JCR Pharmaceuticals Co., Ltd.

2Q Financial Results Briefing for the Fiscal Year Ended March 2022 Presentation

November 2, 2021

Event Summary

[Company Name]	JCR Pharmaceuticals Co., Ltd.
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[Participants]	
[Number of Speakers]	3

Shin Ashida	Representative Director, Chairman, President, and CEO
Kazunori Tanizawa	Corporate Officer, Executive Director, Development Division
Yoshihiro Ohta	Director, Accounting Department Management Division

Presentation

Ashida: I am Ashida from JCR Pharmaceuticals Co., Ltd. We would like to express our sincere gratitude to all of you for your continued understanding and support of our company.

At today's financial results briefing, each of our staff members will provide a detailed explanation of the overview of financial results for the second quarter of the fiscal year ending March 2022 and the status of research and development later on.

I would like to talk about the partnership with Takeda Pharmaceutical Company Limited for the global development and marketing of JR-141, which was announced on September 30.

Under the terms of the agreement, we will receive an upfront payment from Takeda for the non-US portion of the license agreement, consideration for the grant of US option rights, milestone fees based on progress in development and commercialization, and royalties on product sales once launched.

Through our partnership with Takeda, we will be able to bring new treatment options to patients with Hunter syndrome around the world as quickly as possible. During the course of negotiations, I strongly felt that the 2 companies' passions for rare diseases are aligned. We are very pleased to have been able to conclude this contract, including the financial terms.

With regard to the lysosomal disease drug currently under development, we will carefully examine the region and whether the disease is ultra-rare or not, and consider whether we will market the drug in-house or license it out to other companies.

Several companies have already expressed interest in JR-171, and we will proceed with negotiations, taking various conditions into consideration.

We believe that the global licensing for JR-141 is the result of Takeda, a biopharmaceutical company, evaluating our blood-brain barrier penetration technology, J-Brain Cargo.

We will continue to develop new drugs in the field of lysosomal diseases on a global basis, while at the same time accelerating out-licensing and actively licensing out our J-Brain Cargo technology.

I believe that we have entered the second stage of our business development, where we can contribute to the creation of innovative drugs in a variety of disease areas. In the second half of this fiscal year and for the next few years, we will make various preparations for global clinical trials and sales, and Team JCR will work as one to achieve our goal of becoming a global specialty pharmaceutical company.

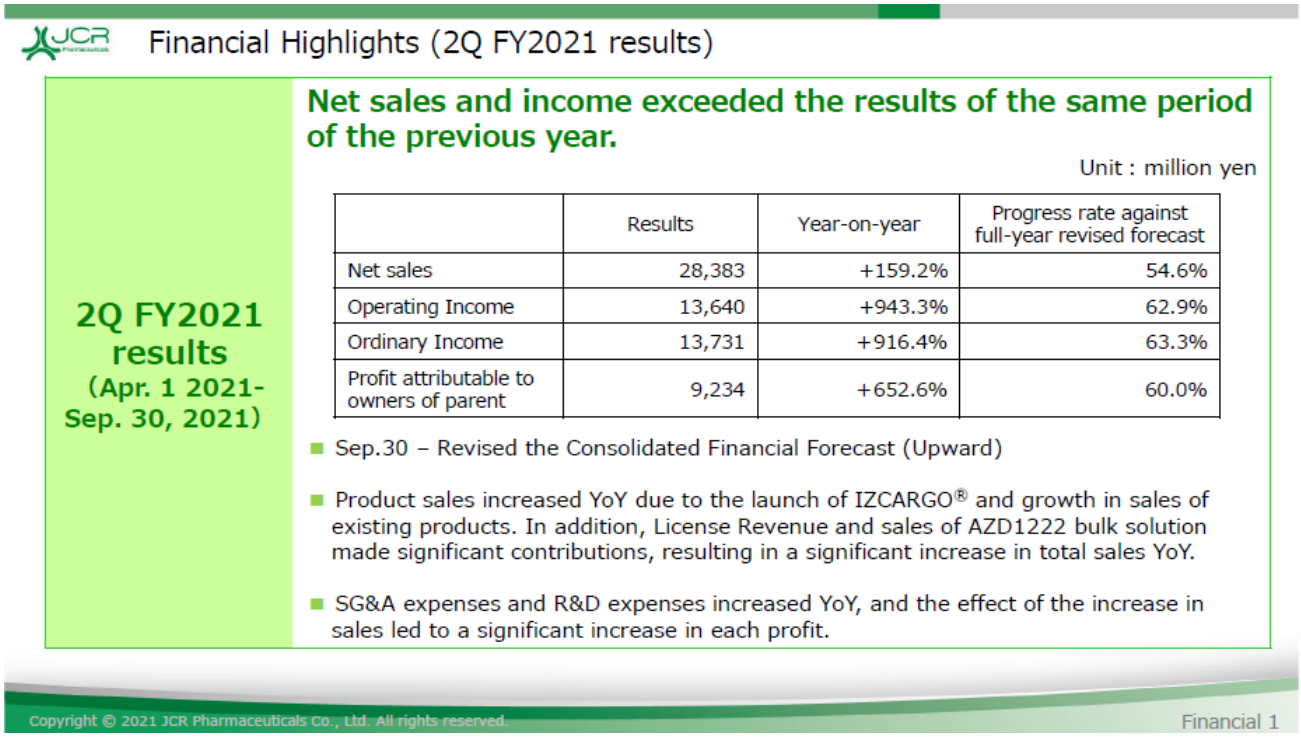
As for the vaccine manufacturing contracted from AstraZeneca, we plan to complete the manufacturing of all the scheduled batches by December.

In addition, we will actively work to further accelerate and expand our existing initiatives based on the principles of the SDGs, which aim to realize a sustainable and better society where no one is left behind.

We look forward to your continued understanding and support.

In addition, we are planning to hold a briefing session on JCR's R&D during this fiscal year to provide a more detailed understanding of JCR's technology and research initiatives, including J-Brain Cargo. We hope that you will pay attention to this as well. Thank you.

Ohta: Ohta of the Accounting Department will now provide an overview of the financial results for the second quarter of the fiscal year ending March 2022. Thank you.



First, I would like to provide an overview of the results for the second quarter. Both net sales and each income exceeded the results of the same period of the previous year.

I will explain the details of sales and others later, but on September 30, we made an upward revision to our full-year consolidated earnings forecast.

In addition, pharmaceutical sales increased YoY due to the new launch of IZCARGO and growth in sales of existing products.

In addition, contract revenue and the increase in sales of AZD1222 stock solution, which is a stock solution for coronavirus vaccine, made a significant contribution to the large increase in total sales YoY.

At the same time, selling, general and administrative expenses and research and development expenses also increased YoY, and the effect of the increase in sales led to a significant increase in each profit.

Consolidated Results

Unit : million yen

Consolidated	Six Months Ended Sep. 30, 2020	Six Months Ended Sep. 30, 2021 A	Year-on-year	FY2021 (Apr. 1, 2021- Mar. 31, 2022) Forecast (revised) B	Progress rate A/B
Net sales	10,951	**28,383**	**+159.2%**	52,000	54.6%
Cost of Sales	3,513	**4,485**	**+27.7%**	8,300	54.0%
Gross Profit	7,438	**23,898**	**+221.3%**	43,700	54.7%
SG&A	3,723	**6,737**	**+81.0%**	11,700	57.6%
R&D Expenses	2,407	**3,520**	**+46.2%**	10,300	34.2%
Operating Income	1,307	**13,640**	**+943.3%**	21,700	62.9%
Ordinary Income	1,351	**13,731**	**+916.4%**	21,700	63.3%
Profit*	1,227	**9,234**	**+652.6%**	15,400	60.0%

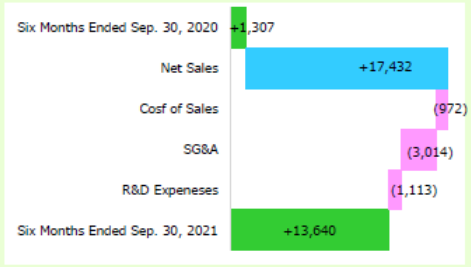
*Profit attributable to owners of parent

(Reference)

R&D Expenses**	2,607	**3,570**	**+36.9%**	11,080	32.2%

**R&D Expenses before deducting contribution amount by collaborative R&D partners

◆**Net Sales 13,640 million yen**
Year-on-year: +12,333 million yen



Factors of change

- Significant increase in License Revenue and AZD1222
  +17,432 million yen
- Increase in the cost of sales due to increase in net sales
  (972) million yen
- Increase in SG&A expenses
  (3,014) million yen
- Increase in R&D expenses
  (1,113) million yen

I will continue with an overview of the consolidated financial results. Net sales increased significantly to JPY28.383 billion, up 159.2% or JPY17.432 billion YoY.

As I mentioned earlier, the main reason for this is the large increase in contract revenue and vaccine sales.

Although the cost of sales has increased slightly in line with the increase in sales, gross profit has also increased significantly to JPY23.898 billion, up 221.3% YoY.

Selling, general and administrative expenses totaled JPY6.737 billion, an increase of 81% or JPY3.014 billion in value YoY. Reasons for a large increase in SG&A expenses are the increase in personnel expenses resulting from an increase in the number of employees, as well as an increase in expenditures for royalties on product sales and various commissions, many of which are unique to this fiscal year.

Research and development expenses totaled JPY3.52 billion, an increase of 46.2% or JPY1.113 billion in value YoY. The main reason for this is the increase in R&D expenses due to the progress of clinical trials.

As a result, operating income was JPY13.64 billion, an increase of 943.3% or about 10 times YoY. The same trend can be seen in ordinary income.

Net income for the quarter was JPY9.234 billion, an increase of 652.6% or JPY8 billion in value YoY, which is a significant increase.

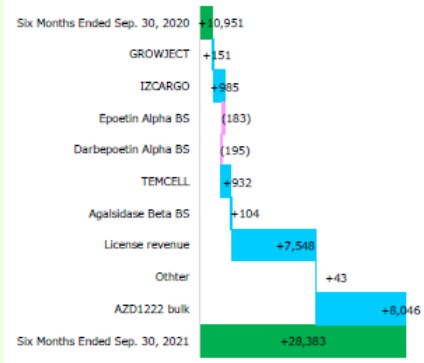
The forecast for the current fiscal year is shown on the right. These are the figures that we announced and revised our forecast on September 30. For the full year, we are forecasting net sales of JPY52 billion, operating income of JPY21.7 billion, and net income for the quarter of JPY15.4 billion. The progress rate for each stage of profit is between over 50% and 60%, and we are making good progress.

Breakdown of net sales (Consolidated)

Unit : million yen

	Six Months Ended Sep. 30, 2020		Six Months Ended Sep. 30 2021			FY2021 (Apr. 1, 2021- Mar. 31, 2022)	
		Composition ratio	A	Composition ratio	Year-on-year	Forecast (revised) B	Progress rate A/B
GROWJECT®	6,538	59.7%	6,689	23.6%	+2.3%	13,900	48.1%
IZCARGO®	–	–	985	3.5%	–	2,800	35.2%
Treatment for renal anemia	3,390	31.0%	3,011	10.6%	(11.2)%	6,400	47.0%
Epoetin Alpha BS Inj. [JCR]	1,696	15.5%	1,512	5.3%	(10.8)%	2,700	56.0%
Darbepoetin Alpha BS Inj.[JCR]	1,694	15.5%	1,498	5.3%	(11.6)%	3,700	40.5%
TEMCELL® HS Inj.	784	7.2%	1,717	6.1%	+118.9%	3,200	53.7%
Agalsidase Beta BS I.V. Infusion [JCR]	220	2.0%	323	1.1%	+47.0%	800	40.4%
Total Core products	10,934	99.8%	12,728	44.9%	+16.4%	27,100	47.0%
License Revenue	10	0.1%	7,557	26.6%	+74,360%	10,200	74.1%
Other	7	0.1%	51	0.2%	+565.8%	0	–
AZD1222 stock solution	–	–	8,046	28.3%	–	14,700	54.7%
Total Net Sales	10,951	100.0%	28,383	100.0%	+159.2%	52,000	54.6%

◆**Net sales 28,383 million yen**
Year-on-year +17,432million yen



Factors of change

- Launch of IZCARGO®
  +985 million yen
- Increase in License Revenue
  +7,547 million yen
- Shipment of AZD1222 stock solution according to the contract schedule
  +8,046 million yen

I will now explain the breakdown of net sales. Sales of our mainstay product, GROWJECT, increased 2.3% or JPY151 million YoY to JPY6.689 billion. Although the sales of this product were affected by the NHI price revision, sales increased due to higher sales volume.

Sales of IZCARGO, which started in May this year, amounted to JPY985 million.

Sales of therapeutic products for renal anemia totaled JPY3.011 billion, a decrease of 11.2% YoY. One of them, Epoetin alpha, was affected by a shipment adjustment at the beginning of the current fiscal year.

TEMCELL sales totaled JPY1.717 billion, up 118.9% or JPY932 million in value YoY. In the first half of the previous fiscal year, shipping restrictions were imposed on these products, so the number of these products was reduced in the previous fiscal year. Compared to the same period 2 years ago, sales increased.

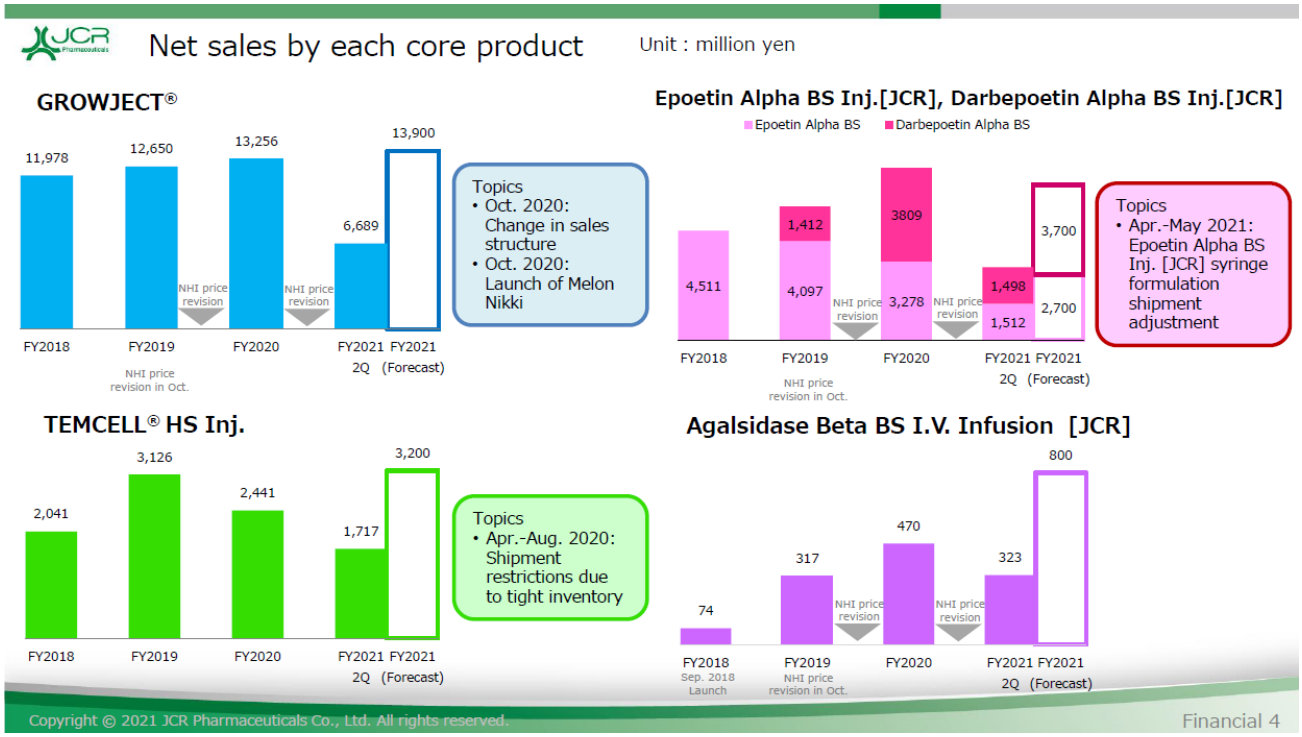
Sales of Agalsidase beta were JPY323 million, up 47% YoY.

As a result, total sales of pharmaceuticals and other products, or existing products, amounted to JPY12.728 billion, up 16.4% YoY.

Contract revenue was JPY7.557 billion, which contributed significantly to an increase in sales, as it was only JPY10 million in the same period last year.

For the AZD1222 stock solution, JPY8.046 billion was recorded in the first half of the fiscal year.

As a result, total sales increased significantly to JPY28.383 billion, up 159.2% YoY.



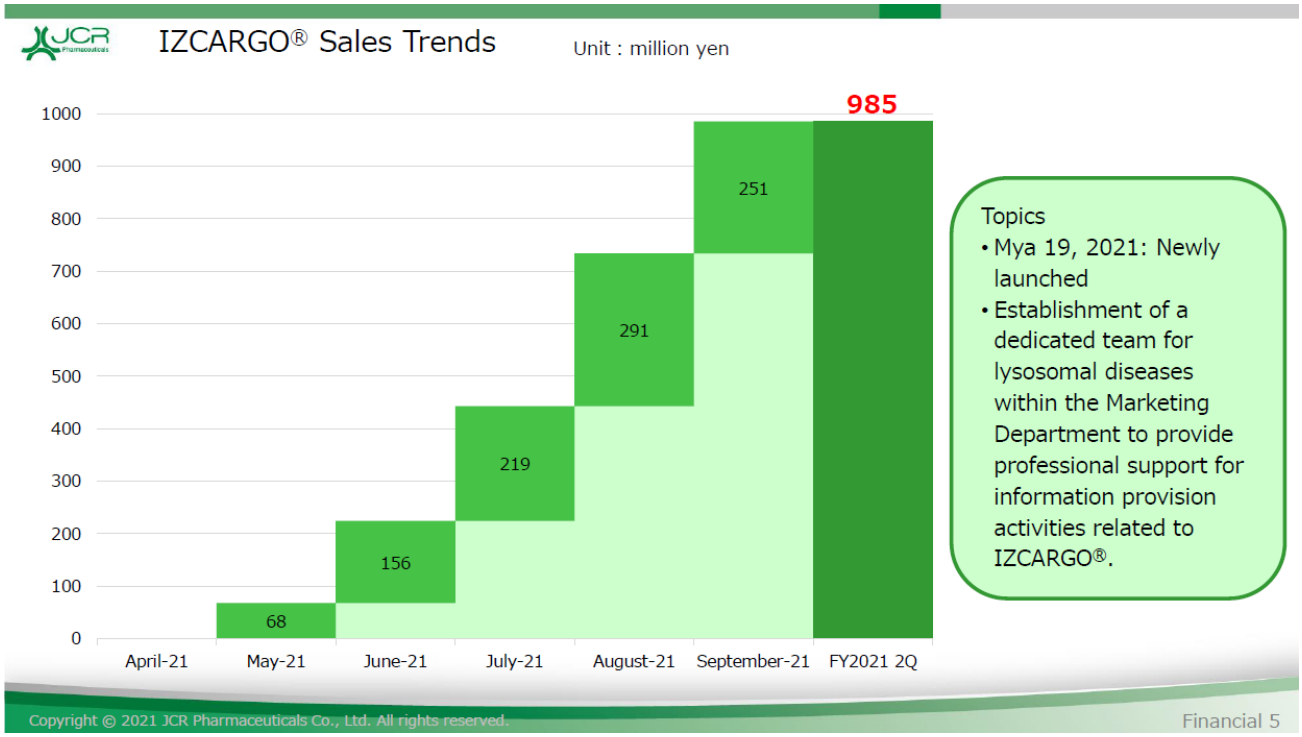
Next, this graph shows the sales trend by each product.

In the upper-left corner of the screen, you can see the GROWJECT. The NHI price revisions took place after the fiscal year ending March 2020 and after the fiscal year ending March 2021, but despite this, sales have been steadily increasing, and we are forecasting the same for the current fiscal year.

On the right is a graph showing the total of therapeutic product for renal anemia which is Epoetin alpha and Darbepoetin alpha. The sales of these products were steady until FY2021, but are expected to decline slightly in the current fiscal year due to the impact of price cuts caused by the NHI price revision.

As I mentioned earlier, TEMCELL's sales are expected to decline in FY2021, but we are forecasting JPY3.2 billion for the current fiscal year. This forecast exceeds the result in the fiscal year ending March 2020.

Agalsidase beta was launched in the fiscal year ending March 2019, and sales have been growing steadily since then.

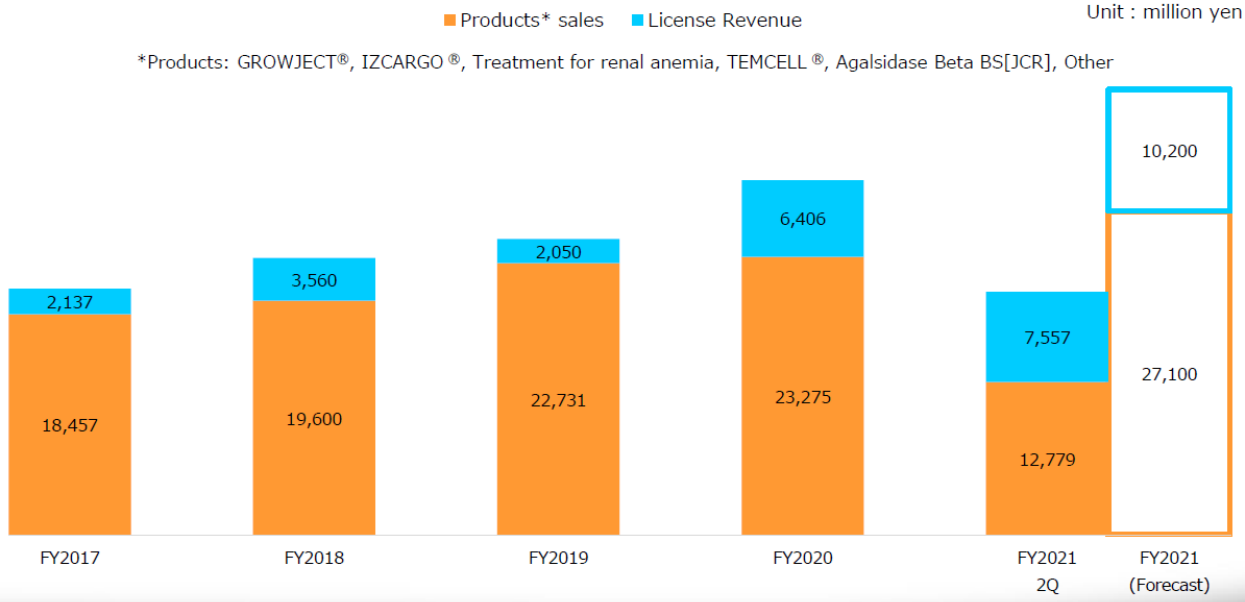


Next, I would like to show you the monthly trend of IZCARGO, which we started selling this year. You can see that the sales have been rising steadily since its release in May. As a result, we have recorded sales of JPY985 million through September.

We newly started to sell this in May 19. Since then, a dedicated team for lysosomal disease has been set up within the marketing department to support the provision of specialized information on IZCARGO, and sales have been increasing as a result.

Changes in sales (Except AZD1222 stock solution)

Unit : million yen



Continuing on, this page shows the trend of net sales excluding vaccine sales. The orange area at the bottom shows product sales, and if you take a look at it, you will see that product sales have been steadily increasing.

In addition, contract revenue is shown in blue on top of that, and if you add it up, you can see that the revenue has been on a steady rise all along, with a particularly notable increase in the current fiscal year.

Balance sheet (Consolidated)

Unit : million yen

	Mar. 2021	Sep. 2021	Change ・Main change		Mar. 2021	Sep. 2021	Change ・Main change
Current assets	48,545	**58,422**	**Total +9,876** ・Cash and deposits (5,848) ・Accounts receivable +13,956 ・Inventories +1,491	**Current liabilities**	29,028	**35,586**	**Total +6,558** ・Special suspense account for tax purpose reduction entry +4,345 ・Short-term loans payable +2,200
				Non-current liabilities	6,199	**4,024**	**Total (2,174)** ・Long-term loans payable (2,200)
Non-current assets	25,238	**28,197**	**Total +2,958** ・Property, plant and equipment +3,343	**Total liabilities**	35,227	**39,610**	**+4,383**
				Total net sales	38,557	**47,008**	**Total +8,451** ・Dividends (929) ・Profit appropriation +9,233
Total	73,784	**86,619**	**+12,834**	**Total**	73,784	**86,619**	**+12,834**
				Equity ratio	51.3%	**53.4%**	

Next, I will explain our financial position.

Total assets as of the end of September 2021 were JPY86.619 billion, an increase of JPY12.834 billion from the beginning of the fiscal year under review. The main reason for this increase is that current assets increased by JPY9.876 billion compared to the end of the previous fiscal year. The main reason for this increase is that accounts receivable increased by JPY13.956 billion from the beginning of the fiscal year under review, while cash and deposits decreased by JPY5.848 billion.

The increase in accounts receivable was due in part to the fact that the contract revenue mentioned earlier for this fiscal year was mostly recorded in September, and all of it was recorded in accounts receivable. In addition, the balance of accounts receivable is large due to the fact that there was a large balance of accounts receivable as of the end of September related to sales of IZCARGO and vaccines, which have been launched this fiscal year. It should be noted that a large part of this accounts receivable has been eliminated during the month of October.

In addition, fixed assets increased by JPY2.958 billion. By major breakdown, property, plant and equipment increased by JPY3.343 billion, mainly due to an increase in construction in progress related to the new plant currently under construction.

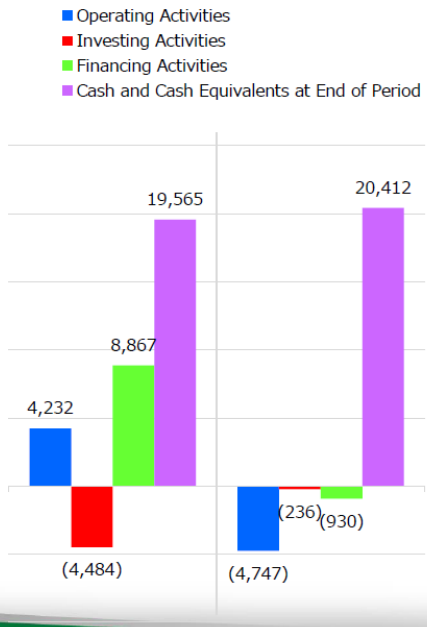
On the other hand, total liabilities amounted to JPY39.610 billion, an increase of JPY4.383 billion from the end of the previous fiscal year. The main reason for this was an increase in current liabilities of JPY6.558 billion. The increase in current liabilities was mainly due to a JPY4.345 billion increase in the special suspense account for tax purpose reduction entry. The amount in this special suspense account for tax purpose reduction entry is the subsidies we receive currently from the government in relation to the construction of new plant, and it was recorded under the current liabilities account because it is currently under construction.

Total net assets were JPY47.008 billion, an increase of JPY8.451 billion from the end of the previous fiscal year. This is the result of paying JPY929 million in dividends out of the JPY9.233 billion in profits recorded.

As a result, the equity ratio improved by 2.1 percentage points, from 51.3% at the end of the previous fiscal year to 53.4% at the end of the second quarter of this fiscal year.

Cash Flows (Consolidated)

Unit : million yen



	Six Months Ended Sep. 30, 2020 A	**Six Months Ended Sep. 30, 2021 B**	Year-on-year B-A
Income before income taxes	1,381	**12,729**	11,348
Depreciation and amortization	872	**922**	49
Accounts receivable-trade	1,462	**(13,934)**	(15,397)
Inventories	(1,562)	**(1,491)**	71
Other	2,078	**(2,972)**	(5,050)
Operating Activities	4,232	**(4,747)**	(8,979)
Securities	0	**0**	0
Capital investment	(1,437)	**(4,514)**	(3,076)
Other	(3,047)	**4,277**	7,324
Investing Activities	(4,484)	**(236)**	4,247
Borrowings	9,420	**0**	(9,420)
Dividends·treasury stock	(516)	**(920)**	(404)
Other	(36)	**(9)**	(26)
Financing Activities	8,867	**(930)**	(9,798)
Increase/ decrease of cash and cash Equivalents at end of Period	8,637	**(5,848)**	(14,485)
Cash and Cash Equivalents at End of Period	19,565	**20,412**	847

(Reference)	FY2020		FY2021	
	2Q	4Q	2Q	4Q (Forecast)
Depreciation and amortization	872	1,892	**922**	**1,860**
Capital investment	306	3,965	**583**	**4,190**

Next, I would like to explain the status of cash flows. As I explained earlier in the balance sheet section, the decrease in cash and cash equivalents was JPY5.848 billion. The main reason for this is that net cash used in operating activities was JPY4.747 billion.

As I mentioned earlier, the main reason for this is that trade receivables increased by JPY13.934 billion.

Net cash used in investing activities was JPY236 million, which is considerably less than the previous year. The main reason for this is that subsidies have been received for capital investment.

As for the cash flow from financing activities, since there was no change in borrowings during the current fiscal year, the major variable factor was the payment of dividends.

As a result, the balance of cash and cash equivalents at the end of the fiscal year was JPY20.412 billion, a decrease of JPY5.848 billion from the end of the previous fiscal year.

As I mentioned earlier, we received a large amount of payment for accounts receivable in October, so as of October 25, the balance of cash and deposits has increased by more than JPY10 billion over the JPY20.4 billion.

For your reference, capital investment and depreciation expense were listed at the bottom. As I mentioned earlier, the subsidy for the new plant will be used for the capital investment, so the capital investment of JPY583 million does not include the amount for the new plant.

The above is an overview of our financial results.

Thank you very much.

Contents

- Research and Development Topics(Period : June to October 2021)
- Lysosome treatment pipeline
  - JR-171
  - JR-141
  - Others, Expected timeline
- Growth hormone, Regenerative medicine area
  - JR-401X
  - Others, Expected timeline

Tanizawa: I am Tanizawa from the Development Division. I would like to explain the progress of our research and development.

Here is the table of contents for today.

Research and Development Topics (Period : June to October 2021)

2021

◆Jul. Presentation at 16th International Symposium on MPS and Related Diseases (MPS2021)
Development pipeline for lysosomal storage diseases which apply the J-Brain Cargo® (JR-141, 171, 441, 446) were conducted oral and poster presentations in MPS2021.

◆Sep. Conclusion of **an exclusive co-development and commercialization agreement for JR-141 with Takeda Pharmaceutical** Co., Ltd in certain regions.
The two companies will collaborate to bring this therapy to patients as quickly as possible upon completion of the global Phase 3 program, which will be conducted by JCR.

◆Sep. **JR-171** was granted **Fast Track Designation** from US FDA.
Fast track is a process that expedite the review of drugs to treat serious conditions and fill an unmet medical need, so accelerated clinical development and early approval can be expected.

◆Oct. **JR-141** was granted **PRIME Designation** from the EMA.
PRIME is a scheme launched by EMA to enhance support for the development of medicines that target an unmet medical need. With PRIME designation, JCR can expect to be eligible for accelerated assessment of JR-141 at the time of application for a marketing authorization in Europe.

As for R&D topics, in September this year, we concluded an agreement with Takeda Pharmaceutical Company Limited for the joint development and commercialization of JR-141. Also, in the same month, September, JR-171 was designated as a fast track by the FDA. In October, we received PRIME designation from EMA for JR-141. This is the equivalent of breakthrough therapy in the US.

Development Pipeline

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

Code	Indication	Preclinical / Clinical Trials / Filed / Approved	Remarks
JR-141	MPS type II (Hunter Syndrome)	Filed / Phase 3	• ERT • J-Brain Cargo®
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 IIIA (Sanfilippo A Syndrome)	Preclinical	• ERT • J-Brain Cargo®
JR-443	MPS type VII (Sly Syndrome)	Preclinical	• ERT • J-Brain Cargo®
JR-446	MPS type IIIB (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® • Recombinant long-acting GH
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

R&D 4

Today, I would like to explain the progress of lysosomal disease therapeutic enzymes, growth hormone-related development, and the development status of regenerative medical products.

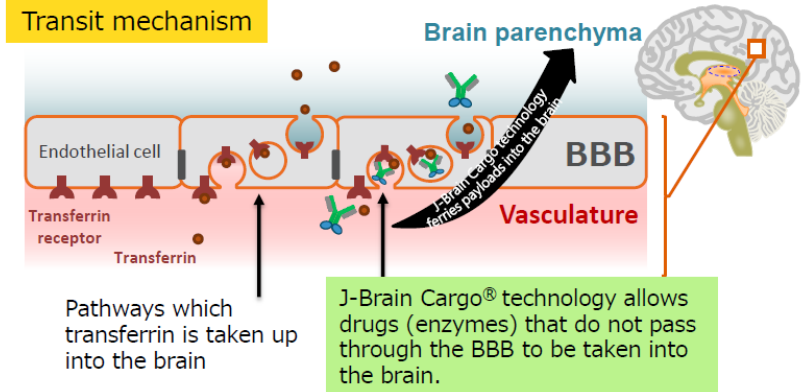
JCR's proprietary blood-brain-barrier (BBB)-penetrating technology, J-Brain Cargo®

Penetrating BBB through transferrin receptor to deliver the active ingredient into the brain

Molecular concept

TfR-targeting mAb + Effector (enzyme) = J-Brain Cargo® Antibody-enzyme fusion protein

Transit mechanism



Pathways which transferrin is taken up into the brain

J-Brain Cargo® technology allows drugs (enzymes) that do not pass through the BBB to be taken into the brain.

Possibility of development

- Lysosomal storage diseases
- Alzheimer's disease
- Parkinson's disease
- Neuro-Oncology
- Neuro-Inflammation

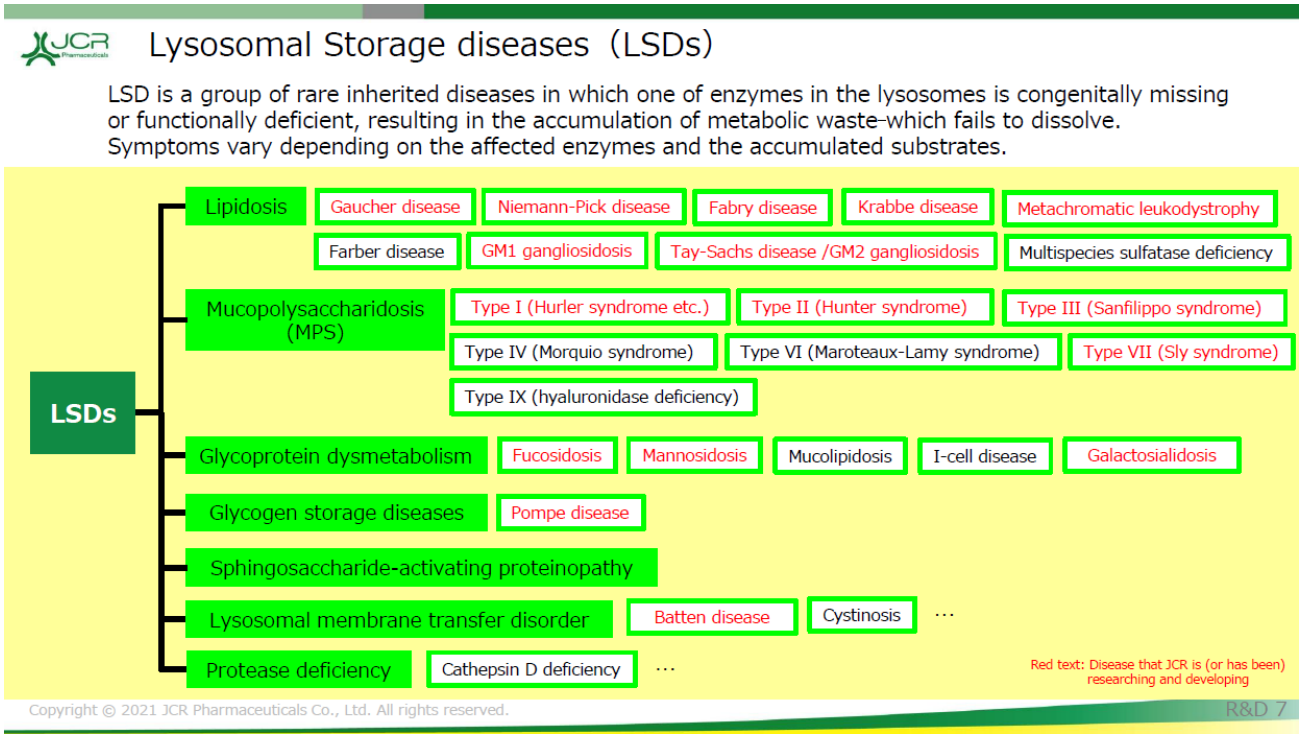
R&D 6

This is an overview of our core technology, the blood-brain barrier penetration technology, J-Brain Cargo. J-Brain Cargo is a technology that delivers drugs into the brain by passing through the BBB via the transferrin receptor.

As shown here, the J-Brain Cargo fusion protein consists of a transferrin receptor antibody and a drug, which binds to the transferrin receptor expressed on the endothelial cells of the blood–brain barrier and transports the drug to the brain parenchyma. This is the mechanism.

We are currently developing this technology for lysosomal disease therapeutic enzymes, but it has the potential to be applied to other diseases that cause central nervous system symptoms in the future.

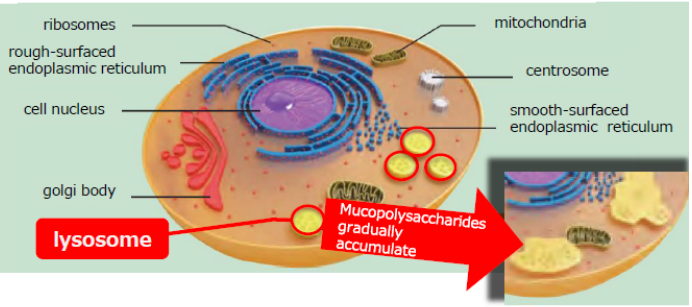
We have many years of experience in researching the J-Brain Cargo, and there are many variations of the J-Brain Cargo. The details will be explained at the next R&D presentation scheduled separately.



Here is the overall picture of lysosomal disease. Lysosomal diseases are a type of inborn error of metabolism, and are classified as shown here according to the substances that accumulate. At present, JCR is working on the area in red, and is expanding the scope of the project.

MPS (Mucopolysaccharidosis)

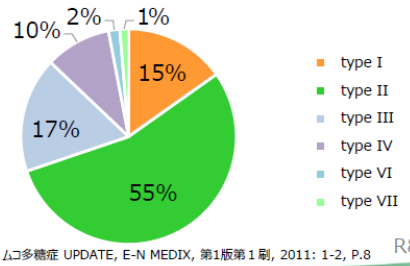
MPS is a group of LSD in which mucopolysaccharides such as dermatan sulfate (DS) and heparan sulfate (HS) accumulate.
Accumulation of mucopolysaccharides causes severe central nervous system (CNS) disorders, organ enlargement, soft tissue disorders, osteoarthritis, and cartilage disorders.



Classification of MPS (some excerpts)

MPS type	Enzyme deficiency	Accumulated substances
I	α-L-iduronidase	HS, DS
II	Iduronate-2-sulfatase	HS, DS
IIIA	Heparan N-sulfatase	HS
IIIB	α-N-acetylglucosaminidase	HS
VII	β-glucoronidase	DS, HS

Frequency of Incidence by MPS Type (Japan)*



*折居 忠夫ら, ムコ多糖症 UPDATE, E-N MEDIX, 第1版第1刷, 2011: 1-2, P.8

R&D 8

The development in the area of mucopolysaccharidosis has advanced the most. It is a disease in which mucopolysaccharides, such as dermatan sulfate and heparan sulfate, accumulate in cells.

There are several types, such as Type I, Type II, Type III, Type IV, and Type VII. Type II is the most major type in Japan. The next major disease is MPS type III.

MPS type I (Hurler, Hurler-Scheie, Scheie syndrome)

MPS I (ratio) *1	Symptoms*2	Central nervous system symptoms (CNS)*2	Conventional treatments*3
Hurler (≒60%)	the most severe form, symptoms emerge shortly after birth and progress rapidly	significant developmental delay and cognitive decline	HSCT* ERT**
Hurler-Scheie (≒20%)	an intermediate phenotype	mild cognitive impairment	
Scheie (≒10%)	typically milder symptoms and a slower disease progression	mostly nomal intelligence	

※Approximately 10% of patients were classified as having an unknown or undetermined phenotype.

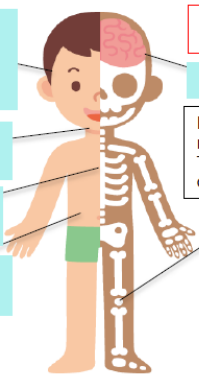
*HSCT: Hematopoietic Stem Cell Transplantation
**ERT: Enzyme Replacement Therapy

characteristic coarse facial features
corneal clouding
hearing loss

airway obstruction
→ respiratory failure

heart valve disease
→ cardiac failure

hepatosplenomegaly
umbilical hernia



Main symptoms*2

CNS symptoms

Develop symptoms such as psychomotor retardation.
The developmental age peaks at 2-3 years of age.

short stature
cervical spine compression
joint stiffness and contractures

◆It greatly reduces quality of life (QOL) in patients with CNS or systemic symptoms.

JR-171

Drugs are delivered to both the body and the brains, by adapting **J-Brain Cargo®** and passing the BBB, can be **expected to improve** the systemic symptoms and **CNS symptoms.**

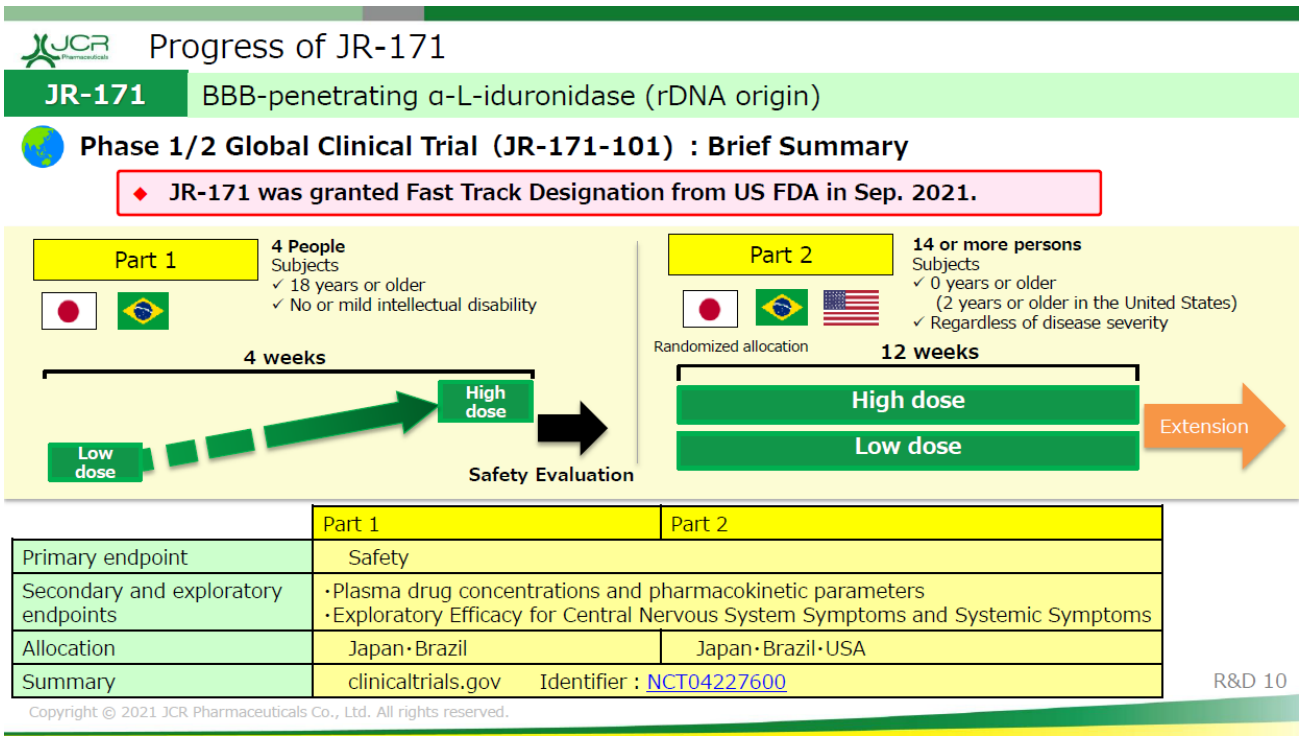
*1:Tomatsu S, Lavery C, Giugliani R, Harmatz P, Scarpa M, Wegrzyn G, et al. Mucopolysaccharidoses Update (2 Volume set); 2018. Chapter 9, Mucopolysaccharidosis type I: clinical feautures biochemistry, diagnosis, genetics, and treatment. Mucopolysaccharidoses update; p. 143-64.
*2:折居 忠夫ら, ムコ多糖症 UPDATE, E-N MEDIX, 第1版第1刷, 2011: P.xii,2,102-103
*3:Michael Beck, MD, The natural history of MPS I: global perspectives from the MPS I Registry, Genetics in Medicine, October 2014: P.759-765.

R&D 9

I would like to explain a little bit about MPS Type I here. There are 3 disease names for MPS type I, depending on the severity of the disease, ranging from Hurler syndrome to Scheie syndrome, and from severe to mild.

In terms of clinical symptoms, it is not much different from other MPS, but it is characterized by physical symptoms such as valvular heart disease and hepatosplenomegaly, as well as central nervous system symptoms.

Currently, enzyme therapy is being used, but it is not effective in treating central nervous system symptoms, so we are currently conducting clinical development of JR-171 using J-Brain Cargo.



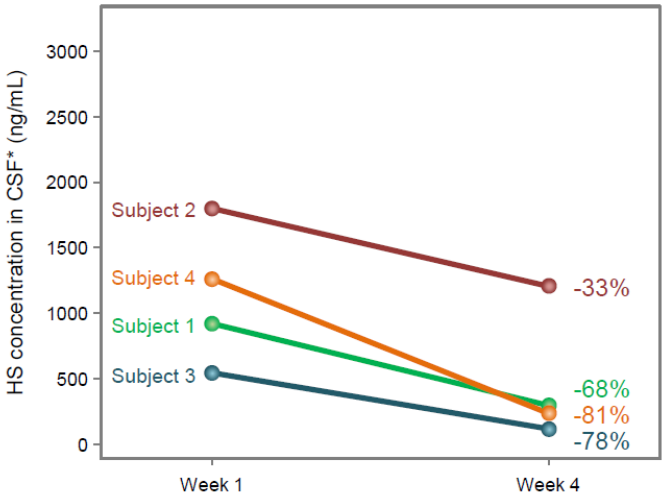
Here is the trial outline for the global Phase I/II trial. The part on the left is Part 1, which confirms safety, and the part on the right is Part 2, which examines the 2 dosages. These 2 parts are being conducted together as a Phase I/II trial. Part 1 has already finished, so I would like to show you the data in the next slide.

Progress of JR-171

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

Phase 1/2 Global Clinical Trial（JR-171-101）：CSF*-heparan sulfate (HS) levels in Part 1 subjects

*CSF: Cerebrospinal fluid



Subjects background（N＝4）

- Scheie syndorome
- No intellectual disability
- Prior treatment with existing ERT
- No history of HSCT

Results

CSF HS concentrations decreased in all subjects (mean decrease of 65%)

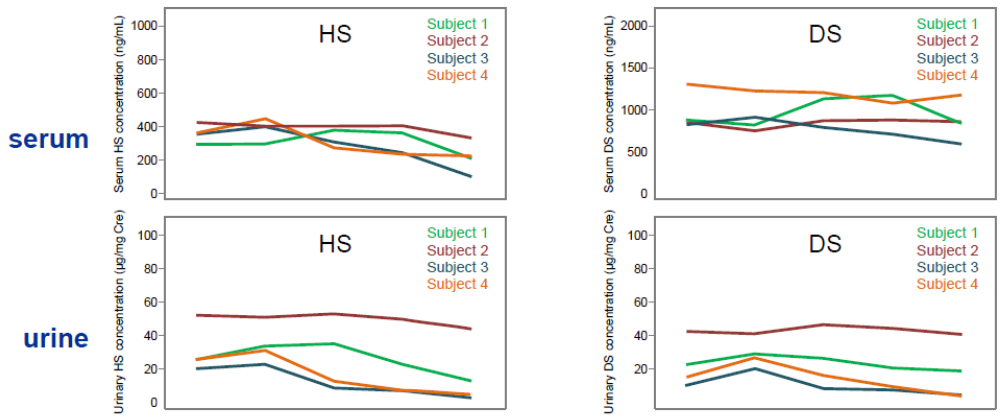
R&D 11

This is a very important result, showing the concentration of heparan sulfate (HS) in the cerebrospinal fluid (CSF) of the subjects in Part 1. As you can see, we were able to confirm that the concentration of HS in the CSF decreased in all subjects. The average is 65%. The results showed that JR-171 migrated to the central nervous system and reduced the substrate, so we are in a state of further development based on these results.

Progress of JR-171

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

Phase 1/2 Global Clinical Trial（JR-171-101）：heparan sulfate/dermatan sulfate (HS/DS) levels in Part1 subjects



Results

HS/DS concentrations remained stable in all subjects throughout the treatment period.

R&D 12

JR-171 is, of course, expected to have an effect on central nervous system symptoms, but it is also expected to have an effect on physical symptoms. In order to confirm the effect, we are checking the changes in biomarkers in serum and urine.

In conclusion, as you can see below, HS/DS concentrations remained stable in all subjects during the administration period, even after switching from the existing enzyme to 171.

Progress of JR-171

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

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

Part1 : Summary

- CSF HS levels decreased from baseline in all subjects
- There were no serious safety concerns.

Current Status and Future Planning

- JR-171-101 Part 2 with a 12-week treatment is in progress.
- Phase 3 pivotal study to confirm long-term safety and efficacy of JR-171 is planned

R&D 13

Here is a summary.

As described on the top, HS concentration in CSF decreased from baseline in all subjects. We are currently conducting Part 2 and plan to move to global Phase III trial once that is completed.

Progress of JR-141

JR-141 IZCARGO® (Brand name in Japan)
pabinafusp alfa (BBB-penetrating iduronate-2-sulfatase, rDNA origin)

JR-141 Cinical Development Package

	Japan	Brazil	Global (US, Brazil, UK, France, Germany, Spain)
Clinical trials for application for manufacturing and marketing approval	• Phase 1/2 clinical trial • Phase 3 clinical trial Manufacturing and marketing approval (Mar. 23, 2021) Listed in the National Health Insurance (NHI) reimbursement price list and launched (May 19, 2021)	• Phase 2 clinical trial **Application for marketing approval (Dec. 22, 2020)**	• Phase 3 clinical trial **Initiated recruitment for Global Phase 3 clinical trial (2022)**
Clinical trials to obtain long-term clinical data	**Post-marketing clinical trials (approx. 10 years) in progress**	**Long-term administration study ongoing**	

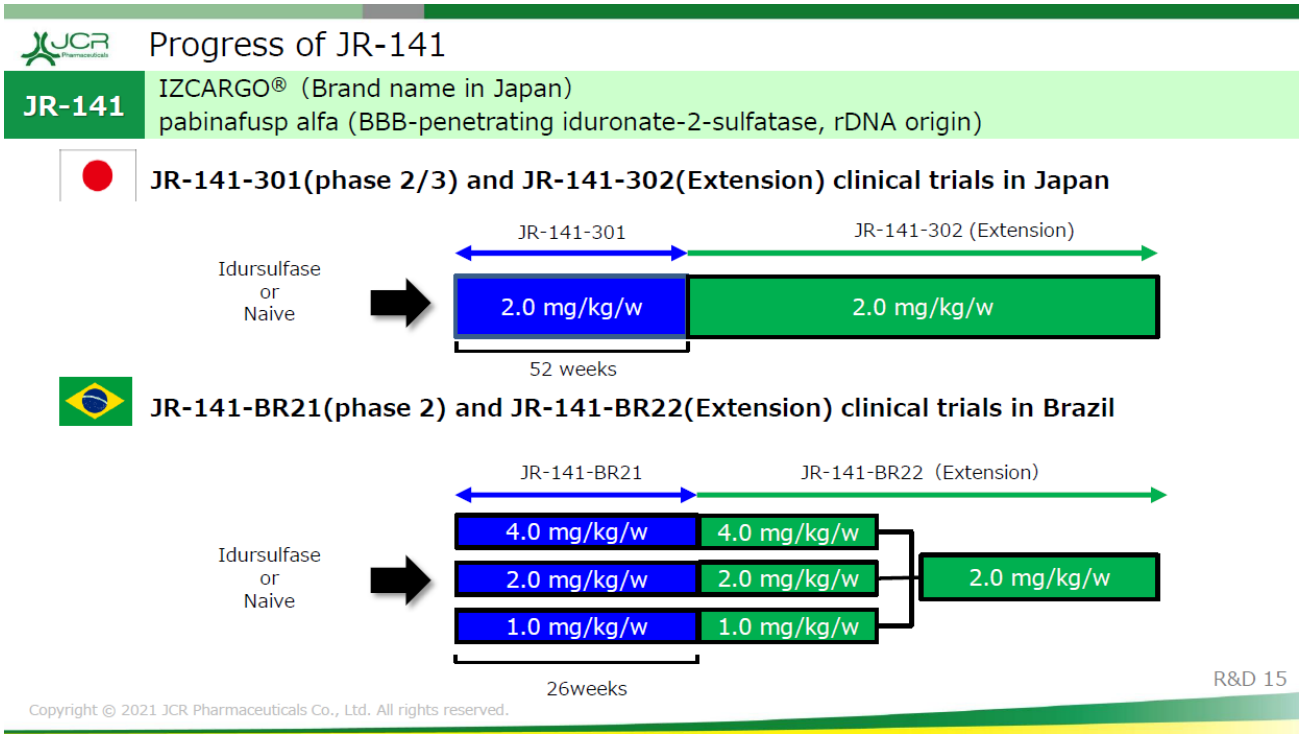
R&D 14

From here, I will explain the global development status of JR-141, IZCARGO.

In Japan, as I have already mentioned, the drug was approved and listed on the NHI drug price list in May of this year. It is currently on sale. We are currently conducting a post-marketing clinical trial.

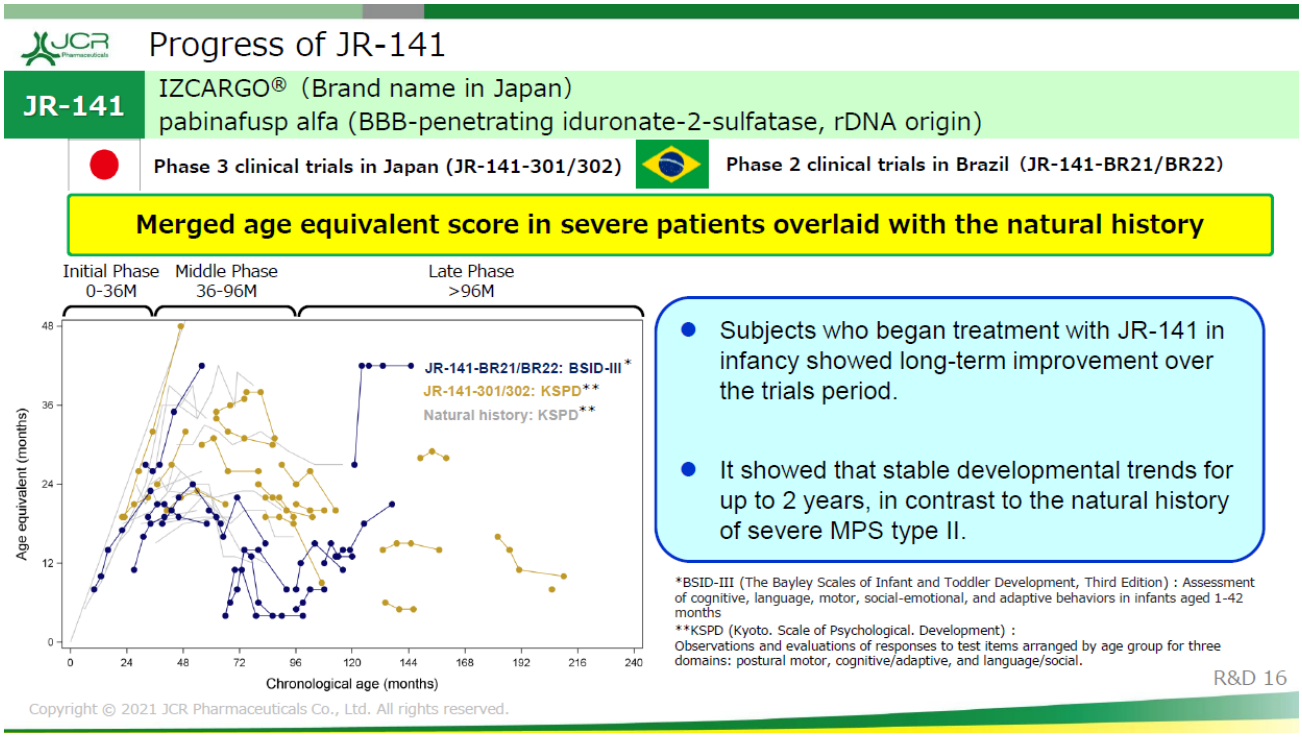
As for Brazil, we completed the application in December last year and are currently negotiating with ANVISA, the authorities. In addition, a long-term administration trial is still ongoing, so patients are still receiving the administration of JR-141.

Globally, we are planning to start trials in the US, Brazil, the UK, France, Germany, and Spain, and we expect to start dosing early next year, in 2022.



Here is the content of the completed trial.

In Japan, the dose was 2 mg/kg/week for a long period of time. In Brazil, 3 doses were established, and the final conclusion was that 2 mg was the most appropriate.



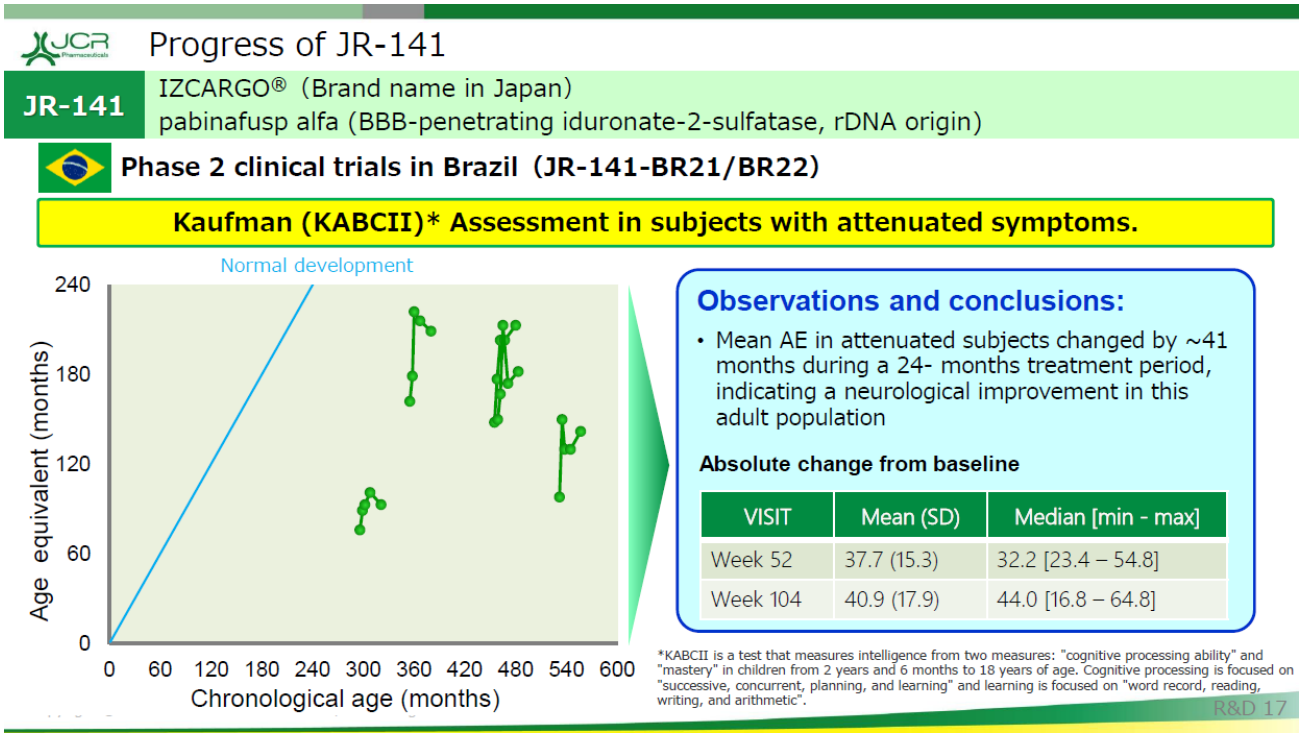
I will explain the data obtained from these trials. The first slide shows the data comparing developmental age and natural history in patients with severe forms of the disease.

The horizontal axis in the table on the left shows the actual age. The vertical axis shows the developmental age. It may be hard to see, but a straight line is drawn, and that is the normal range.

There are 2 important messages here. The first is that patients who are treated early continue to develop close to normal. This shows how very important it is to diagnose early and start treatment.

Another point is that, as you can see from the age of around 8 years old, there is an increase in the developmental age after treatment even in patients who are severely ill and over 8 years old. These data are a narrative report that has been reported separately.

The data are very important because they are consistent with the behavioral improvement of the patients, their facial expressions, and their speech, et cetera. Therefore, we interpret the result that we can expect the effectiveness of IZCARGO for all age groups.



These data are also very important. This is an assessment of the age equivalent of patients with mild forms of the disease. You can see these data in the same way as the previous one. This shows the change in age equivalent after treatment in attenuated patients who are approximately 25 to 40 years old.

As you can see, at the beginning of the administration, the values were lower than the normal range, and after the treatment, you can see that the age equivalent increased significantly.

Specifically, at 52 weeks, an increase in developmental age of 37 months was observed. I think this is a result of the fact that central nervous system symptoms are observed even in patients with mild forms of the disease, and that these symptoms improve with treatment.

JR-141 Clinical Trials

JR-141

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

Narrative Reports (JR-141-301 and JR-141-BR22)

Japan (JR-141-301)

Language

- 12/18 of narrative reports from severe patients showed an improvement in language.
- Changes observed include increase word count, increased number of conversations, and resumed singing.

Liveliness/Expression

- 11/18 of narrative reports demonstrated an improvement in liveliness/expression
- Changes observed include increase in activity, richer facial expression

Brazil (JR-141-BR21/BR22)

General changes observed

- Generally positive changes were found in language, motor skills and liveliness/ expression
- Even the patients without marked improvement in language or motor function showed positive changes in liveliness/ expression

R&D 18

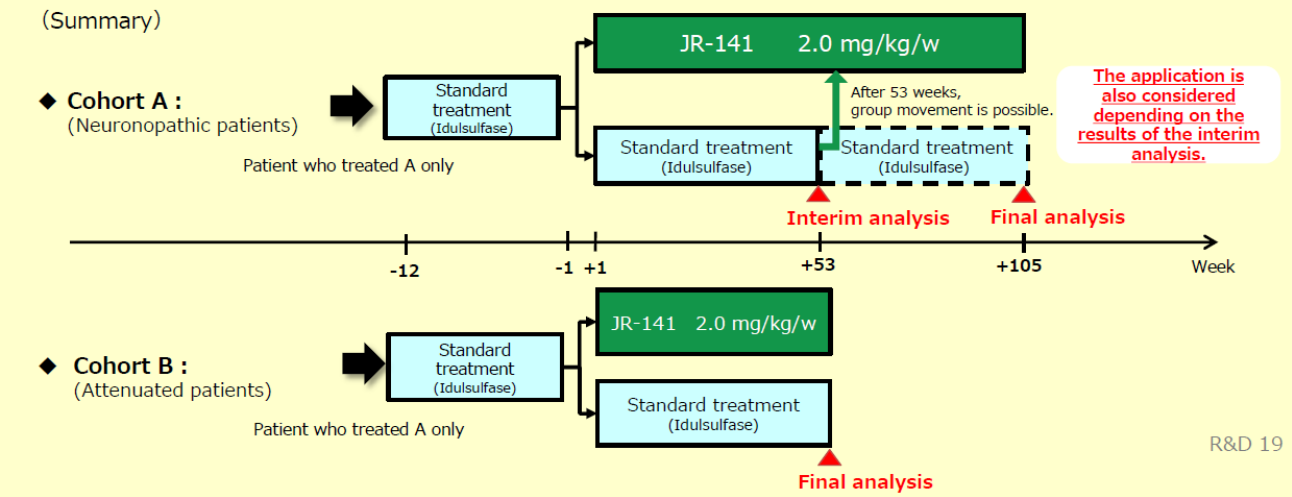
As I mentioned earlier, many narrative evaluations have been made. The results were same in Japan and Brazil. In terms of language, 12 out of 18 subjects with severe disease showed improvement in language. In addition, changes such as increased conversation and singing have been observed. In terms of liveliness and expressiveness, 11 of the 18 subjects showed improvement. The same is true in Brazil, but in addition to this, there have been reports of patients being able to sleep better and being calmer.

JR-141 Global Trial Phase 3 (JR-141-GS31)

JR-141

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

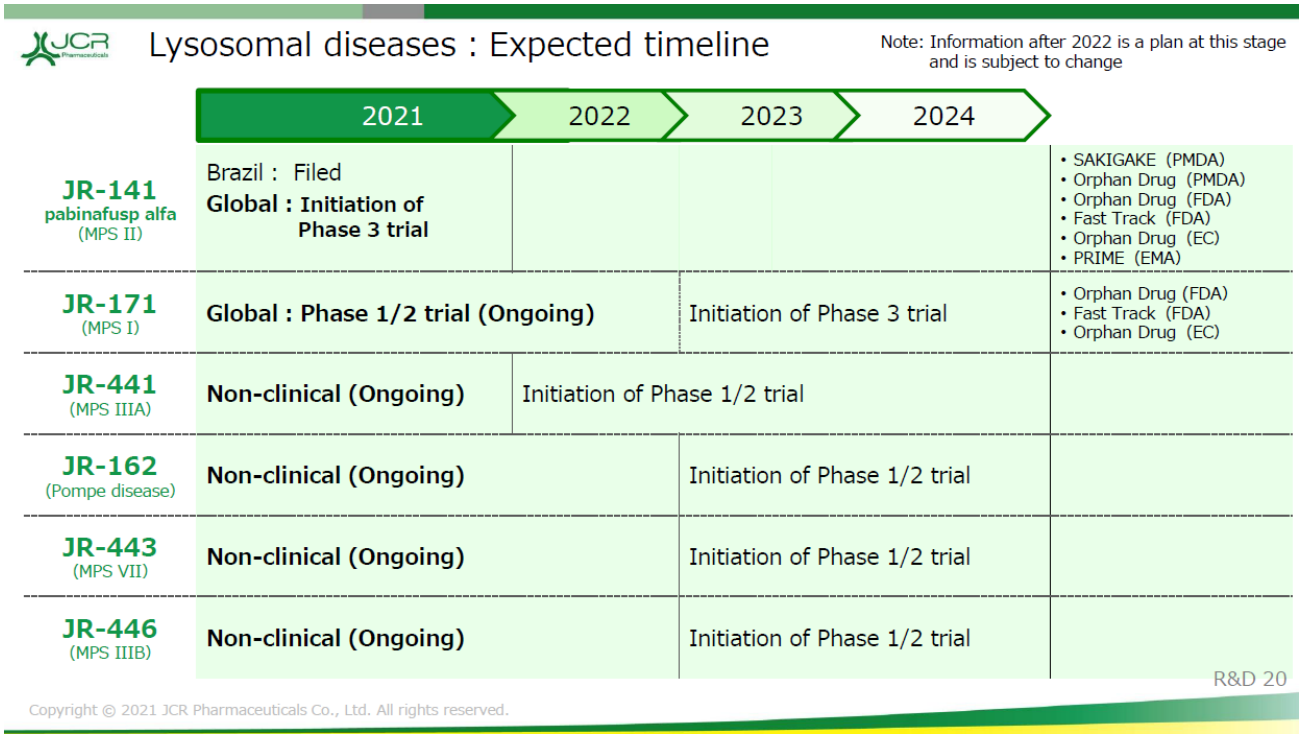
◆ **Designation of PRIME from the EMA in Oct. 2021**



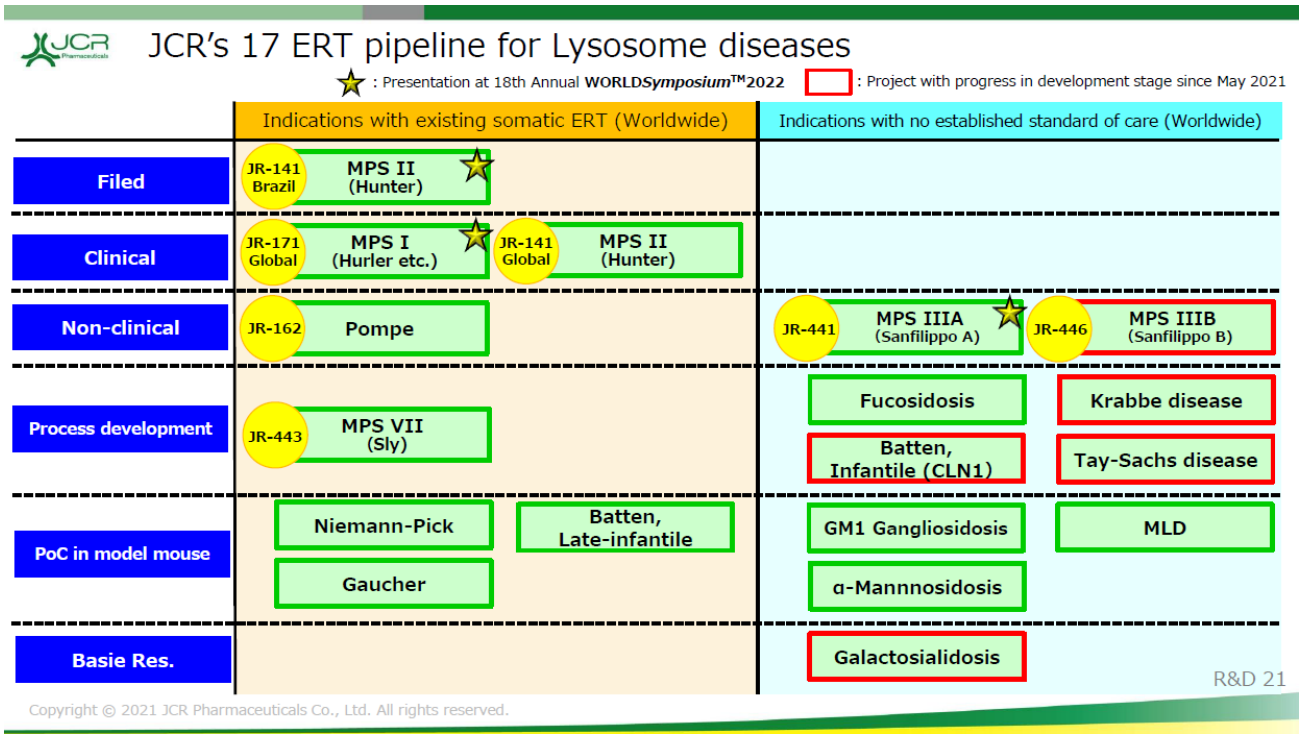
R&D 19

This is the design of the Global Phase III trial that we are planning to conduct. As a feature, 2 cohorts are set up, Cohort A and Cohort B. Cohort A is the recruitment of patients who present with neurological symptoms. As for Cohort B, it is a recruitment of patients with mild forms of the disease.

Cohort A is scheduled to be studied for 2 years, and Cohort B for 1 year. We are planning to study the efficacy of central nervous system symptoms and physical symptoms in comparison with the target group.



As I have explained so far, clinical trial for JR-141 and JR-171 are in progress. Next year, we plan to start Phase I/II trial of JR-441, an enzyme preparation for mucopolysaccharidosis type IIIA. We are also preparing to start trials for the other 3 diseases in 2023.



At present, JCR is conducting research and development on therapeutic agent for 17 lysosomal diseases, and I would like to particularly emphasize the diseases for which there are no existing therapeutic agent listed on

the right side. We are aware that there is currently no cure for these diseases such as mucopolysaccharidosis Type IIIA, Type B, fucosidosis, Krabbe's disease, Batten's disease, Tay-Sachs disease, et cetera. Therefore, we are making a concerted effort to start clinical trials as soon as possible.

JR-401X: About SHOX deficiency

JR-401X Expanded indication of GROWJECT® : SHOX deficiency

- SHOX deficiency is a congenital disorder caused by micro deletions, duplications, or mutations that result in loss of function of a growth-gene SHOX (Short stature homeobox containing gene) present on the sex chromosomes.
- The potential number of patients in Japan is expected to range from 450 to 500 patients/year, but the number of patients diagnosed in clinical practice is extremely small, because of necessary for genetic diagnosis.

Recombinant Human Growth Hormone
GROWJECT®

Indications (As of Nov. 2021)
- Growth Hormone Deficiency
- Turner Syndrome
- Adult Growth Hormone Deficiency
- Small for Gestational Age

R&D 23

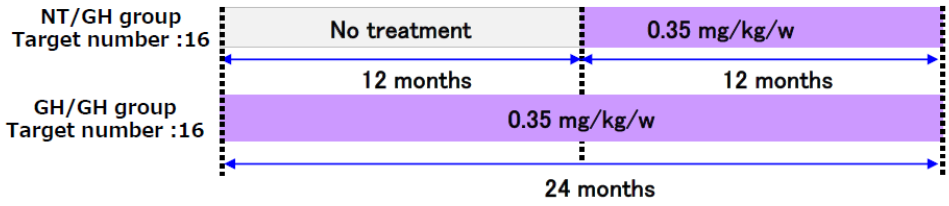
I would now like to explain the development status of growth hormones and regenerative medical products.

The first project is the addition of an indication for GROWJECT, short stature in SHOX abnormalities. The growth gene, SHOX, is a gene involved in growth, and loss of function of this gene causes short stature in patients with this disease.

JR-401X Clinical Trials Phase 3

JR-401X GROWJECT® additional indication: SHOX deficiency

JR-401X-301 : Design (JAPIC trial ID : JapicCTI-183946)



Efficacy endpoints

- Primary endpoint
  - ✓ Δ chronological age - equivalent height SDS (for 12 months after the start of the study)
- Secondary endpoints
  - ✓ chronological age - equivalent height SDS
  - ✓ chronological age - growth velocity SDS
  - ✓ Δchronological age - growth velocity SDS
  - ✓ growth velocity
  - ✓ bone age
  - ✓ Δ bone age
  - ✓ Δ bone age ／Δchronological age
  - ✓ bone age - equivalent height SDS
  - ✓ Δ bone age - equivalent height SDS
  - ✓ IGF-I SDS in serum

R&D 24

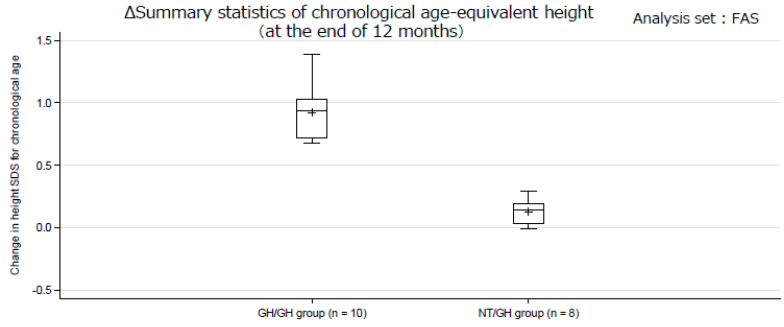
We are currently conducting Study 301, a Phase III trial, and this is the study design. In the first year, we will compare the treated group with the untreated group, and after 12 months, the untreated group will be treated with growth hormone. In this study, we compared the growth of height with the target group.

JR-401X: Results of efficacy data analysis (At the end of 12 months)

JR-401X Long-acting recombinant growth hormone
Growject ® additional indication: SHOX deficiency

		GH/GH group N=10	NT/GH group N=9	Difference
Change in height SDS for chronological age	N	10	8	
	mean(SD)	0.932(0.213)	0.127(0.105)	0.796(0.174)
	median	0.935	0.142	p<0.001
	[min-max]	[0.67 - 1.39]	[-0.01 - 0.29]	
	95%CI	0.771 – 1.075	0.040 - 0.215	0.621 - 0.971

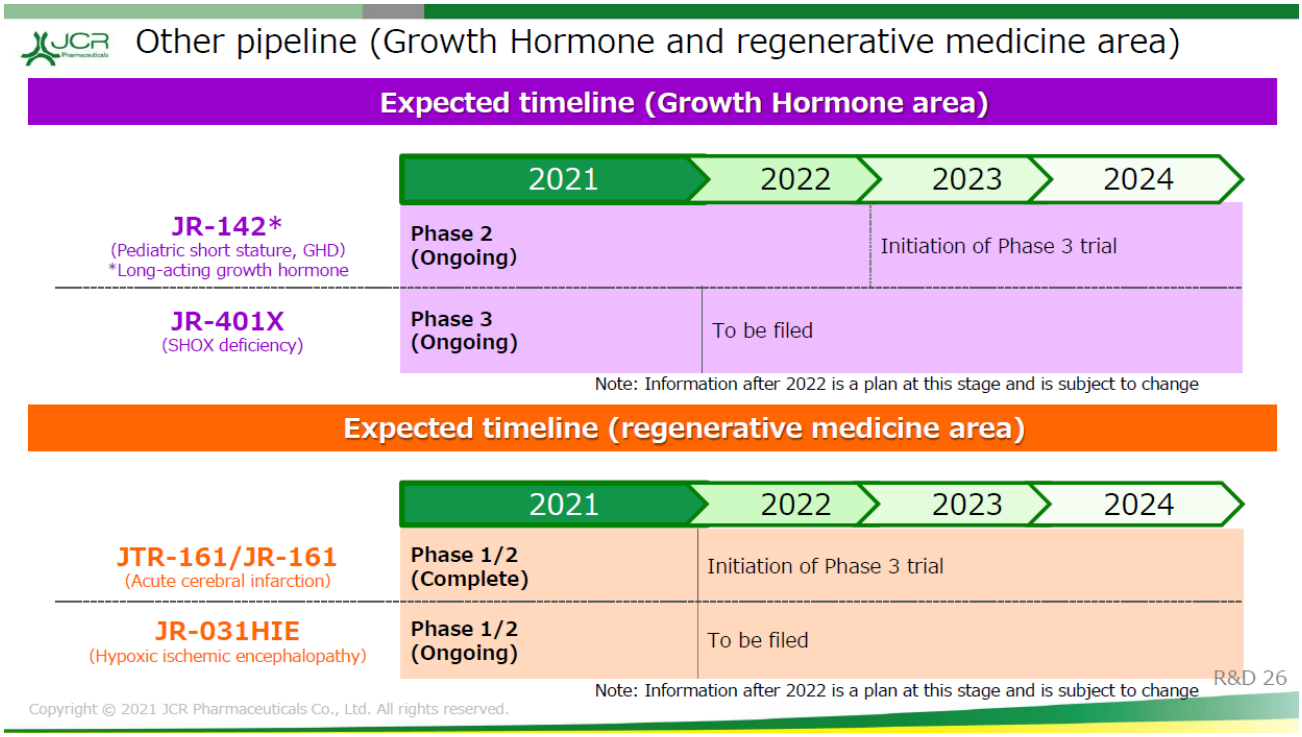
CI : confidence interval, SD : standard deviation



Statistically significant differences were observed in the primary and secondary endpoints between the GROWJECT® group and the no-treatment group.

R&D 25

In conclusion, we are pleased to report that the primary endpoint has been met. The primary endpoint is the Δ calendar age equivalent height SDS, where the left side is the treatment group and the right side is the no-treatment group. The untreated group on the right was treated for 1 year and showed almost no improvement, while the treated group showed an improvement of 0.9 SD or more, which is a very clear and statistically significant difference.



As for growth hormone-related projects, JR-142, a long-acting growth hormone, is currently undergoing Phase II trial. With the cooperation of many doctors, this trial is still being implemented.

We are planning to submit an application for SHOX abnormality next year, mainly based on the data I have just presented.

With regard to regenerative medical products, we will continue to develop JTR-161 in collaboration with Teijin Pharma Ltd.

In addition, JR-031HIE, for the treatment of neonatal hypoxic-ischemic encephalopathy, is currently undergoing Phase I/II trials.

That is all for my explanation.

[END]

Document Notes

1. *Portions of the document where the audio is unclear are marked with [Inaudible].*
2. *Portions of the document where the audio is obscured by technical difficulty are marked with [TD].*
3. *This document has been translated by SCRIPTS Asia.*

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