



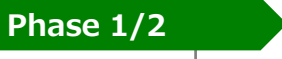


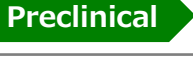









# FY2020 First-Half Results Briefing Session - Research and Development Highlights -

November 2, 2020

JCR Pharmaceuticals Co., Ltd.


Code	Indication	Preclinical	Clinical trials	Filed	Approved	Remarks	
<b>JR-141</b>	MPS type II (Hunter Syndrome)	 <b>Filed</b>				<ul style="list-style-type: none"> <li>• ERT</li> <li>• J-Brain Cargo®</li> </ul>	
		 <b>Phase 2 completed</b>					
<b>JR-171</b>	MPS type I (Hurler Syndrome etc.)	<b>Phase 1/2</b>				<ul style="list-style-type: none"> <li>• ERT</li> <li>• J-Brain Cargo®</li> <li>• J-MIG System®</li> </ul>	
<b>JR-162</b>	Pompe disease	<b>Preclinical</b>				<ul style="list-style-type: none"> <li>• ERT</li> <li>• J-Brain Cargo®</li> </ul>	
<b>JR-441</b>	MPS type III A (Sanfilippo A Syndrome)	<b>Preclinical</b>				<ul style="list-style-type: none"> <li>• ERT</li> <li>• J-Brain Cargo®</li> </ul>	
<b>JR-443</b>	MPS type VII (Sly Syndrome)	<b>Preclinical</b>				<ul style="list-style-type: none"> <li>• ERT</li> <li>• J-Brain Cargo®</li> </ul>	
<b>JR-446</b>	MPS type III B (Sanfilippo B Syndrome)	<b>Preclinical</b>				<ul style="list-style-type: none"> <li>• ERT</li> <li>• J-Brain Cargo®</li> </ul>	
<b>JR-401X</b>	SHOX deficiency	<b>Phase 3</b>				<ul style="list-style-type: none"> <li>• Expanded indication of GROWJECT®</li> </ul>	
<b>JR-041</b>	Infertility	<b>Phase 1/2</b>				<ul style="list-style-type: none"> <li>• Out-licensed to ASKA Pharmaceutical Co., Ltd.</li> </ul>	
<b>JR-142</b>	Pediatric growth hormone deficiency	<b>Phase 1 completed</b>				<ul style="list-style-type: none"> <li>• J-MIG System®</li> </ul>	
<b>JR-031EB</b>	Epidermolysis bullosa	<b>Suspended (Application withdrawn)</b>					<ul style="list-style-type: none"> <li>• Expanded indication of TEMCELL®HS Inj.</li> </ul>
<b>JR-031HIE</b>	Hypoxic ischemic encephalopathy in neonates	<b>Phase 1/2</b>				<ul style="list-style-type: none"> <li>• Expanded indication of TEMCELL®HS Inj.</li> </ul>	
<b>JTR-161/ JR-161</b>	Acute cerebral infarction	<b>Phase 1/2</b>				<ul style="list-style-type: none"> <li>• Co-developed with Teijin Limited</li> </ul>	

**Research & Development News (Jun.-Oct.)**

JR-141 Development Status

Other Pipeline Products

2020

- Jun. 17 : **Agalsidase Beta BS. I.V. Infusion** for Fabry Disease:  
Publication of The Clinical Trial Results for Fabry Disease in Molecular Genetics and Metabolism
- Jul. 31 : **Completion of Phase 1/2 Clinical Trial Notification of JR-171**  
as a Global Clinical Trial in Japan 
- Jul. 31 : **Capital Expenditures to Increase Production Capacity** at the Seishin Plant
- Aug. 26 : Decision for **Business Expansion in Brazil** 
- Sep. 15 : PHC and JCR Offer **Growth Hormone Adherence Application** for Use in Clinical Research
- Sep. 18 : MHLW **Orphan Drug Designation for JR-141(Pabinafusp Alfa)**  
for Hunter Syndrome 
- Sep. 29 : **Filing for Marketing Approval of JR-141(Pabinafusp Alfa)**  
for Hunter Syndrome under the SAKIGAKE Designation System in Japan 
- Oct. 15 : **JR-141 (Pabinafusp Alfa)** for Hunter Syndrome:  
Publication of The Phase2/3 Clinical Trial Results in Japan in Molecular Therapy
- Oct. 23 : **Growth Hormone Therapy Medication Management App Melon Nikki™**  
Launched to Help Improve Medication Adherence

Research & Development News (Jun.-Oct.)

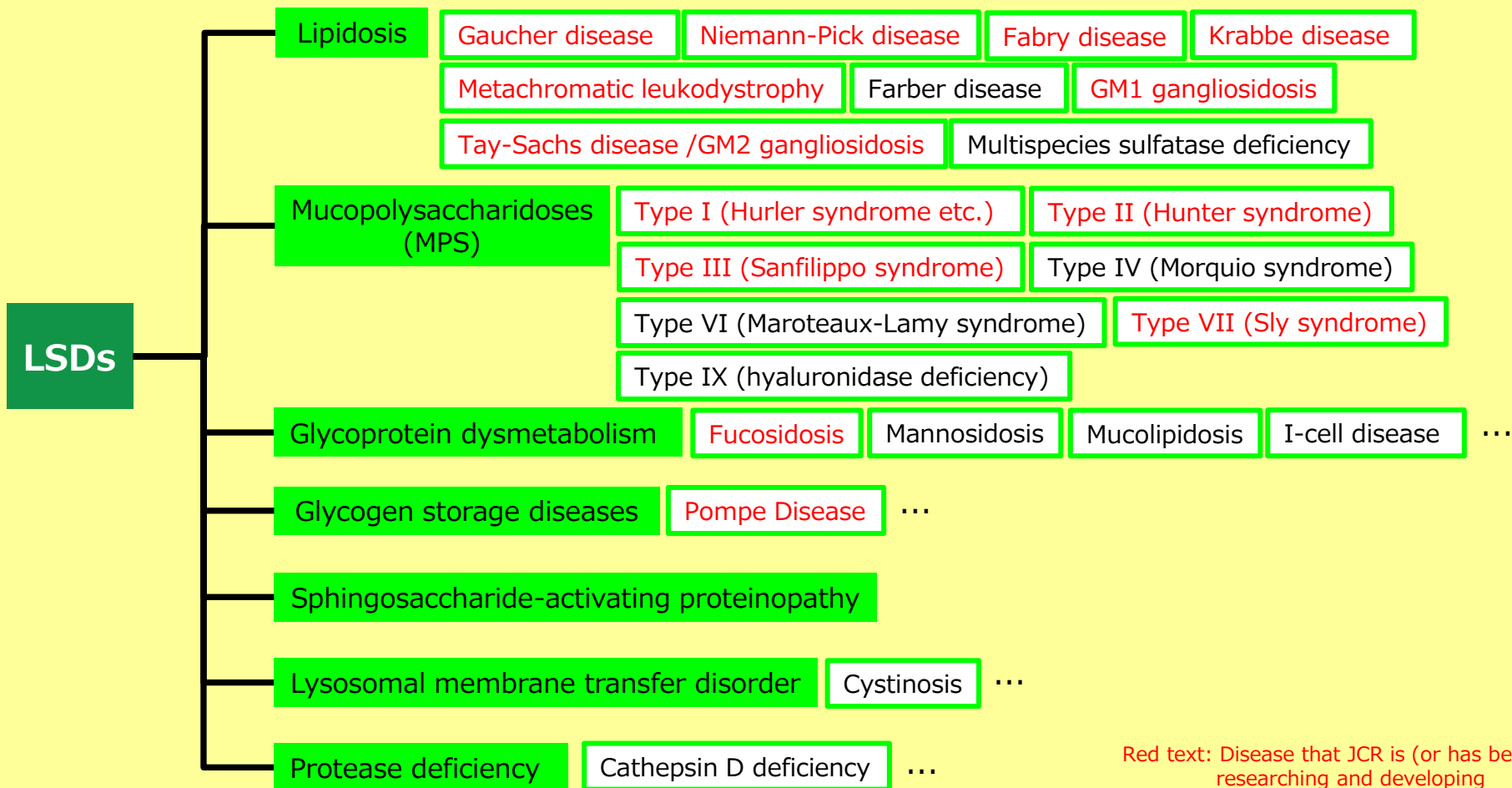
**JR-141 Development Status**

Other Pipeline Products

# 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.



## Pabinafusp alfa (BBB-penetrating iduronate-2-sulfatase, rDNA origin)

**Status : Filed for MAA in Japan**

Indication : **MPS type II (Hunter Syndrome)**

Patient population\*<sup>1</sup> : 250 (Japan), 7,800 (WW)

Market size\*<sup>2</sup> : 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.

Heparan Sulfate (HS) and Dermatan Sulfate (DS) accumulating in tissues causes various clinical symptoms such as retinal degeneration, decreased intelligence, exudative otitis media, hearing loss, obstructive breathing disorder, restrictive lung disease, cardiac valve disease, splenohepatomegaly, arthrogryposis, bone deformation and macroglossia.

Current standard of care : Supportive measures for each symptom and HSCT or ERT as causal therapy

**ERT** : Global, first-line choice. Relatively safe.

Clinical benefit including decrease in HS and DS in urine, improvement of splenohepatomegaly, increase of 6 minute walk distance/forced vital capacity/range of joint motion.

\*<sup>1</sup> Calculated internally based on the data from MHLW \*<sup>2</sup> Actual sales of existing ERT and data from Evaluate Pharma and IQVIA

# Unmet medical needs of Hunter Syndrome

Hunter Syndrome\*1\*2



Intellectual disability: Yes  
Life expectancy: Approximately 10 years w/o treatment

Intellectual disability : None or moderate  
Life expectancy : Approximately 20 years w/o treatment

## ◆ CNS symptoms disrupt QoL of patients

CNS symptoms including intellectual disability, aberrant behavior, hyperactivity, sleep disturbance and convulsion are highly prevalent. Some of these symptoms are observed even in the attenuated patients.

## ◆ Existing ERT cannot address CNS symptoms due to blood brain barrier (BBB)\*2\*4

(MPS type II practice guideline 2019, Japanese Society for Inherited Metabolic Diseases) \*5  
High-molecular compounds, such as enzymes, cannot cross BBB. Existing ERT cannot ameliorate CNS symptoms including mental retardation and neurological regression which are observed in about 70% patients with Hunter syndrome



HS accumulation in the brain is regarded to cause the onset of CNS symptoms. **Reducing HS in brain parenchyma is important as a direct approach to improve CNS symptoms.**\*6\*7\*8\*9

### [Reference]

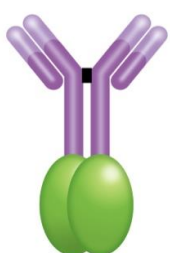
- \*1 : Muenzer J, et al. Eur J Pediatr. 2012; 171: 181-8. \*2 : Tanaka A, et al. Mol Genet Metab. 2012; 107: 513-20. \*3 : Okuyama T. Ped. Int. Med; 2009; 41: 466-70.  
\*4 : Tanaka A, Inherited Metabolic Disorder Syndrome (2<sup>nd</sup> Edition) Vol.2; 2012. p. 533-8. \*5 : Japanese Society for Inherited Metabolic Diseases. SHINDAN TO CHIRYO SHA; 2019. 24p.  
\*6 : Tomatsu S, et al. Mucopolysaccharidosis UPDATE. EN MEDICS; 2011. p. 15-9. \*7 : Tanaka A, SHINDAN TO CHIRYO SHA; 2011. p. 190-6.  
\*8 : Mano T, et al. SHINDAN TO CHIRYO SHA; 2011. p. 51-5. \*9 : Sato Y. et al. Int J Mol Sci. 2020; 21: 400.

**JR-141**

Pabinafusp alfa (BBB-penetrating iduronate-2-sulfatase, rDNA origin)  
**Status : Filed for MAA in Japan**

**JR-141 Summary and Estimated delivery route of J-Brain Cargo®**

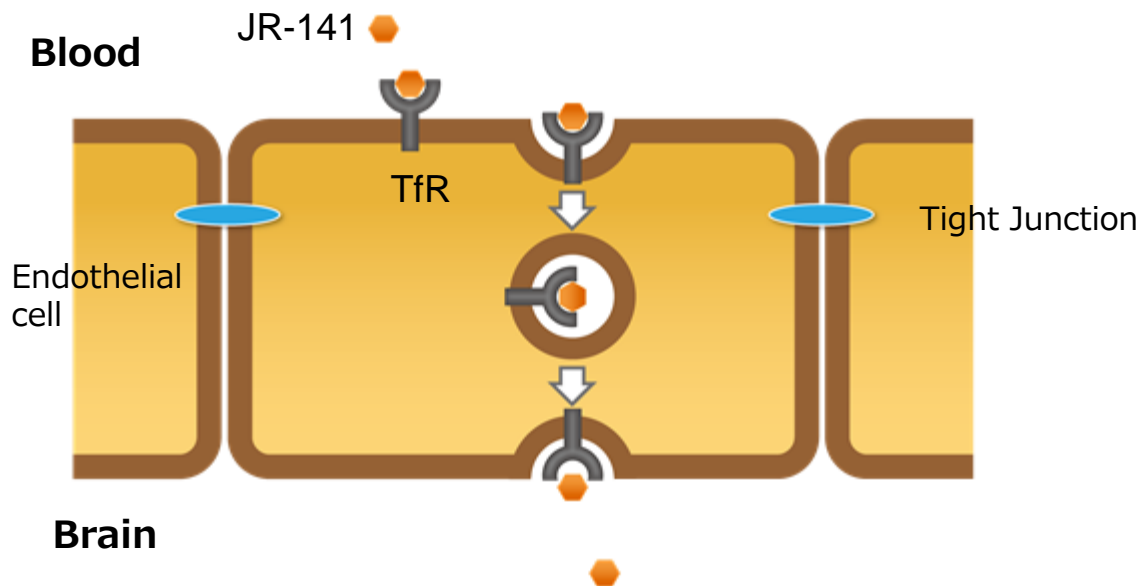
<JR-141>



**J-Brain Cargo®**  
 (Anti human-Transferrin Receptor antibody)

**hIDS** (2 molecules)

- Recombinant fusion protein of humanized antibody (J-Brain Cargo®) specifically binding human transferrin receptor (TfR) and human Iduronate-2-Sulfatase (hIDS)
- Produced by CHO
- Intravenously infusion, Lyophilized.



2005

- Initiation of BBB-penetrating technology research

(2007)

(ERT for Hunter syndrome launched in Japan)

2014

- Initiation of JR-141 development
- Initiation of non-clinical testing
  - Confirmation of BBB penetration into CNS  
(Sonoda H, et al. Mol Ther. 2018; 26(5):1366-74.)
  - Suppression of CNS symptom in MPSII mouse  
(manuscript submitted)

2017

- Initiation of Phase 1/2 clinical trial in Japan
  - Indicating clinical significance of J-Brain Cargo®  
(Okuyama T, et al. Mol Ther. 2019; 27(2):456-64.)

2018

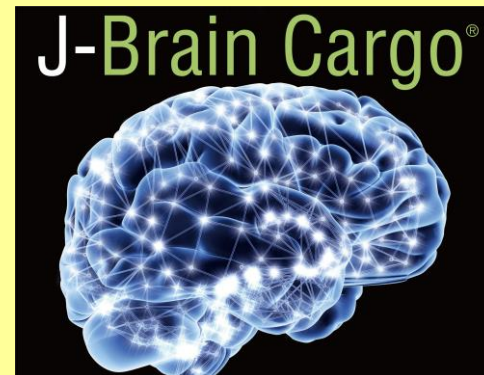
- Designation under SAKIGAKE system in Japan
- Initiation of Phase 2 trial in Brazil
- Initiation of Phase 2/3 trial in Japan  
(Okuyama T, et al. Mol Ther. 2020; 2020 Sep 30;S1525-0016(20)30496-2)

2019

- Orphan drug designation in U.S.
- Orphan drug designation in EU.

2020

- Orphan drug designation in Japan.
- Application for marketing authorization in Japan

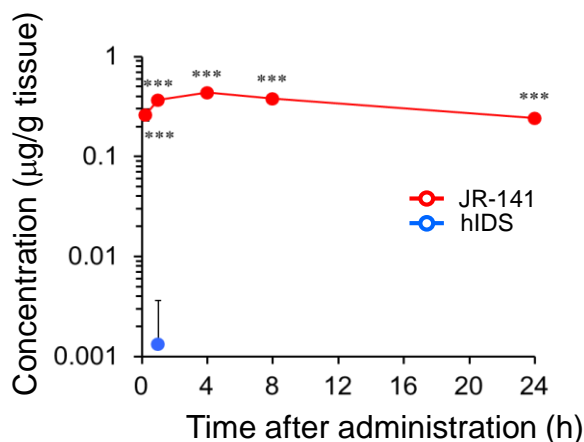


## JR-141

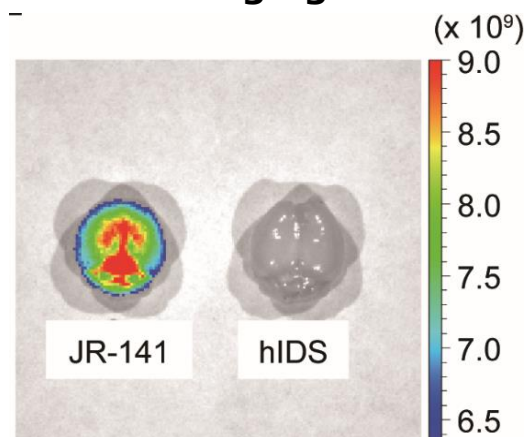
Pabinafusp alfa (BBB-penetrating iduronate-2-sulfatase, rDNA origin)  
**Status : Filed for MAA in Japan**

➤ Incorporation of JR-141 to neuronal tissues in of the brain following penetration via BBB intravenous administration into hTfR-KI Mice

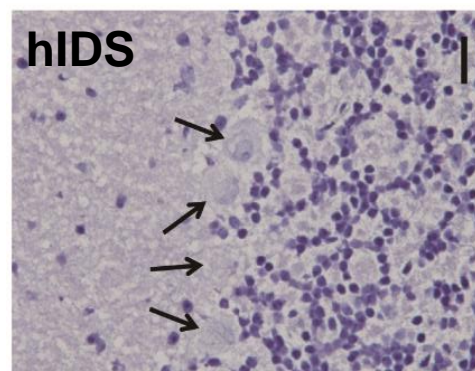
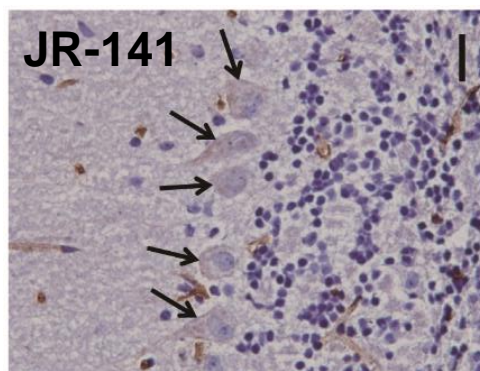
### A Distribution to the brain



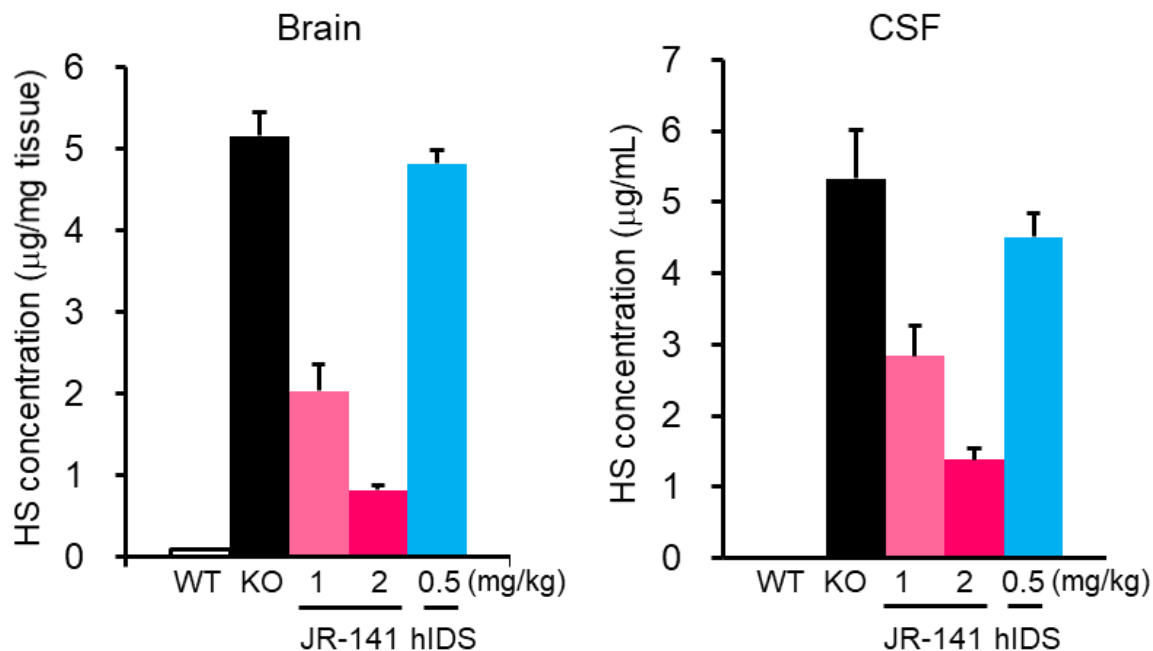
### B Fluorescent imaging of mouse brains



### C Immunohistochemical detection of JR-141 in the brain



**Effect on HS accumulation in MPS II mice**



- JR-141 decreases HS in brain and Cerebral spinal Fluid (CSF)
- A correlation between HS in brain tissues and CSF indicates utility of CSF HS as a biomarker to measure HS levels in the brain

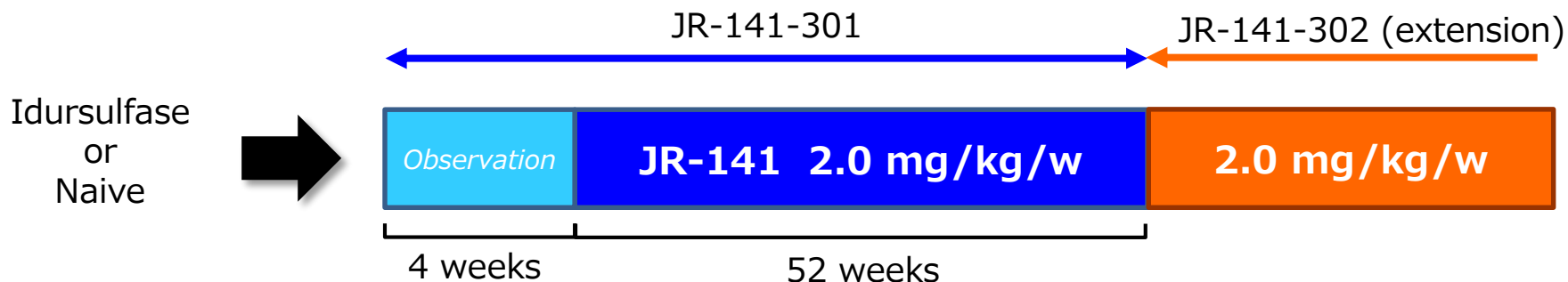
Tanaka et al., Mol Genet Metab. 2018; 125: 53-58 (DOI: <https://doi.org/10.1016/j.ymgme.2018.07.013>)

## JR-141

Pabinafusp alfa (BBB-penetrating iduronate-2-sulfatase, rDNA origin)  
**Status : Filed for MAA in Japan**



### Phase 3 trial (JR-141-301) : Brief Summary

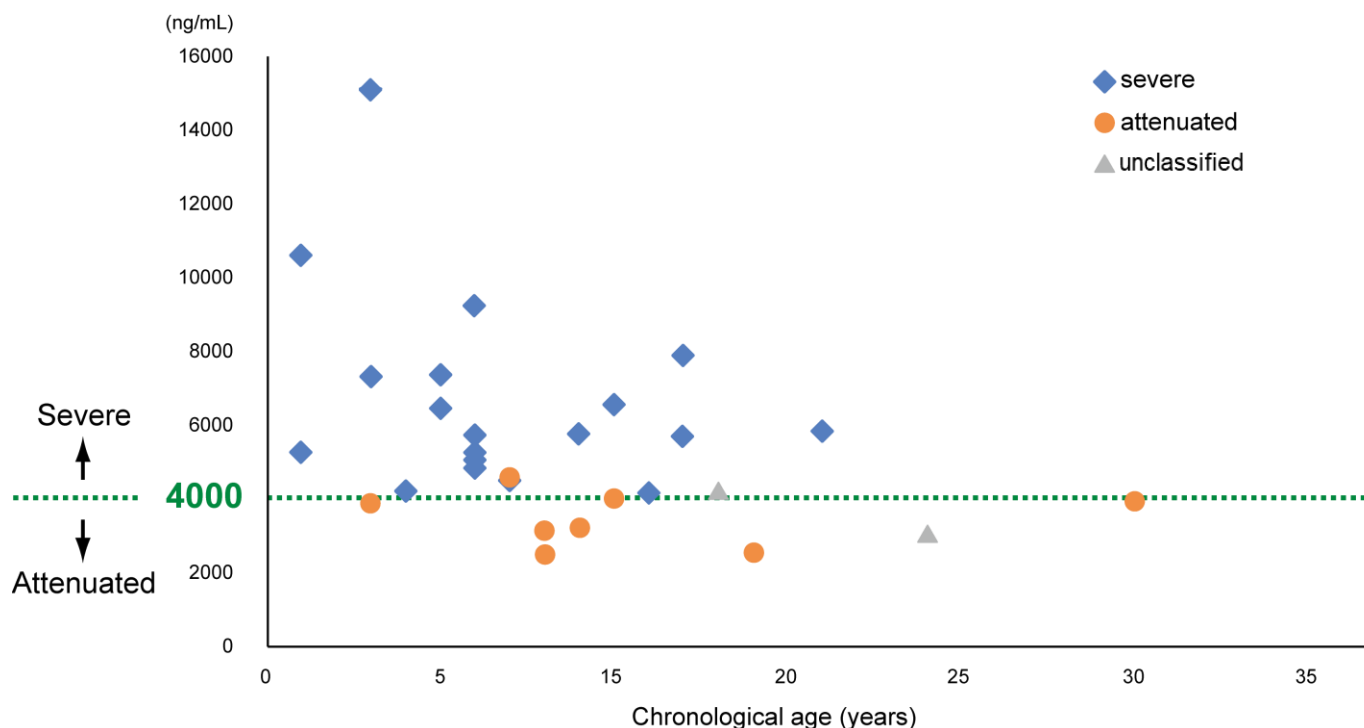


Primary endpoint	Heparan Sulfate (HS) in CSF
Secondary endpoint	<ul style="list-style-type: none"> <li>Developmental evaluation (cognitive, adoptive behavior)</li> <li>Dermatan Sulfate (DS) reduction in CSF</li> <li>HS and DS reduction in blood and urine</li> <li>Liver volume, spleen volume</li> <li>6 minute walk distance</li> <li>Joint range of motion</li> </ul>
Number of subjects	28 (Target number of subjects: 20)
Manuscript	Okuyama T, et al. DOI: <a href="https://doi.org/10.1016/j.ymthe.2020.09.039">https://doi.org/10.1016/j.ymthe.2020.09.039</a>



### Phase 3 trial (JR-141-301) : Results

#### Individual CSF HS Levels in Trial JR-141-301 at Baseline



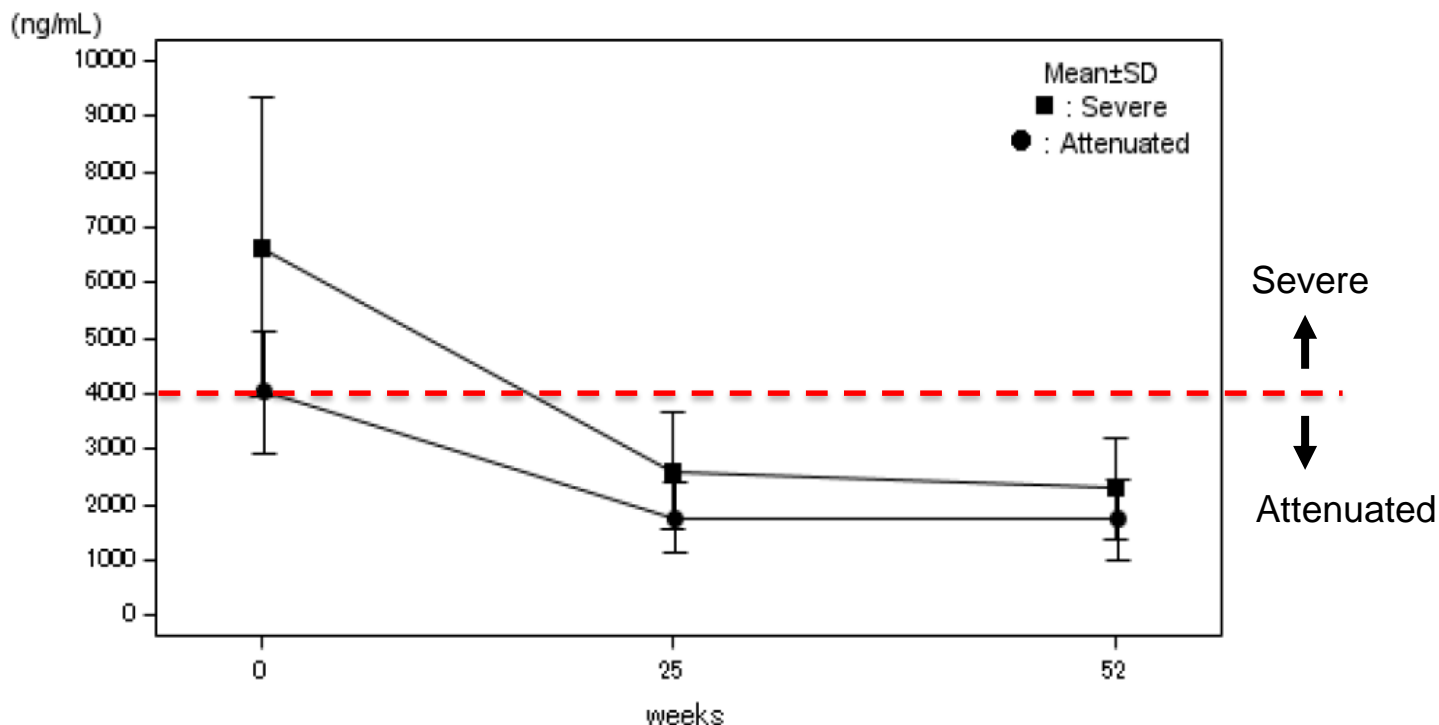
#### Findings

➤ The CSF HS concentration is a biomarker that correlates well with disease severity



**Phase 3 trial (JR-141-301) : Results**

**Time course of HS reduction in CSF**



**Findings**

- CSF levels decreased in almost all patients to a level comparable with attenuated patients

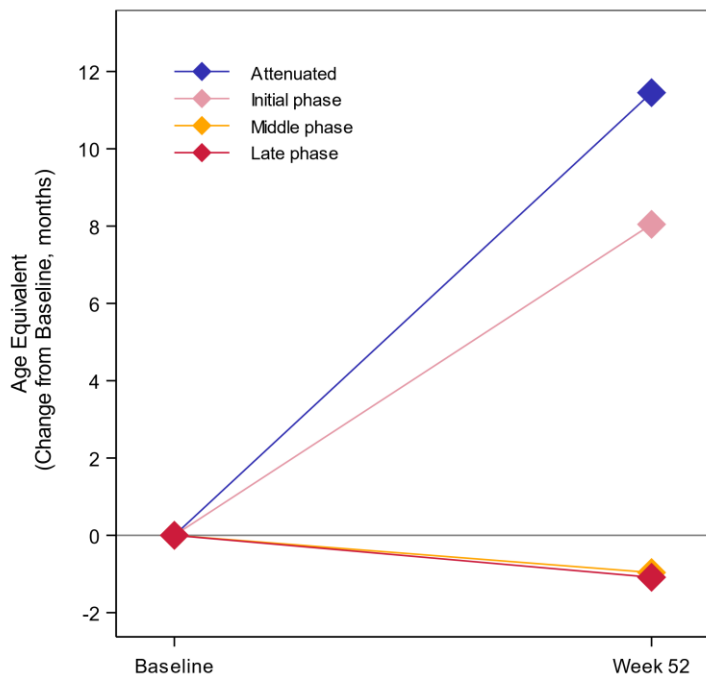
## JR-141

Pabinafusp alfa (BBB-penetrating iduronate-2-sulfatase, rDNA origin)  
**Status : Filed for MAA in Japan**



### Phase 3 trial (JR-141-301) : Results

#### Mean Changes in Age Equivalent Score (AES) observed in various Disease Severity Groups



Disease phenotype	No Subjects	Slope
Attenuated	8	0.9543
Severe: initial phase	2	0.6705
Severe: middle phase	11	-0.0802
Severe late phase	5	-0.0904

#### Findings:

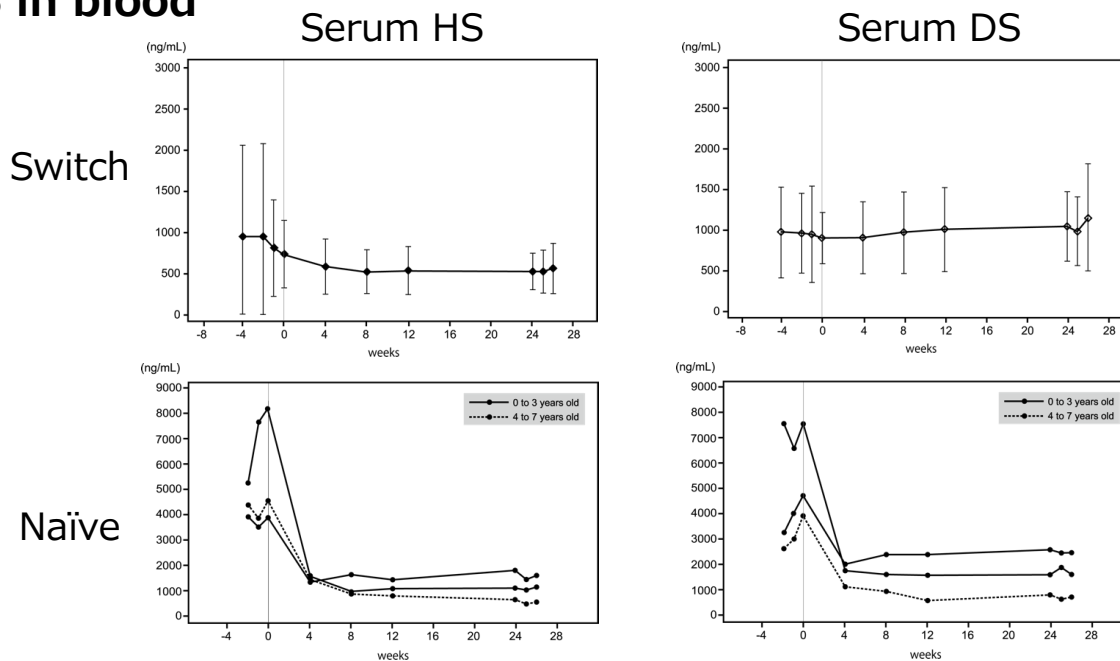
- Increases in AES from baseline were observed in attenuated and severe patients in the initial phase
- Stabilization of AES was observed in patients in the middle and late disease phase

Initial phase : <3y and <80 of Development Quotient  
 Middle phase : ≤8y or ≥20 of Development Quotient  
 Late phase : >8y or ≤20 of Development Quotient



### Phase 3 trial (JR-141-301) : Results

#### HS and DS in blood



#### Findings:

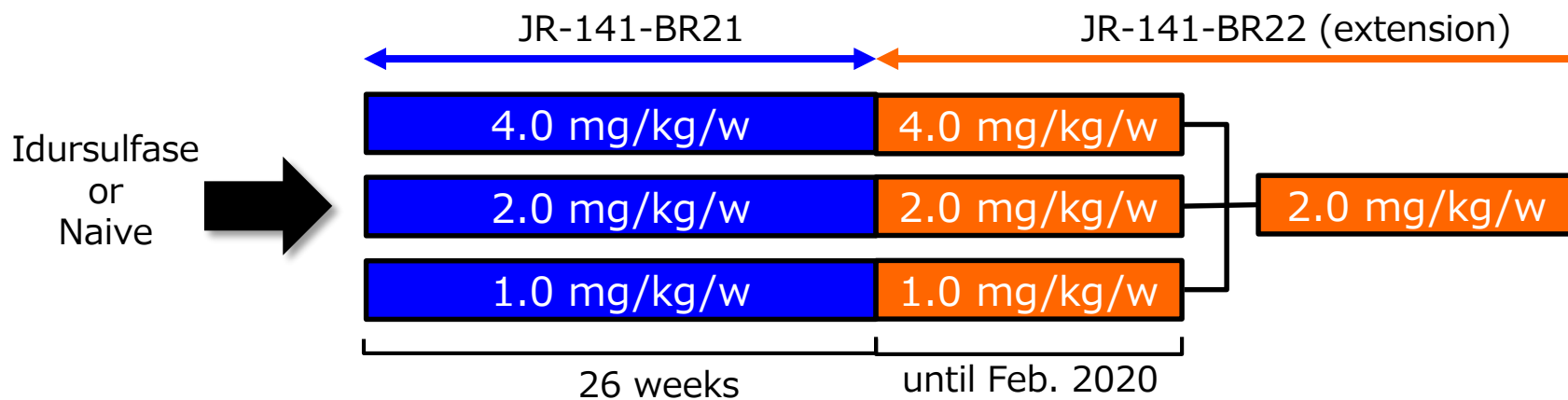
- Serum HS and DS remained stable in patients switched from IDS to JR-141
- Serum HS and DS rapidly decreased in ERT-naïve patients treated with JR-141
- These results including other secondary endpoints indicate that JR-141 has comparable efficacy on systemic symptom to existing ERT

## JR-141

Pabinafusp alfa (BBB-penetrating iduronate-2-sulfatase, rDNA origin)  
**Status : Filed for MAA in Japan**



### Phase 2 trial (JR-141-BR21) : Brief Summary

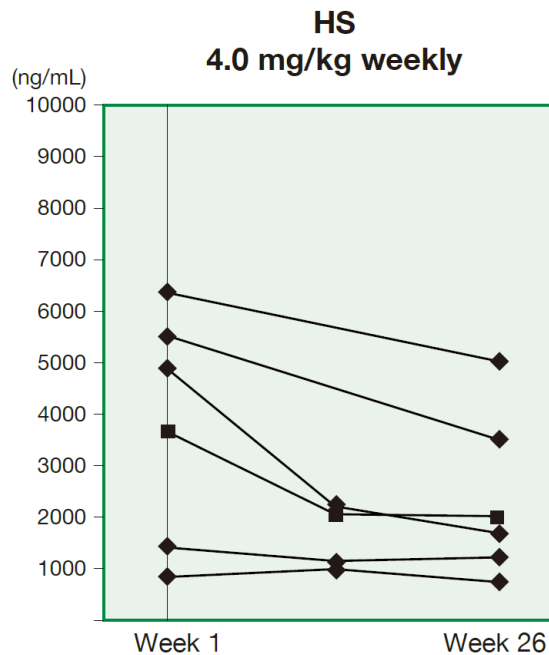
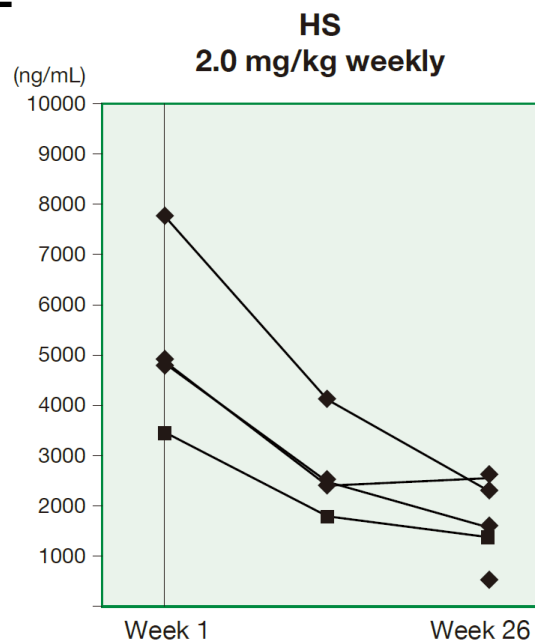


Primary endpoint	Safety
Secondary and exploratory endpoints	<ul style="list-style-type: none"> <li>HS and DS concentration in CSF, serum and urine</li> <li>Developmental evaluation (cognitive, adoptive behavior) etc.</li> </ul>
Number of subjects	20 (Target number of subjects: 18)
Presentation	Oral and Poster presentations at the <i>WORLDSymposium 2020</i>



### Phase 2 trial (JR-141-BR21) :Results

#### HS in CSF



#### Findings

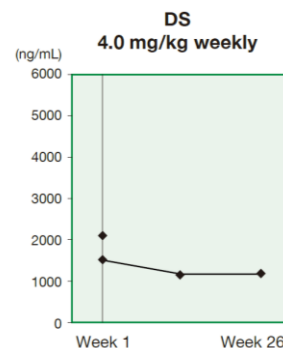
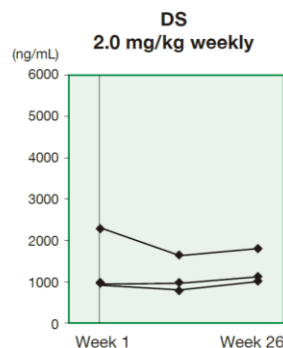
- Decrease of HS concentration in CSF in all subjects of the 2.0 mg and 4.0 mg treatment group



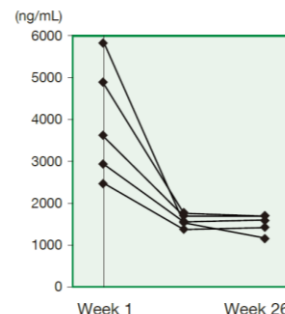
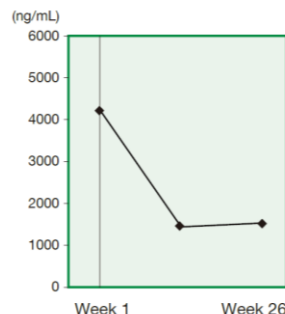
### Phase 2 trial (JR-141-BR21) :Results

#### DS in serum

<Switch>



<Naïve>



#### Findings:

- Serum DS remained stable in patients switched from IDS to JR-141
- Serum DS rapidly decreased in ERT-naïve patients treated with JR-141
- These results indicate that JR-141 has comparable efficacy to existing ERT in reducing serum DS

## Investigators' reports on patients



### Phase 3 trial (JR-141-301)

#### 【Speech】

Utters meaningful words, More verbally responsive to greetings, Resumes singing, Tries to speak in sentences

#### 【Facial expression Liveliness】

Livelier and more active than before, Smiles and hums, Often in better mood than before, More facial expressions

#### 【Physical movement】

Walks longer distances, Has resumed sitting up, Muscular strength improved



### Phase 2 trial (JR-141-BR21)

#### 【Speech】

Vocabulary and oral comprehension improved

#### 【Facial expression Liveliness】

Smiles more, More stable mood, Sleeps better

#### 【Physical movement】

Walks longer distance, Becoming able to perform activities not possible before

- No severe adverse event related to JR-141 reported
- Efficacy on CNS signs and symptoms was demonstrated
- Easy for initiation and continuation of treatment of MPS II patients: Intravenous infusion interval same as existing ERT.
- Consistent findings of reduction in HS concentration in CSF in non-clinical to clinical studies correlating with reduction of brain HS in disease models indicate the utility of CSF HS as surrogate biomarker for brain substrate reduction in human subjects
- The world's first ERT drug, which is capable to address CNS symptoms in MPS II, has now been submitted for market authorization application in Japan

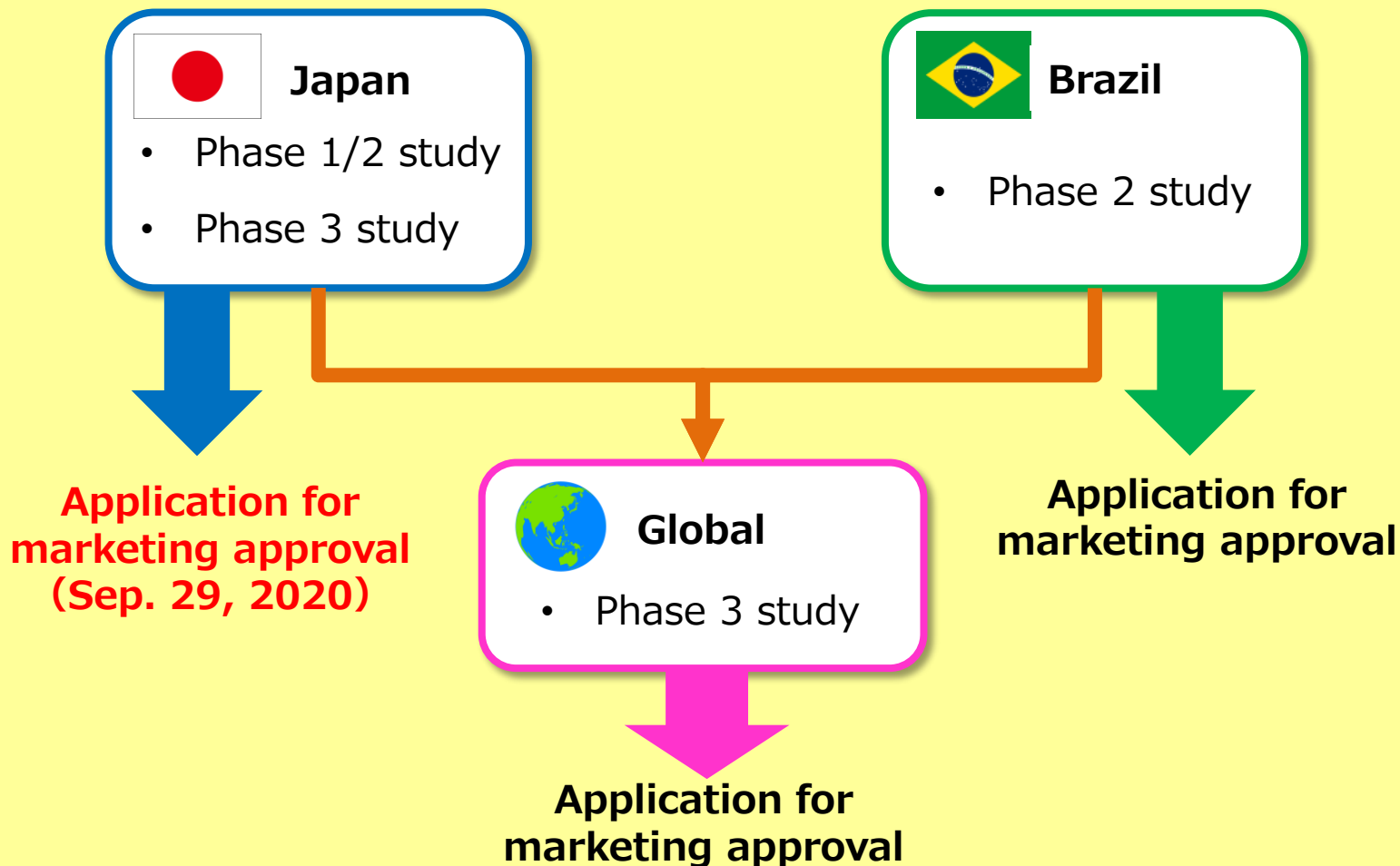


JR-141 has the potential to become a Breakthrough and first choice drug for MPS type II patients, capable to address somatic and CNS symptoms

**JR-141**

Pabinafusp alfa (BBB-penetrating iduronate-2-sulfatase, rDNA origin)  
**Status : Filed for MAA in Japan**

## JR-141 Study Design





**Global Phase 3 trial (JR-141-GS) : 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	<ul style="list-style-type: none"> <li>• <b><u>Neuronopathic patients</u></b></li> <li>• 3-6 years old, IQ=55-85</li> </ul>	<b><u>15</u></b>	<b><u>15</u></b>	105 weeks
CohortB	<ul style="list-style-type: none"> <li>• <b><u>Attenuated patients</u></b></li> <li>• &gt;6 years old, IQ≥85</li> </ul>	<b><u>10</u></b>	<b><u>10</u></b>	53 weeks

Endpoints : • HS in CSF, CNS symptoms (cognitive, behavior, attention)  
 • Systemic symptoms

ClinicalTrials.gov : [Identifier : NCT04573023](https://clinicaltrials.gov/ct2/show/study/NCT04573023)

## JR-141

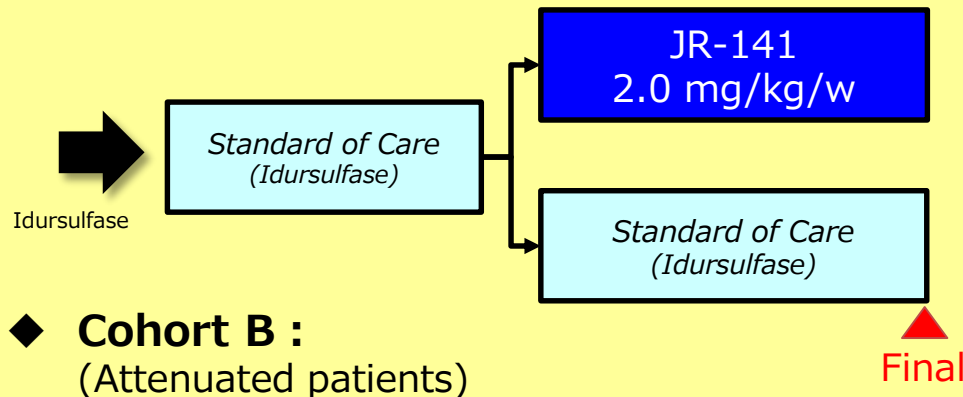
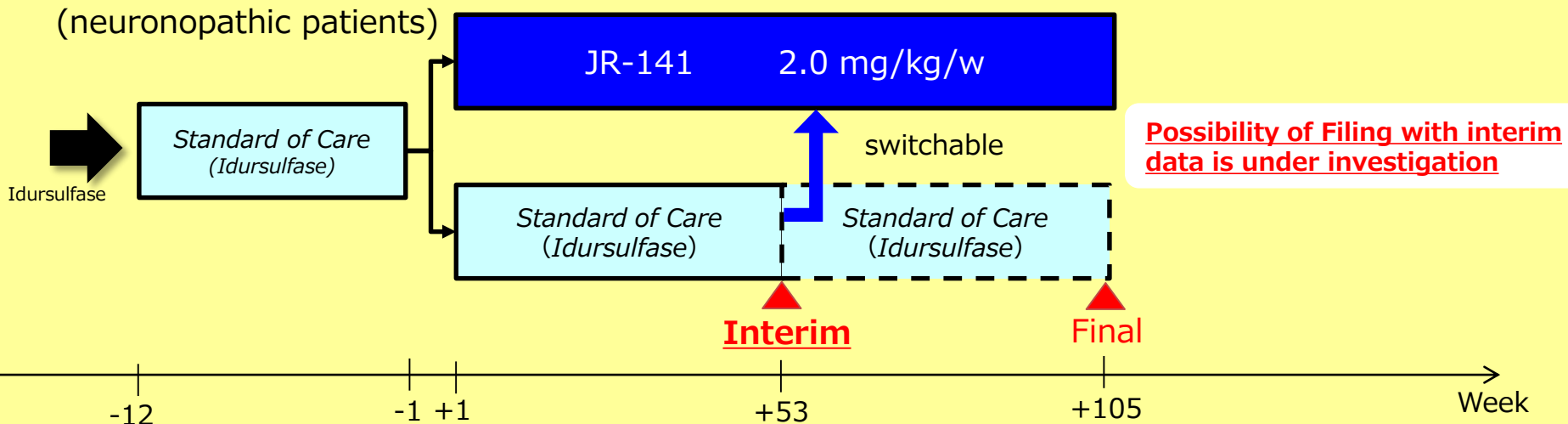
Pabinafusp alfa (BBB-penetrating iduronate-2-sulfatase, rDNA origin)  
**Status : Filed for MAA in Japan**



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

#### ◆ Cohort A :

(neuronopathic patients)



#### ◆ Cohort B :

(Attenuated patients)

## JR-141

Pabinafusp alfa (BBB-penetrating iduronate-2-sulfatase, rDNA origin)  
**Status : Filed for MAA in Japan**



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



- Mar. 2018: Designated under  
**“SAKIGAKE Designation System”**
  - All patients enrolled in Phase 3 trial participate in the extension study (JR-141-302)
- Will be presented at **WORLDSymposium 2021**
- **Sep. 9: Orphan drug designation**  
**Filing for marketing authorization**  
**⇒Approval may occur as early as Mar. 2021**



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



- All patients enrolled in Phase 2 trial participate in the extension study (JR-141-BR22)

Will be presented at  
**WORLDSymposium 2021**



Application for marketing approval planned in 2020  
**⇒Approval may occur as early as May, 2021**



**Phase 3 global study planned to start in FY2020**

Research & Development News (Jun.-Oct.)

JR-141 Development Status

Other Pipeline Products

## JR-171

## BBB-penetrating $\alpha$ -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  $\alpha$ -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 data from MHLW \*2 Actual sales of existing ERT and data from Evaluate Pharma and IQVIA

### ● Outline Global Phase 1/2 study

**Completion of the Investigational New Drug submission,**  
**Jul. in Japan, and Oct. in Brazil**

- Number of subjects : 19
- Country : Japan, USA, Brazil
- Administration period : 12 weeks
- Primary Endpoint : Safety
- Secondary Endpoint : Effects for CNS symptoms and Somatic symptoms  
Plasma pharmacokinetics

# JCR's pipeline for Lysosome diseases

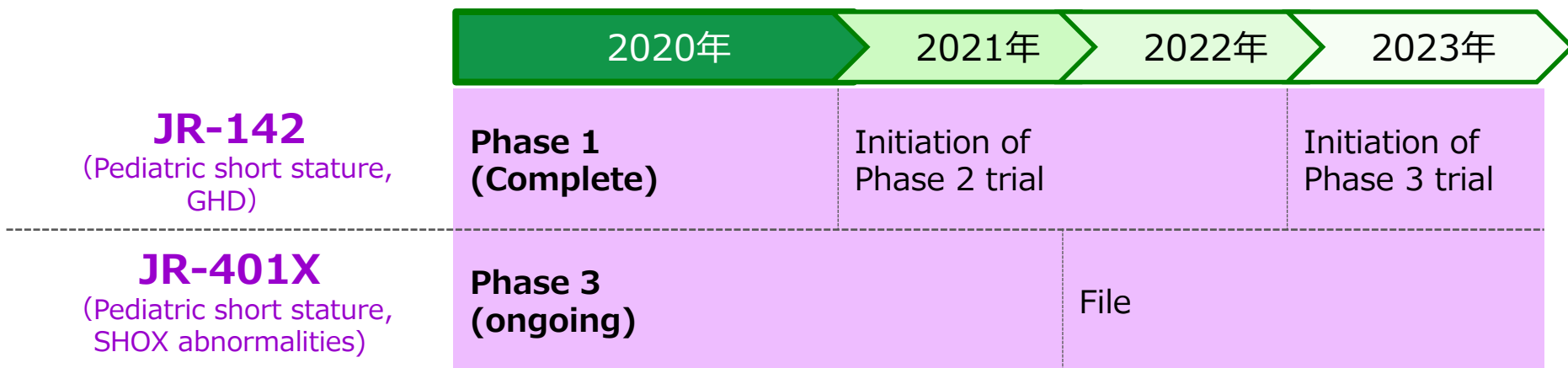
	Indications with existing somatic ERT (WW)	Indications with no established standard of care (WW)
<b>Filed</b>	JR-141 MPS type II (Hunter)	Red frames: Clinical studies to start within 3years
<b>Clinical</b>	JR-171 MPS I (Hurler etc.)	
<b>Non-clinical</b>	JR-162 Pompe	JR-441 MPS IIIA (Sanfilippo A)
<b>Process development</b>	JR-443 MPS VII (Sly)	JR-446 MPS IIIB (Sanfilippo B) GM1 gangliosidosis Fucosidosis
<b>PoC in model mouse</b>	Niemann-Pick Gaucher Batten, late-infantile (CLN2)	Batten, Infantile (CLN1) MLD Krabbe $\alpha$ -Mannosidosis
<b>Basic Res.</b>		Tay-sachs

## Expected timeline (Lysosome diseases)

	2020	2021	2022	2023
<b>JR-141</b> <b>Pabinafusp alfa</b> (MPS II)	<b>Japan : Filed</b>  Brazil : To be filed	Global : Initiation of Phase 3 trial		
<b>JR-171</b> (MPS I)	<b>Global : Phase 1/2 trial (ongoing)</b>			Initiation of Phase 3 trial
<b>JR-441</b> (MPS IIIA)	<b>Non-clinical (ongoing)</b>		Initiation of Phase 1/2 trial	
<b>JR-162</b> (Pompe)	<b>Non-clinical (ongoing)</b>			Initiation of Phase 1/2 trial
<b>JR-443</b> (MPS VII)	<b>Non-clinical (ongoing)</b>			Initiation of Phase 1/2 trial
<b>JR-446</b> (MPS IIIB)	<b>Non-clinical (ongoing)</b>			Initiation of Phase 1/2 trial

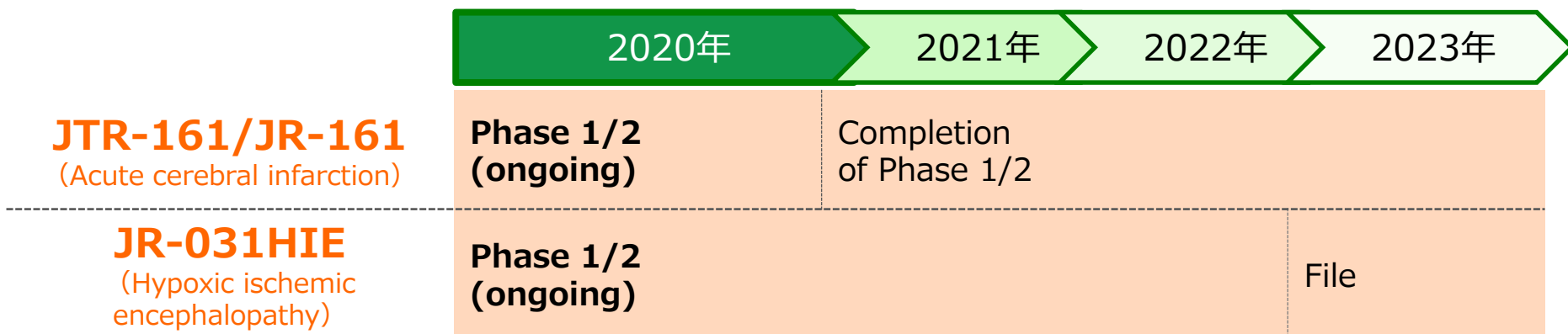
Note: Information after 2021 is a plan at this stage and is subject to change

## Expected timeline (GH area)



Note: Information after 2021 is a plan at this stage and is subject to change

## Other pipeline (regenerative medicine)



Note: Information after 2021 is a plan at this stage and is subject to change

变革

**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 : 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.

**JR-162** J-Brain Cargo<sup>®</sup>-applied acid  $\alpha$ -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  $\alpha$ -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

## JR-443 BBB-penetrating $\beta$ -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,  $\beta$ -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 $\alpha$ -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  $\alpha$ -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

**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** Somatotropin (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**

\*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 .