FY2018 Results Briefing Session

- Research and Development Highlights -

May 16, 2019

JCR Pharmaceuticals Co., Ltd.

【Securities code】4552, 1st Sec. TSE

Development Pipeline

Lysosomal Storage Disorder (LSD) / Regenerative Medical Product / Other Recombinant Protein Therapeutics

As of May 16, 2019

Code	Indication	Pre-clinical	Ph I/II	Ph III	Filed	Approved	Remarks
JR-141	Hunter syndrome						• ERT • J-Brain Cargo®
JR-162	Pompe disease						• ERT • J-Brain Cargo® • J-MIG System®
JR-171	Hurler syndrome						• ERT • J-Brain Cargo® • J-MIG System®
JR-441	Sanfilippo syndrome type A						• ERT • J-Brain Cargo® • J-MIG System®
JR-131	Renal anemia						• Co-developed with Kissei Pharmaceutical Co., Ltd. • Biosimilar
JR-401X	SHOX deficiency						• Expanded indication of GROWJECT®
JR-142	Growth disorders						• Long-acting human growth hormone product • J-MIG System®
JR-041	Infertility						• Out-licensed to ASKA Pharmaceutical Co., Ltd.
JR-031EB	Epidermolysis bullosa						• Expanded indication of TEMCELL®HS Inj.
JTR-161/JR-161	Acute cerebral infarction						• Co-developed with Teijin Limited

Research & Development News

since Nov. 28, 2018

2018 **Nov. 28 :** Launch of **Agalsidase Beta BS I.V. Infusion [JCR]** for Fabry Disease

Dec. 21 : A blood-brain-barrier (BBB)-penetrating recombinant iduronate-2-sulfatase (**JR-141**):
Notice on The Publication of The Phase 1/2 Clinical Trial Results for Hunter Syndrome in *Molecular Therapy*

Dec. 28 : JCR Completes Enrollment in Phase 3 Clinical Trial of **JR-141** for Hunter Syndrome in Japan

2019 **Feb. 6 :** Administration of "**JTR-161**" Dental Pulp Stem Cells Product Starts in Clinical Trial in Japan

Feb. 12 : JCR Announces Presentation on **JR-171** for Hurler Syndrome
at the 15th Annual WORLD*Symposium*™ 2019

Feb. 28 : JCR Completes Patient Enrollment in Phase 2 Clinical Trial
of **JR-141** for Hunter Syndrome in Brazil

Feb. 28 : JCR Receives EMA Orphan Designation for **JR-141** for Hunter Syndrome

Mar. 22 : JCR Files for Additional Marketing Approval
of TEMCELL® HS Inj. (**JR-031EB**) for the Indication of Epidermolysis Bullosa

Apr. 1 : JCR Announces Completion of Phase 1 Clinical Trial Notification of **JR-142**,
A long-acting growth hormone -Phase 1 clinical trial to commence in May 2019-

May 10 : PeptiDream and JCR Pharma Announce Development of BBB Carrier Peptides
Capable of Targeting Therapeutic Payloads to the Brain

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LSD	**JR-141** BBB-penetrating iduronate-2-sulfatase (rDNA origin)	**Japan:** Phase III **Brazil:** Phase II	Hunter syndrome
LSD	**JR-171** BBB-penetrating α-L-iduronidase (rDNA origin)	Preclinical	Hurler syndrome
LSD	**JR-441** BBB-penetrating heparan N-sulfatase (rDNA origin)	Preclinical	Sanfilippo syndrome type A
LSD	**JR-162** J-Brain Cargo® -applied acid α-glucosidase (rDNA origin)	Preclinical	Pompe disease
Regenerative Medical Product	**JR-031EB** Expanded indication of TEMCELL®HS Inj.	Filed	Epidermolysis bullosa
Regenerative Medical Product	**JTR-161/JR-161** Dental pulp stem cells (DPCs)	Phase I/II	Acute cerebral infarction
Biosimilar	**JR-131** Darbepoetin alfa (rDNA origin)	Filed	Renal anemia
Growth Hormone	**JR-142** Long-acting growth hormone (rDNA origin)	Phase I/II in preparation	Growth disorders

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

➢ Hunter syndrome (MPS type II)

MHLW designated intractable disease

- Disease condition
  - Bone : characteristic face, bone deformity, arthrogryposis
  - Heart : cardiac valvular disease
  - Soft tissue : thick skin, hairiness, macroglossia
  - Liver : hepatomegaly
  - CNS* :**CNS disorders**

*CNS: Central nervous system

- Patient population* : **250** (Japan), **7,800** (WW) est.

*Internal analysis

- Market size* : **8 billion JPY** est. (2018 Japan) , **91 billion JPY** est. (2018 WW)

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

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

➢ Hunter syndrome (MPS type II)

MHLW designated intractable disease

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

- Mar. 2018: Designated under **"SAKIGAKE Designation System"**
- Aug. 2018; Ph III clinical trial initiated
  ⇒started of administration to all subjects

JCR USA, Inc.

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

- Jun. 2018:
  Ph II clinical trial initiated
  ⇒started of administration to all subjects.

Application for marketing approval planned in FY2020 in Japan

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

➢ Hurler syndrome (MPS type I)

MHLW designated intractable disease

- Patient population* : **60** (Japan), **3,600** (WW) est.

*Internal analysis

- Market size* : **1.5 billion JPY** est. (2018 Japan)
  24 billion JPY est. (2018 WW)
- Disease condition
  - Bone : characteristic face, bone deformity, arthrogryposis
  - Eye: cloudy cornea
  - Heart : cardiac valvulopathy
  - Soft tissue : thick skin, hairiness, macroglossia
  - Liver : hepatosplenomegaly
  - CNS : **CNS disorders**

Phase I/II trial is planned in FY 2019

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

➢ Sanfilippo syndrome Type A（ MPS IIIA ）

MHLW designated intractable disease

- Patient population* : **60** (Japan), **6,900** (WW) est.

*Total of Type A&B (Internal analysis)

- Disease condition : CNS disorders, sleep disorders, hepatosplenomegaly, seizures
- Cause : an inborn deficiency or defect in heparan N-sulfatase within lysosomes in cells throughout the body
- Treatment : **effective treatment is not available** → **development of a new treatment option has been long awaited**

- Animal studies demonstrated delivery of JR-441 not only into peripheral tissues but also into the brain, along with significant reduction of heparan sulfate accumulated in these tissues.

Phase I/II trial is planned in FY 2020

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

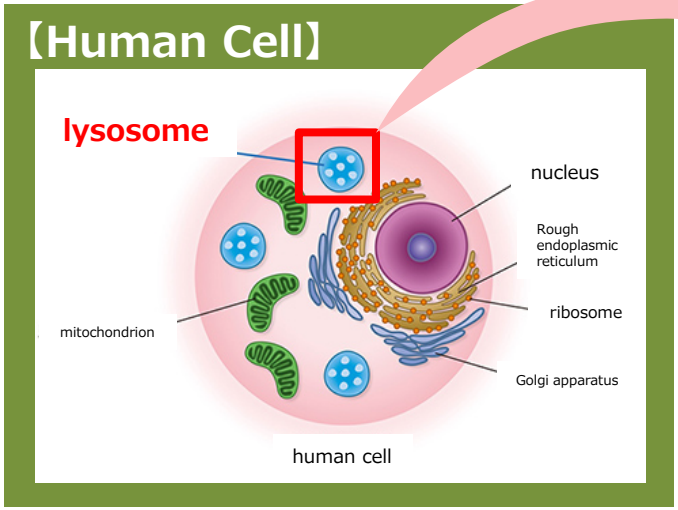
➢ Pompe disease

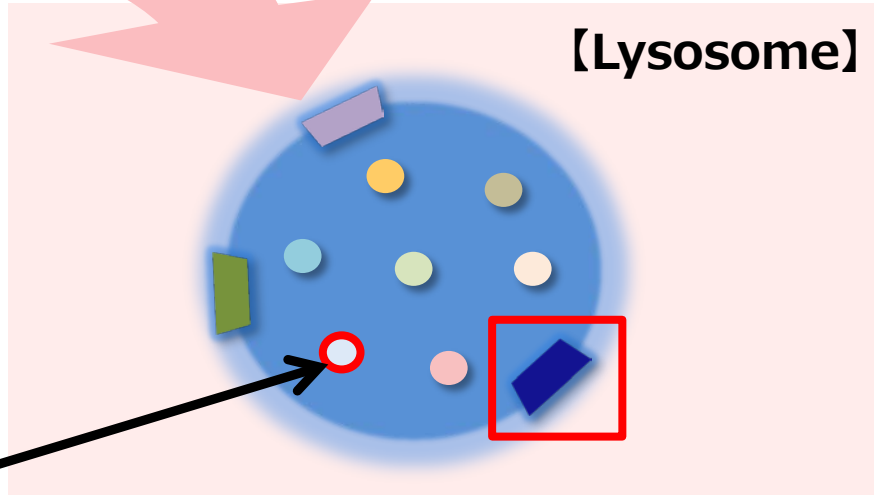
MHLW designated intractable disease

- Patient population* : **80** (Japan), **10,600** (WW) est. *Internal analysis
- Market size* : **3 billion JPY** est. (2018 Japan), **99 billion JPY** est. (2018 WW)
- Disease condition - Primarily affects **skeletal muscles**, Respiratory, motor and cardiac dysfunctions
  - **Infantile onset :** Cardiac dysfunction, muscle weakness, dyspnea, respiratory infections, aspiration pneumonia, delayed growth
  - **Late onset :** Cardiac dysfunction, headache, muscle weakness/lumber pain, dyspnea, respiratory infections, aspiration pneumonia, delayed growth, nutritional deficiency

JR-162 demonstrated the significant proof of concept not only in the skeletal muscles, the respiratory muscle, and the myocardium **but also in CNS**.

Gene Therapy





enzyme

- Enzyme replacement therapy can be applied

J-Brain Cargo® is applied

Membrane protein

- Replacement therapy is not appropriate
- The gene needs to be expressed in the cell

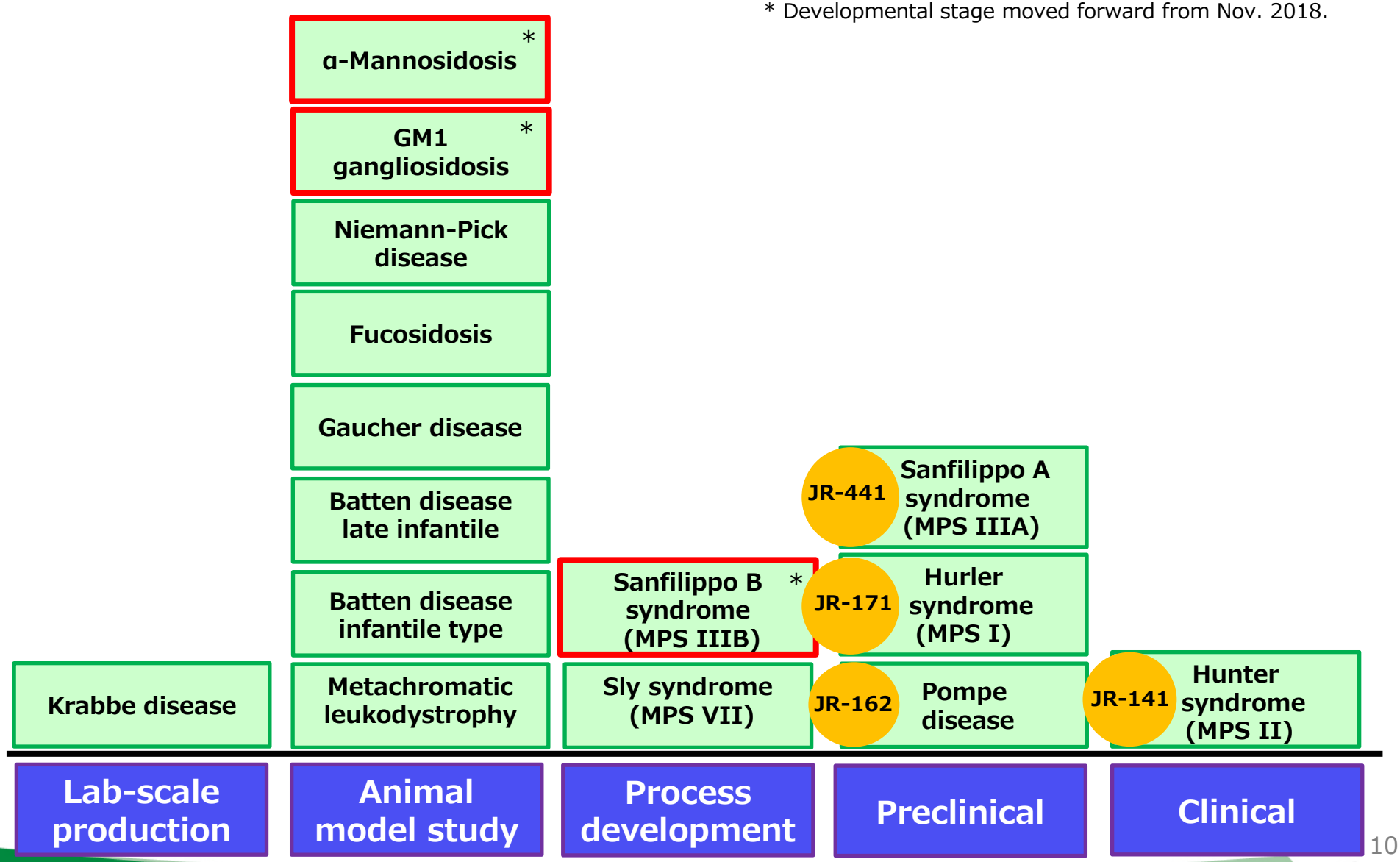
Gene therapy has potential to treat

Clinical trials planned in FY 2021

Progress of developmental stage of LSD pipeline

-15 early to late stage J-Brain Cargo® programs-

* Developmental stage moved forward from Nov. 2018.



Potential of J-Brain Cargo®

Collaboration **PeptiDream Inc.,**

2016 Started the joint research collaboration

2019 **Successful development of constrained peptides across the BBB**

PeptiDream

JCR Pharmaceuticals

potential applications to various CNS disorders

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

➢ Epidermolysis bullosa : EB

MHLW designated intractable disease

- Cause: Hereditary disorder of abnormal gene expressed in the cutaneous basement membrane zone
- Disease condition: Slight friction may cause the skin to detach from its basement membrane, producing burn-like blisters and ulcers
- Treatment: Basically, none. Gauze dressings and Vaseline are used to protect wounds
- Patient population* (Japan): **500-640** est**. (approx. 300 severe cases eligible for treatment)**

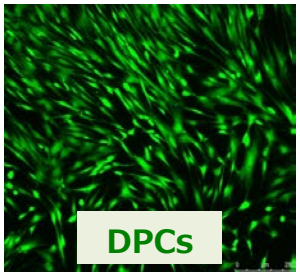
*Internal analysis

- In 2018 : **Designed the orphan regenerative medical product** for EB in Japan

Mar. 2019 : Application for marketing approval filed

Marketing approval planned in FY 2019

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



➢ Acute cerebral infarction

- Cause : Major risk factors are generally the same as for atherosclerosis (high blood pressure, diabetes mellitus, tobacco smoking, obesity, and dyslipidemia)
- Patient population* (Japan): **300,000** est.

*Internal analysis

- Treatment : Use of thrombolytic therapy, antiplatelet therapy, and anticoagulant therapy is advocated within a few hours of onset

TEIJIN

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

Feb. 2019 : Started of administration in Phase I/II

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JR-131 Darbepoetin alfa (rDNA origin)

➢ Renal anemia

- Co-development agreement with Kissei Pharmaceutical Co., Ltd. in Sep. 2013

Leveraging JCR's proprietary Glycoengineering Technology to approach complex sugar chain structure

Patent filed

- Phase III study : demonstrated equivalence in efficacy and safety compared with darbepoetin
  - In a primary endpoint of efficacy, the equivalence was verified for variations in hemoglobin concentration
  - Similarity with regard to the safety profile was confirmed

Sep. 2018 : Application for marketing approval filed

Marketing approval planned in FY 2019

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

➢ Pediatric growth hormone deficiency

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

Patent filed

- ✓ Prominently extended circulatory half-life can be achieved compared to a native albumin-fused technology
- ✓ Reduced dosage and dose frequency were achievable in animal studies using a pharmacological biomarker

- **Apr. 2019 : Completion of Phase I clinical trial notification**

Phase I study design

Subjects : 31 healthy adult male
Assessment : safety and pharmacokinetics

Phase I planned in May 2019

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Regenerative Medical Product

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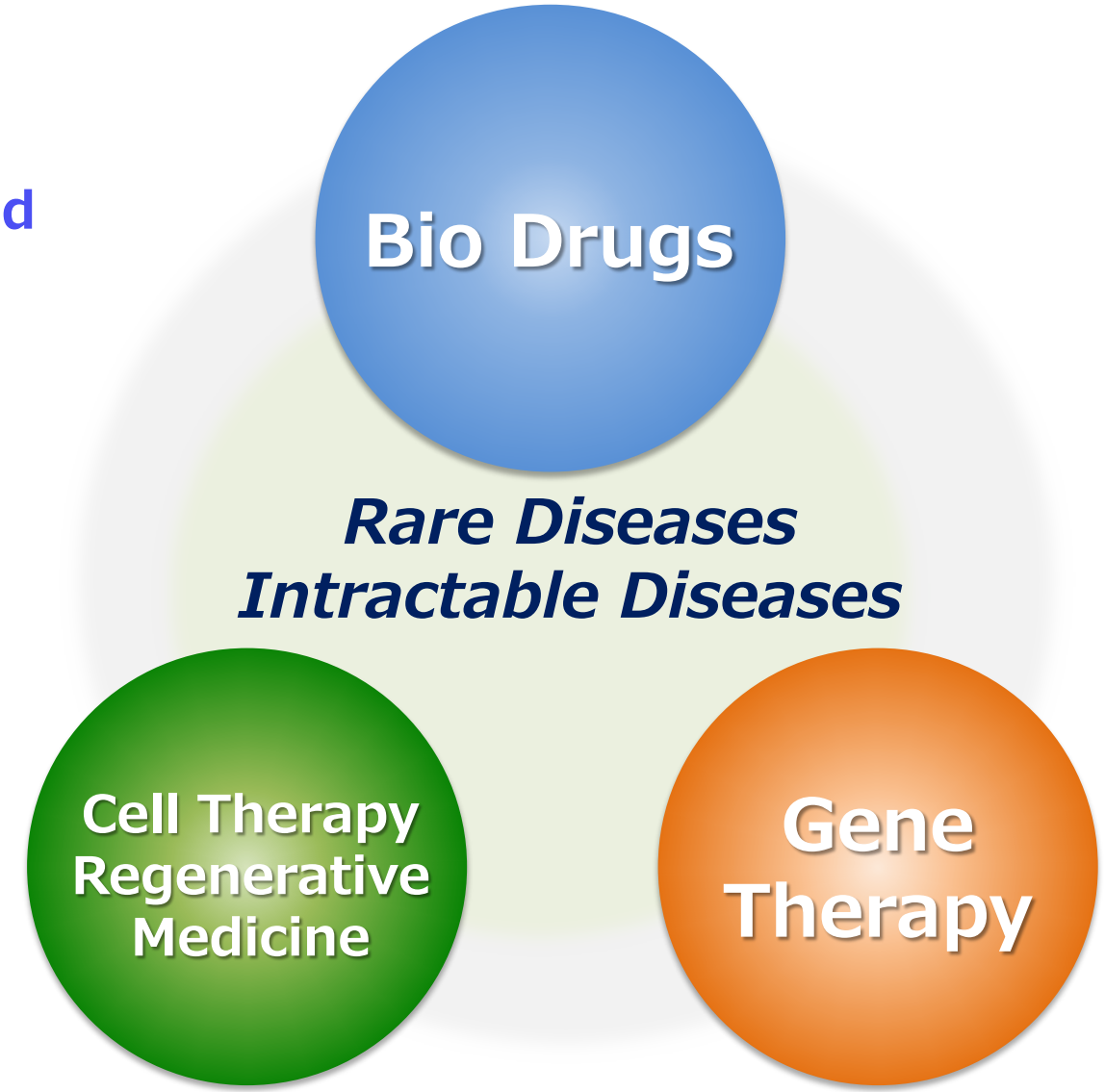
Taking one step ahead,
JCR aims to develop
First-in-class drugs
From Japan to the world



– JCR Biotech for a New Tomorrow –

FORWARD- LOOKING STATEMENT

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

All forward-looking statements speak only as of the date of this presentation.
Except as required by law, we assume no obligation to update these forward-looking statements publicly or to update the factors that could cause actual results to differ materially, even if new information becomes available in the future.