclinical	-	-
JR-443	MPS type VII (Sly Syndrome)	Preclinical	-	-
JR-401X	SHOX deficiency	Filed	-	• Expanded indication of GROWJECT®
JR-142	Pediatric growth hormone deficiency	Phase 2 (Analysis Completed)	FY2023 Phase 3	• Recombinant long-acting Growth Hormone
JR-031HIE	Hypoxic ischemic encephalopathy in neonates	Phase 1/2 (Under Analysis)	-	• Expanded indication of TEMCELL®

– REVOLUTION into the Future –

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.

Appendix

Pipeline of LSDs

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

Indication :	MPS type II (Hunter syndrome)
Patient population*1 :	250 (Japan) , 7,800 (WW) est.
Est. Market size*2 :	7.6 billion JPY (2019 Japan), 87.0 billion JPY (2019 WW)
Disease overview :	Hunter syndrome is an X-linked recessive LSD caused by a deficiency of iduronate-2-sulfatase, an enzyme that breaks down glycosaminoglycans (mucopolysaccharides) in the body. MPS II gives rise to a wide range of somatic symptoms and central nervous system (CNS) symptoms.

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

Indication :	MPS type I (Hurler, Hurler-Scheie, Scheie syndrome)
Patient population*1 :	60 (Japan), 3,600 (WW) est.
Est. Market size*2 :	70.0 billion JPY (2019 WW)
Disease overview :	MPS I is an autosomal recessive LSD caused by a deficiency of α-L-iduronidase, an enzyme that breaks down glycosaminoglycans (mucopolysaccharides) in the body. MPS I gives rise to a wide range of somatic and neurological symptoms. A major limitation to current ERT is that it does not address central nervous system (CNS) symptoms because of the enzyme's inability cross the BBB.

*1 Calculated internally based on the date from MHLW and own research *2 Internal analysis

ERT: enzyme replacement therapy(ERT)

Pipeline of LSDs

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.
Est. Market size*2 :	>70.0 billion JPY (2019 WW: Total of Type A&B)
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), 10,000 (WW) est.
Est. Market size*2 :	3 billion JPY (2019 Japan), 110 billion JPY (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 Internal analysis

Pipeline of LSDs

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

Indication :	MPS type VII（Sly syndrome）
Patient population*1 :	several (Japan) , 200 (WW) est.
Est. Market size*2 :	9.8 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) , 1,800 (WW) est.
Est. Market size*2 :	>70.0 billion JPY（2019 WW: Total of Type A&B）
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 Internal analysis

Pipeline of LSDs

JR-479 BBB-penetrating β-Hexosaminidase A (rDNA origin)

Indication :	GM2 gangliosidosis (Tay-Sachs disease, Sandohoff disease)
Patient population*1 :	30 (Japan), TBD(WW) est.
Est. Market size*2 :	TBD
Disease overview :	GM2 gangliosidosis is an autosomal recessive LSD caused by a deficiency in the GM2 ganglioside-metabolizing enzyme β-Hexosaminidase A. GM2 ganglioside is abundant in the brain, and GM2 gangliosidosis gives rise to progressive central nervous system (CNS) symptoms. It is difficult to distinguish between Tay-Sachs and Sandhoff disease by clinical symptoms.

JR-471 BBB-penetrating α-L-fucosidase (rDNA origin)

Indication :	Fucosidosis
Patient population*1 :	TBD
Est. Market size*2 :	TBD
Disease overview :	Fucosidosis is an autosomal recessive LSD caused by a deficiency in the glycoprotein-metabolizing enzyme (α-L-fucosidase) . Symptoms include psychomotor symptoms, muscle hypotonia, visceromegaly, and skeletal abnormalities. The disease can be classified in the rapidly progressive form, causing severe, life-threatening complications in children or in the mild form develop during adolescence and with slower progression, but causing serious complications in adulthood.

*1 Calculated internally based on the date from MHLW and own research *2 Internal analysis

Pipeline 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）

*Internal analysis

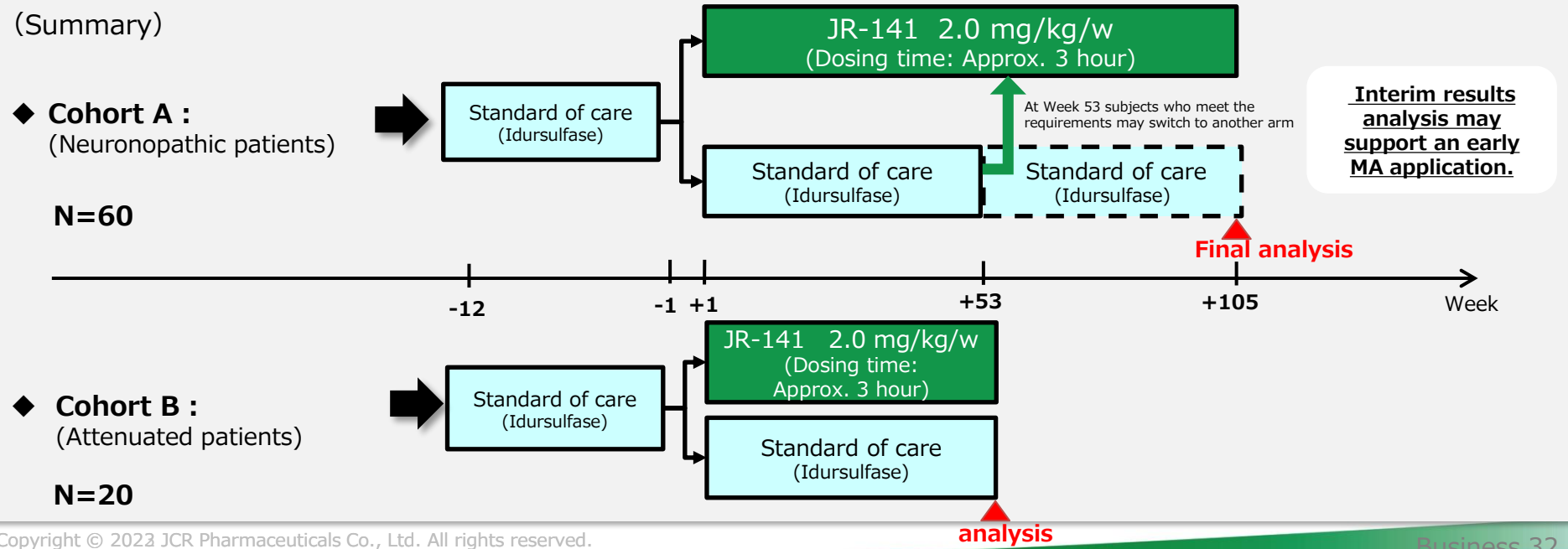
Progress on JR-141 (JR-141-GS31)

JR-141

IZCARGO® (Brand name in Japan)
pabinafusp alfa: BBB-penetrating iduronate-2-sulfatase (rDNA origin)

- **Expansion of clinical trial sites in the US, Brazil, and Europe and patient enrollment is in progress. Also, prepare the initiation of the study in several new areas.**

(Summary)



Interim results analysis may support an early MA application.

Progress on JR-141 (JR-141-GS31)

JR-141

IZCARGO® (Brand name in Japan)
pabinafusp alfa: BBB-penetrating iduronate-2-sulfatase (rDNA origin)

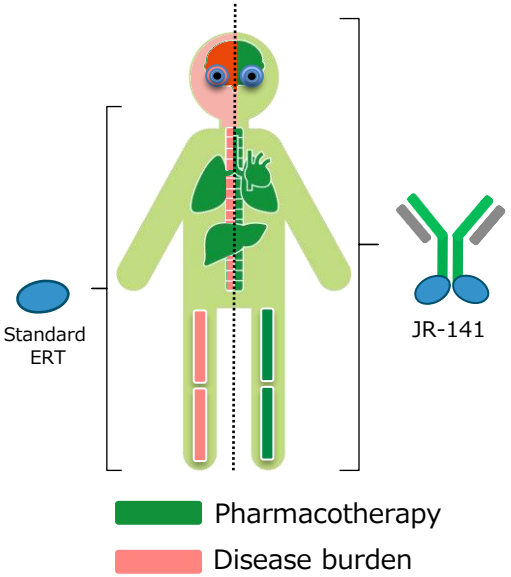
Objective : JR-141-GS31

1. **To demonstrate the significant efficacy of JR-141 on CNS signs and symptoms in MPS-II subjects relative to standard ERT.**

   JR-141 is expected to have superior activity on neurologic signs and symptoms of MPS-II by reducing substrate in the brain.

2. **To demonstrate control of somatic signs and symptoms by JR-141 that is comparable to standard ERT.**

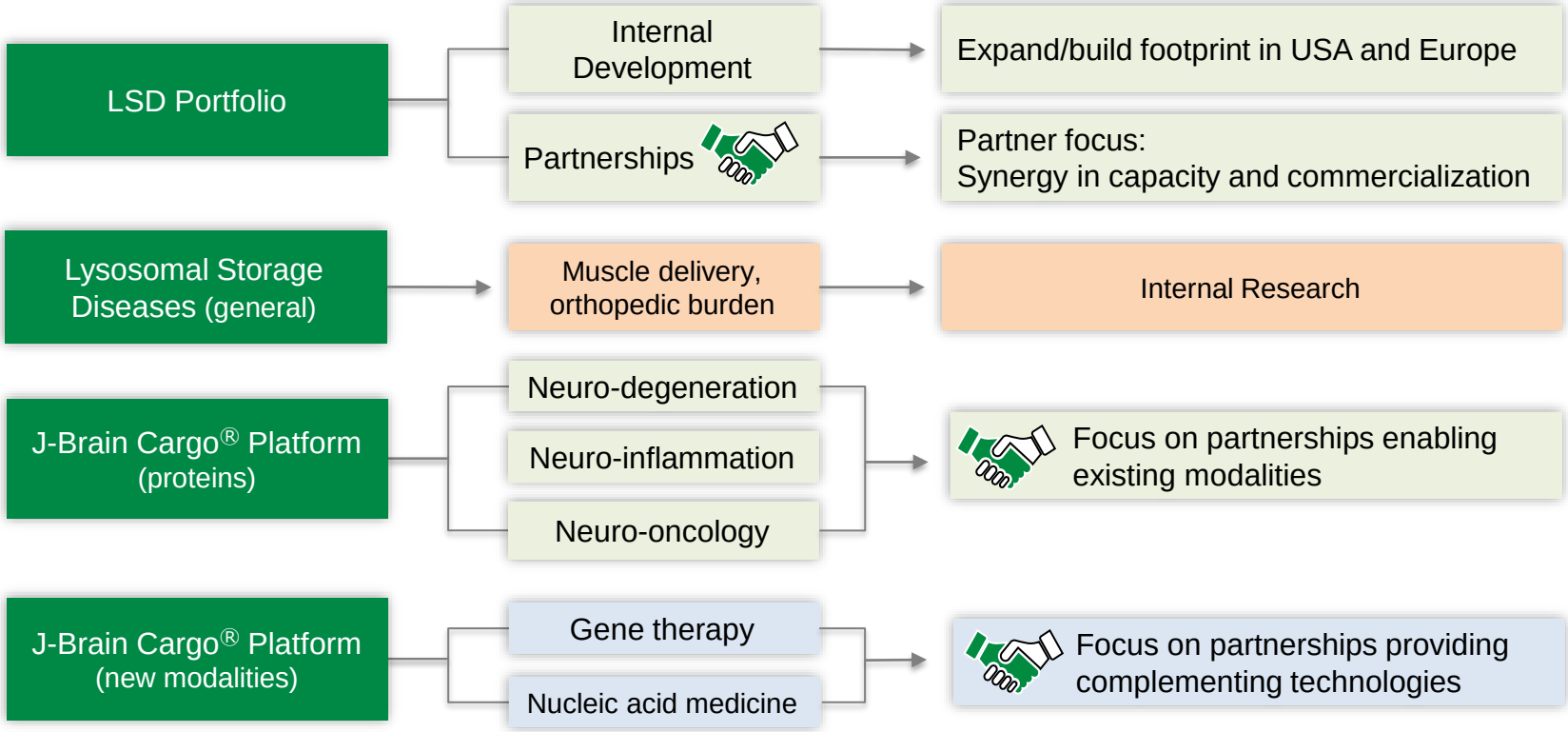
   JR-141 is expected to control somatic symptoms and biomarkers comparable to standard ERT (even though some improved symptom control may be seen due to dual uptake mechanism by JR-141)



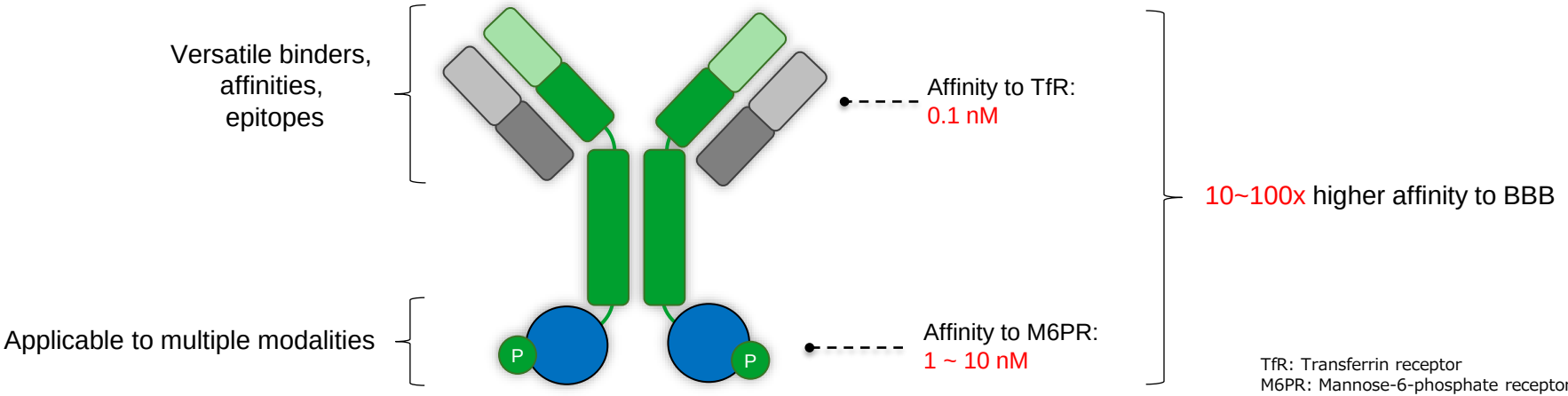
Leveraging Growth Opportunities from J-Brain Cargo® Technology

Partnerships are at the core of JCR's growth and acceleration strategy

LSD: Lysosomal diseases
CNS: Central central nervous system



Design Uniqueness of the J-Brain Cargo® Technology



TfR: Transferrin receptor
M6PR: Mannose-6-phosphate receptor
BBB: Blood-brain barrier

Differentiator	Why does it matter?
Preferential BBB targeting	• Higher uptake to brain compared to somatic tissue
High affinity	• Lower doses resulting in shorter infusion times, manageable infusion reactions
Versatility in binders, affinities, epitopes, modalities	• Customizable to different diseases and modalities
Safety	• Best characterized safety profile in the industry