Kyowa Kirin Co., Ltd.

Agreement to Acquire Shares of Orchard Therapeutics

October 5, 2023

Event Summary

[Company Name]	Kyowa Kirin Co., Ltd.	
[Event Name]	Agreement to Acquire Shares of Orchard Therapeutics	
[Number of Speakers]	2	
	Takeyoshi Yamashita	Director of the Board, Senior Managing Executive Officer and Chief Medical Officer
	Motohiko Kawaguchi	Managing Executive Officer, Head of Finance

Presentation

Moderator: We will now begin the online briefing on Orchard Therapeutics, the acquisition agreement announced at 4:30 PM today.

Today's speaker and person responding to questions and answers are two people: Takeyoshi Yamashita, Director of the Board and Chief Medical Officer, and Motohiko Kawaguchi, Managing Executive Officer and Chief Financial Officer.

Today's conference call is scheduled up to 60 minutes. Yamashita will give an overview of the project and then take questions from the audience. Please download the documents from our IR website.

Then, Dr. Yamashita, please go ahead.

Transaction Summary

Items	Summary
Target	■ Orchard Therapeutics plc (London) — Listed on NASDAQ
Purchase Price*	■ $16.00 per ADS / approx. $387.4 million (approx. JPY 57.3 billion) — Orchard shareholders will hold additional contingent value rights (CVR) of $1.00 per ADS. — Additional $1.00 CVR will be paid for a total of $17.00 per ADS, or approximately $477.6 million (approx. JPY 70.7 billion) if OTL-200 is approved by the U.S. Food and Drug Administration for the commercial marketing and sale in the U.S.
Funding Method	■ Cash on balance sheet
Financial Impact	■ To be announced once allocation of goodwill and intangible assets are determined
Transaction Structure and Process	■ Scheme of Arrangement（SoA） — Requires the approval by Orchard's shareholder meeting, UK court, and regulatory authorities — Closing is expected in 2024Q1 through implementation of SoA

*Refers to the amount required to make payments related to all outstanding Orchard common shares, ADS purchases, options, Restricted Stock Units, and other instruments.

Yamashita: Thank you all for taking time out of your busy schedules and for attending the information session despite the last-minute announcement.

We are pleased to provide an overview of the agreement we signed today to acquire shares of Orchard, a company located in the United Kingdom.

Orchard is one of the leading providers of hematopoietic stem cell gene therapy. Hereinafter, we will refer to this therapy as HSC-GT taking the acronym of "hematopoietic stem cell gene therapy" in English.

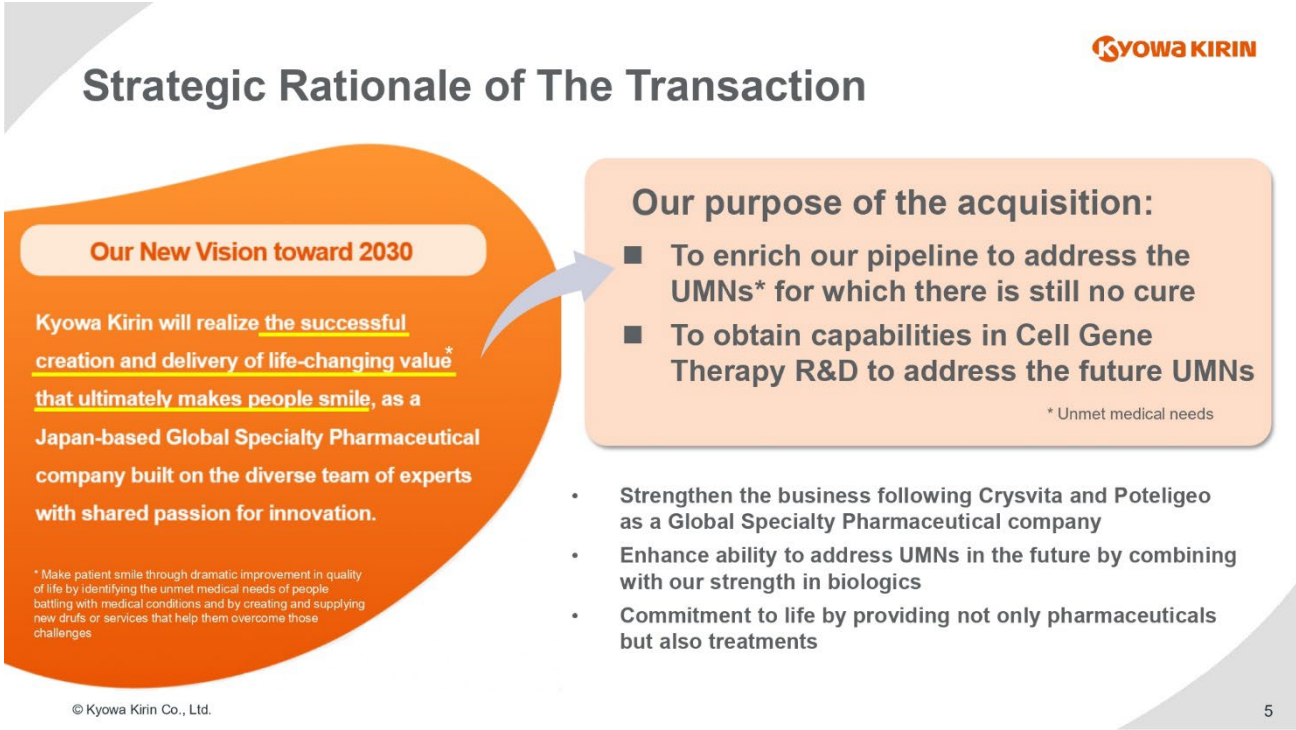
We are making various efforts every day to realize our vision of "the successful creation and delivery of life-changing value that ultimately makes people smile" and by acquiring HSC-GT as a modality that has the potential to cure diseases from the root, we hope to take further steps toward the realization of our vision.

Orchard currently has one marketed product and two development pipelines based on HSC-GT. The marketed product is called Libmeldy and is already available in the EU. In addition to the EU, the company completed a BLA application with the FDA in August of this year, aiming for approval and marketing in the US.

The purchase price will be USD16 per one ADS, for a total purchase price of USD387.4 million. In addition, shareholders will be entitled to receive an additional USD1 per one ADS tied to the approval of the marketing rights of Libmeldy in the US. The total amount in this case would be USD477 million.

The acquisition of the shares will be made by way of a Scheme of Arrangement under the UK Companies Act, whereby the shares held by all shareholders of Orchard will be acquired for cash. Implementation of the Scheme of Arrangement is subject to approval by Orchard's shareholders at a general meeting, and approval by the UK court. At this time, we are targeting a Q1 closing in 2024.

The Company will promptly disclose the impact of the acquisition on our business performance and financial position, if and when it is completed, as soon as it becomes clear.



Orchard already has a steady track record in the area of HSC-GT.

Orchard's medical contributions and business activities fit well with our philosophy, core values, and vision ”the successful creation and delivery of life-changing value that ultimately makes people smile”.

The significance of this acquisition is twofold. One is to enhance our pipeline to address unmet medical needs. The other is to acquire a research and development platform for cellular gene therapy that can challenge to correct the underlying case of a genetic disease.

We hope that both companies will respectfully bring their respective strengths to the table and, by combining them, we strongly hope to promote the creation and delivery of life-changing value and to make people smile, as much as possible.

Overview of Orchard Therapeutics

Orchard Therapeutics plc

Locations	United Kingdom (HQ), United Sates, Netherlands, France, Italy, Germany, Switzerland, Sweden
Business	Biopharmaceutical company with specialty in Hematopoietic Stem Cell Gene Therapy (HSC-GT)
Employees	166 employees (as of Dec. 2022)

Product & Clinical Pipelines

Clinical Asset	Target disease	Status	Next Catalyst	Expected timing of Catalyst
OTL-200 (Libmeldy®)	MLD	Launched in Europe Filed in US	FDA approval	PDUFA: March 18, 2024
OTL-203	MPS-IH	Ph1/2	Initiating pivotal study	Q4 2023
OTL-201	MPS-IIIA	Ph1/2	PoC data readout	Q1 2024

Here is an overview of Orchard.

Headquartered in the United Kingdom, the company operates in Europe and the United States. Orchard has one product on the market, Libmeldy, developed as OTL-200, and two other products in development, OTL-203 and OTL-201, using HSC-GT technology, which can correct the underlying case of a genetic disease.

Libmeldy has already been in the EU market, and a BLA application has been completed with the FDA for approval in the US.

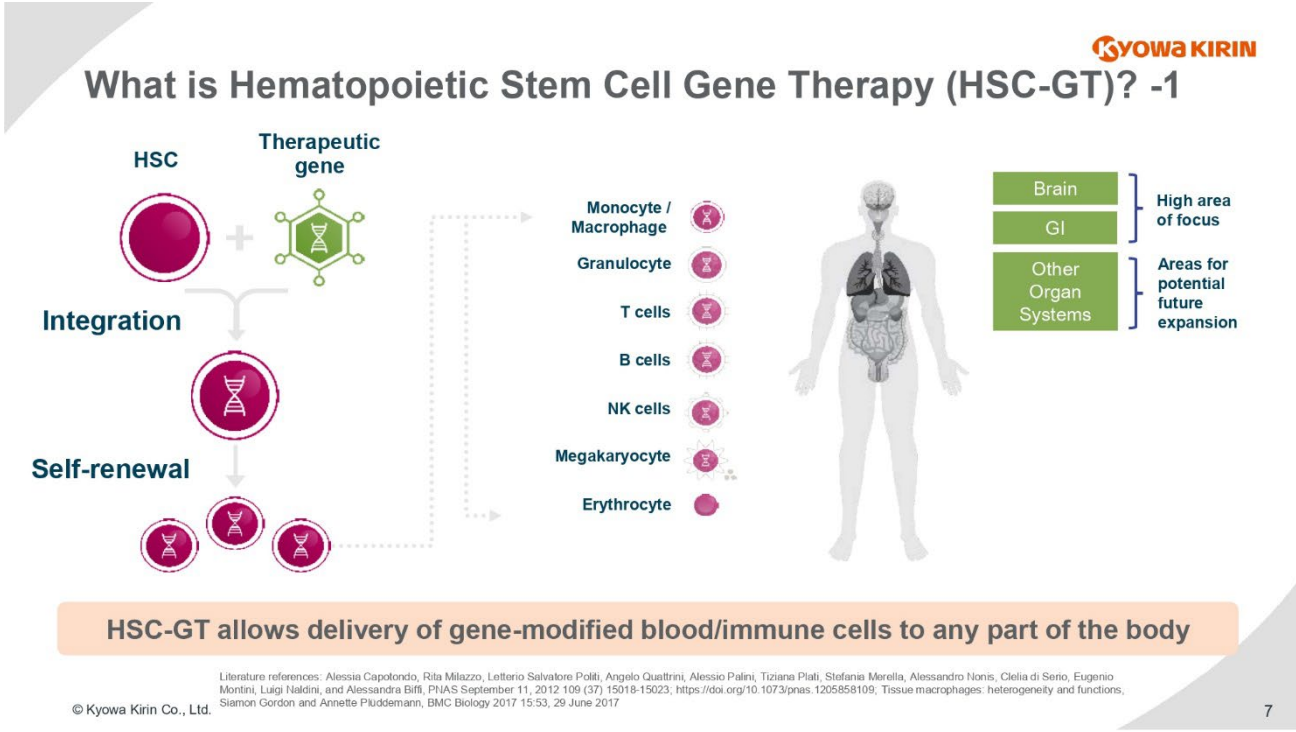
The two development products, both for a disease called mucopolysaccharidosis, are in Phase I/II trials.

For OTL-203, we have already published the results of the PoC study in a paper and plan to begin pivotal study this year. OTL-201 is scheduled to have a data readout of the ongoing PoC study in Q1 of next year.

Common to all three assets is that the targets are classified as lysosomal storage diseases, which are rare diseases caused by metabolic abnormalities due to genetic defects of degrading enzymes in lysosomes. All of these are highly unmet medical needs, and we are trying to realize treatments that can only be achieved with HSC-GT technology.

The market size itself is not large because these targets are rare diseases. On the other hand, there are only a limited number of companies that have established a value chain that can provide HSC-GT and ensure its commercialization.

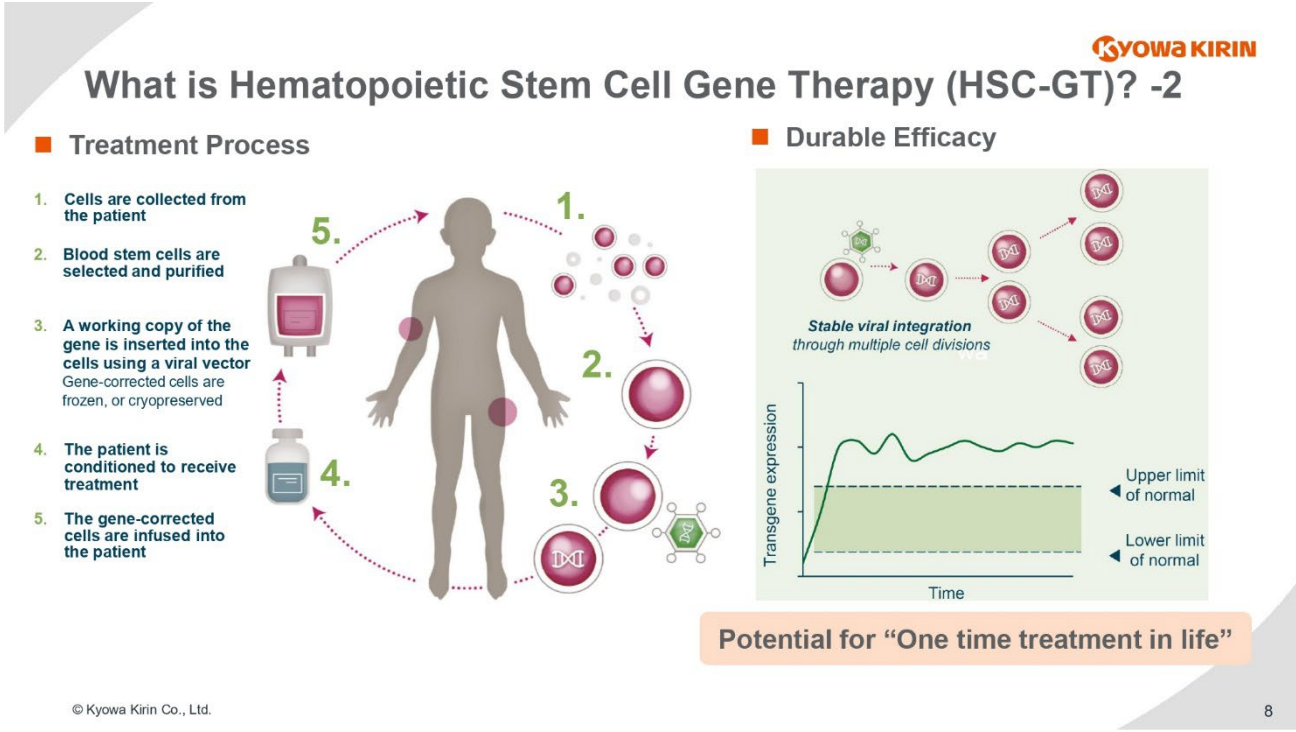
Considering the high degree of perfection of Orchard's business model and infrastructure, combined with the very high level of treatment satisfaction that HSC-GT provides and the extremely small number of patients it targets, we believe that if Libmeldy can be the first to enter the market and establish its position as the one and only treatment, it will be extremely difficult for subsequent companies, with or without patents, to enter the market. In such a case, we have high expectations that the product can be sold steadily over a long period of time.



In this slide, I will give an overview of HSC-GT.

Hematopoietic stem cells, or HSCs, are found primarily in the bone marrow. These cells are capable of differentiating into a variety of blood cells. HSC-GT is characterized by taking these hematopoietic stem cells, introducing a gene for a specific therapeutic purpose, and returning them to the body.

These genetically engineered cells differentiate into a variety of blood cell types in the body, including monocytes/macrophages, T cells, and B cells. These differentiated cells are then distributed to different parts of the body to express the introduced genes. This is a very useful technique for genetic diseases in which gene function has been lost, and by complementing the lost gene function, recovery from the disease state can be expected.

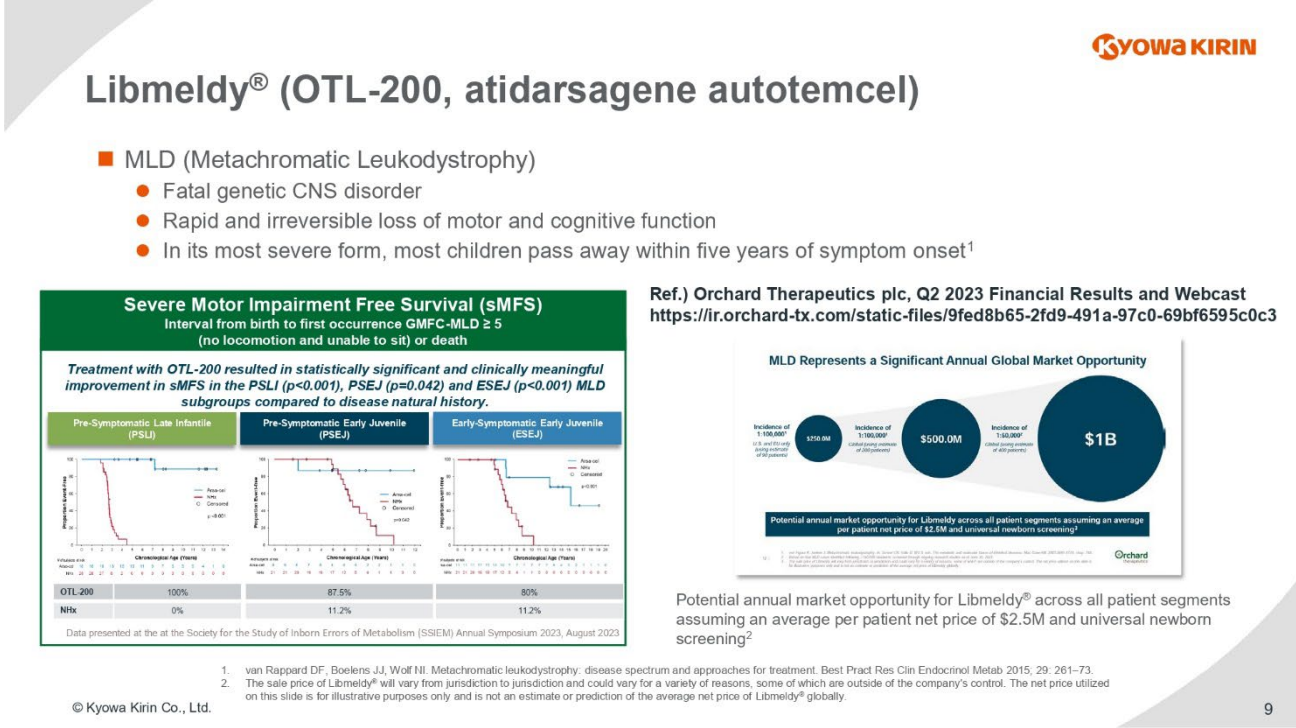


Let me be a little more specific and show you the treatment process.

The patient to be treated has blood stem cells mixed in with the various cells in the patient. Only blood stem cells are taken out from this as shown in number two. In number three, genes that compensate for the impaired function are inserted into the blood stem cells taken out. Here, we use a gene transfer method called lentiviral vectors. Gene-inserted blood stem cells can be cryopreserved and transported.

In number four, the patient then accepts the gene-corrected blood stem cells created in this way, but before this, a conditioning procedure is performed. This is a manipulation to facilitate the replacement of blood stem cells originally in the body with gene-corrected blood stem cells to be transplanted. In number five, the gene-corrected blood stem cells are returned to the patient.

As shown in the figure on the right, the blood stem cells returned to the body differentiate and proliferate in the body, expressing the introduced genes in various parts of the body to produce therapeutic effects.



Next, we will introduce Libmeldy, which is marketed in Europe.

The target disease is metachromatic leukodystrophy. The disease is caused by a genetic defect in the enzyme that degrades sulfatide, a substance consisting of a sugar with a sulfate group attached to it. As a result, glycolipids, which should be broken down, accumulate in the brain, peripheral nerves, kidneys, and other organs, causing impairments in motor and cognitive functions.

The time of onset varies, but those that develop at a young age, from infancy to about six years of age, have a poor prognosis and die before reaching adulthood. The incidence is estimated to be 1 in 40,000 to 160,000 people.

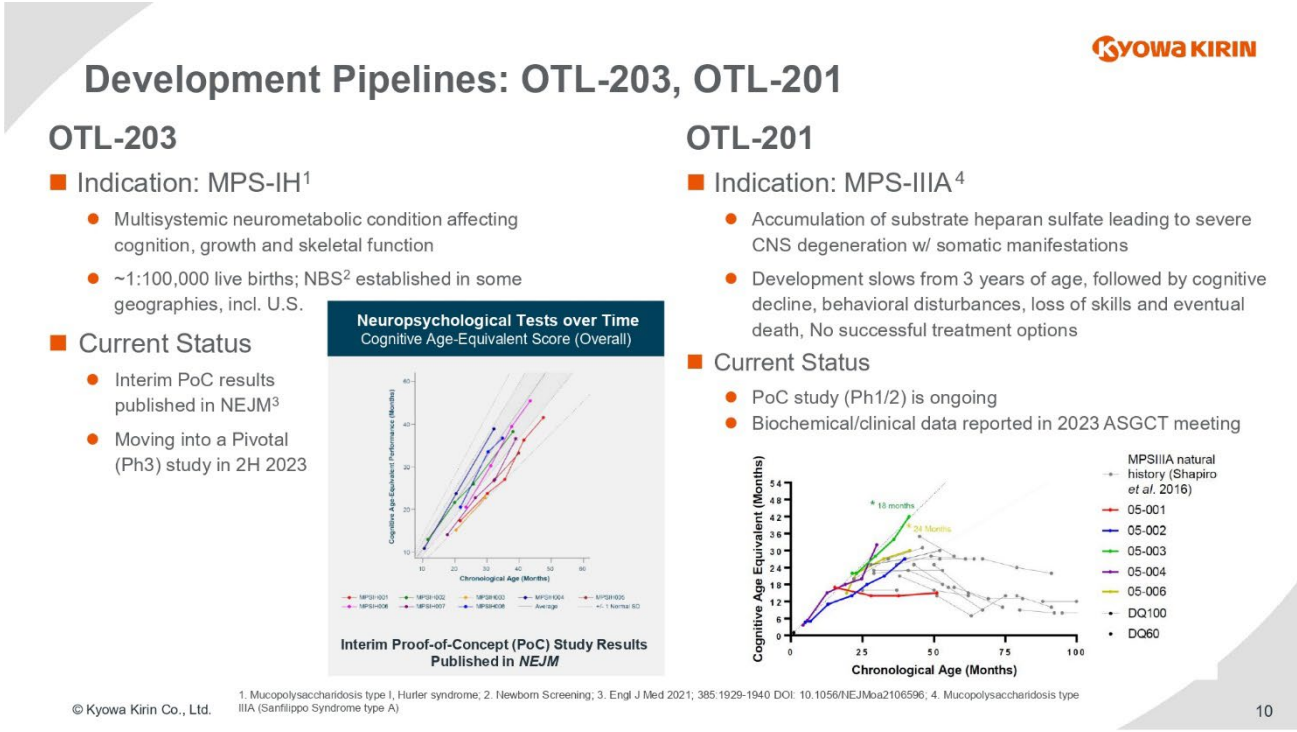
To date, treatment of this disease has been mainly limited to symptomatic therapy. There have been attempts to transplant hematopoietic stem cells from other people, but due to a lack of donors, immune rejection, and other factors, it is not yet widely available.

Libmeldy, on the other hand, uses the patient's own hematopoietic stem cells, so there are no donor search or immune rejection issues. Incorporating the target gene so that it functions well will also make the treatment more effective.

This was approved in Europe in 2020, and we have completed the application in the US and are now awaiting approval. We look forward to Libmeldy's future growth by identifying patients at an early stage, expanding the target area coverage, and pushing forward with these efforts.

The figure on the right is disclosed by Orchard. This is a simple calculation on the assumption that there is 1 in 100,000 patients and that the average drug price per patient is USD2.5 million. In practice, various efforts are needed, including the establishment of a system to find patients by promoting screening of newborns. We have not used this as a variation as it is, but first, we would like to be able to identify and offer treatment to patients born as early as possible in the US and Europe.

In that regard, we consider the market size of USD250 million for about 90 patients, as written in the leftmost circle, to be a rough estimate of the potential in the US and Europe.



Next, we will introduce the development pipelines OTL-203 and OTL-201.

Both target a lysosomal disease called mucopolysaccharidosis and, like Libmeldy, involve taking out the patient's hematopoietic stem cells, introducing the target gene into them, and returning them to the patient for therapeutic effect, basically sharing the same methods and processes as Libmeldy.

OTL-203 is intended for a disease called MPS I, mucopolysaccharidosis type I. This disease is caused by a malfunction of the enzyme that degrades glucosaminoglycans. About 60% of the cases of this disease have an early onset and correspond to what is called Hurler's disease, which is of high severity. Significant cognitive, growth, and skeletal muscle function deficits will occur.

Existing therapies include enzyme replacement therapy, in which enzymes that no longer function are administered externally, and hematopoietic stem cells transplantation from another person. Enzyme replacement therapy has the problem that the administered enzyme does not reach the central nervous system, so the CNS symptoms cannot be improved.

We expect that OTL-203 would also improve the central system and provide better treatment.

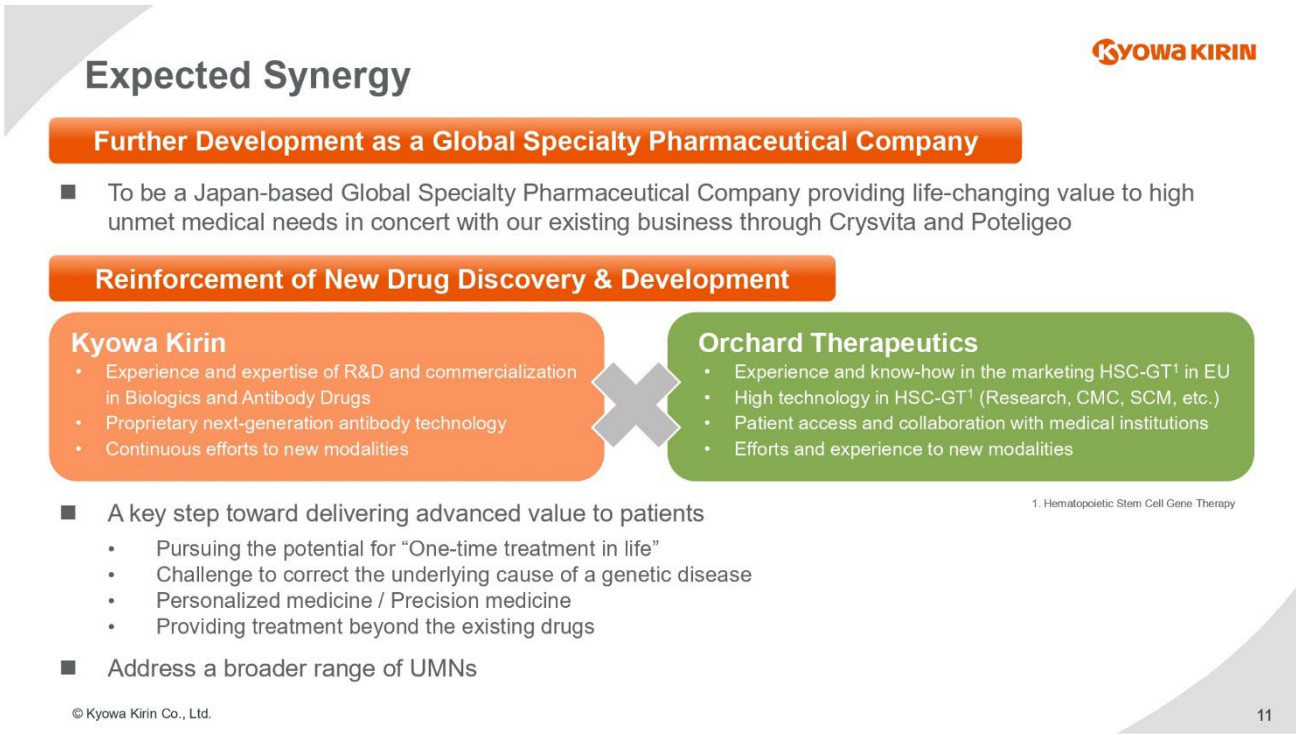
In fact, it has already achieved a PoC in a clinical trial and published the results in *The New England Journal of Medicine*.

One example of the improvement in cognitive function is shown here. In addition to this, improvements in growth, skeletal abnormalities, and motor function have also been observed. Based on these results, Orchard has announced that it will begin pivotal trials during the current fiscal year.

OTL-201 on the right is being developed for MPS IIIA, mucopolysaccharidosis type III. The disease is a malfunction of the enzyme that breaks down heparan sulfate, with the onset of symptoms around age three, developmental delay, and loss of speech by age seven to eight. It is an extremely serious disease, with patients becoming bedridden in their teens and many dying of respiratory infections and other illnesses in their 20s.

As existing treatment options, hematopoietic stem cell transplantation from another person may be considered, but the efficacy is not clear.

OTL-201 is currently undergoing a PoC study, and some of the results of the study have confirmed sustained recovery of the targeted enzyme function in five patients who received the drug, and four of the five patients have achieved cognitive function comparable to that of healthy children, which is the result of the study that was presented at the meeting of American Society of Gene and Cell Therapy (ASGCT) in May.



Now, here are the synergies we expect.

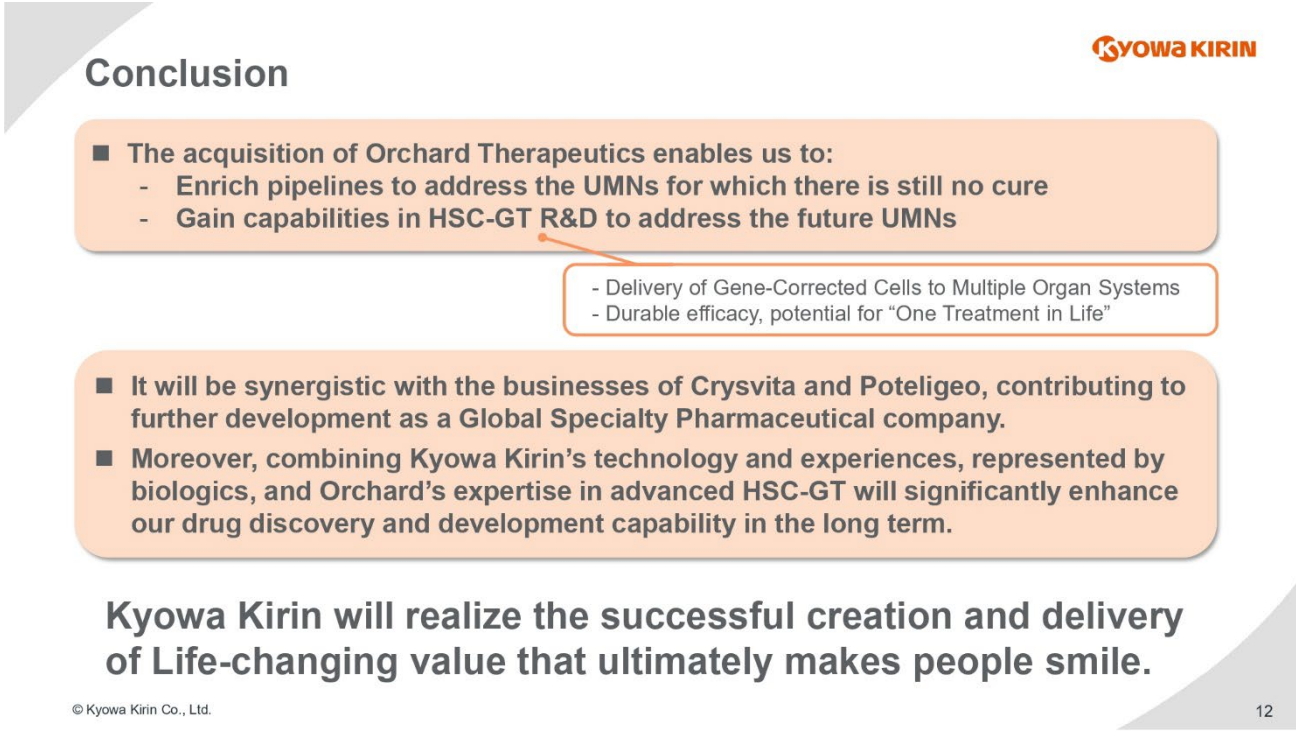
We have already introduced the point of enhancing the pipeline. Apart from that, we are committed to developing as a global specialty pharma through the business expansion of global products such as Crysvita and Poteligeo.

Orchard's product and pipelines I have just introduced fit well with our vision of "the successful creation and delivery of life-changing value that ultimately makes people smile", and we believe that Orchard's technology and expertise and our capabilities complement each other to create new strengths.

Gene therapy has a great advantage as a treatment method, especially if it has the potential to treat the disease fundamentally and only requires one treatment in a lifetime. This is a challenge that we would like to take on to meet the increasingly sophisticated medical needs of the future.

The process of harvesting cells from patients, processing them, and returning them to patients as therapeutic agents also provides us with a whole new opportunity to position ourselves as part of an integrated treatment process in collaboration with medical institutions, rather than simply manufacturing and selling pharmaceutical products.

HSC-GT is truly a personalized medicine or tailor-made medicine, and from this perspective, we expect to gain a new angle for future growth.



The environment around our business is changing rapidly, and we are challenged in terms of our ability to continuously create and realize life-changing value while responding to the speed of change.

We have chosen the approach of acquiring a company to make an early entry into a new disease area with a drug that utilizes a new modality, HSC-GT.

As I have already mentioned, we believe these will be very effective in strengthening our development pipeline and addressing future medical needs.

We will work aggressively to deepen our understanding of Orchard's technologies and rare diseases, and to create synergies by combining the strengths of both companies to quickly create new life-changing value.

Furthermore, we do not think that this acquisition alone is sufficient for our sustainable growth. We will continue to make strategic investments that are expected to contribute to our future growth.

That concludes my explanation.

Question & Answer

Moderator [M]: We would like to start the question-and-answer session.

Muraoka [Q]: Thank you very much. This is Muraoka from Morgan Stanley. Thank you very much.

I took a quick look at the P&L of this company, and the cost to sales ratio is 30%, which is very high. I read it carefully, and I roughly felt that the product was originally purchased from GSK and that the payment to GSK and the payment to other companies and the royalty payment together were indeed about 30%. Based on whether that understanding is correct, if the payments to outside parties are this large, when do you think they will exceed break even before amortization of goodwill?

Kawaguchi [A]: Kawaguchi will answer the question.

As you understand, Libmeldy has already been launched in Europe, and first of all, we expect further sales and earnings growth in 2024, when the product will be launched in the US.

On the other hand, we are still working out the details of the post-acquisition synergies, depreciation costs of intangibles being consolidated after this acquisition, and what to do with the R&D plan afterward.

Nevertheless, the expense-related indicators are supposed to deteriorate due to the high R&D costs for a while. However, over the long term, we expect that it will contribute to the enhancement of our shareholder value, including increases in core operating income and EPS, and we would like to refrain from discussing the specific timing of it at this time.

Muraoka [Q]: I see. Thank you very much. The other question is something that I need to study by myself more. This company's market cap is only USD180 million with European approval and US application pending, which is a very low valuation. Despite the current sales of USD25 million in six months.

In your company's analysis, why do you think the evaluation is so low? What are your thoughts on whether it is product strength, low maximum sales, safety, or some other issue entirely?

Kawaguchi [A]: This is just a guess, but the Orchard’s share price, from our point of view, is quite undervalued, but we assume that this is probably due to concerns about fundraising, and from the analyst's target price, etc., the share price is significantly undervalued.

We believe that this is a reasonable acquisition price, taking comprehensively into account Orchard's growth potential, profitability, synergies with our company, and other factors.

Muraoka [M]: I understand. There are more questions I would like to ask, but since the number of questions is limited to two questions, I will end here.

Kawaguchi [M]: Thank you.

Wakao [Q]: I'm Wakao from JPMorgan.

Excuse me, this is not a question at first, but a confirmation. In your earlier answer to Mr. Muraoka, did you say that you initially had a net deficit? Could you just confirm that part? Should I assume that the cost will be a factor in lowering the OP in net, in the short term?

Yamashita [M]: I'm a little confused about the purpose of your question, so please elaborate a little more.

Wakao [Q]: I'm sorry. At first, I think you said that in the long run, the company will be profitable, but in the short run, it will not be profitable on a net basis, including various amortization expenses. In short, the profit margin will dicrease. Am I understanding this correctly?

Kawaguchi [A]: That's right. This means that a decline in profit indicators is expected in the foreseeable future.

Wakao [Q]: I understand. So, then we have to consider this a negative factor for the next fiscal year.

Kawaguchi [A]: That's right.

Wakao [Q]: I understand. As far as I want to know, I think the original purpose of the M&A this time was to strengthen the pipeline, that is, the pipeline with synergies for your company, and also the short-term contribution to earnings. If we think about this acquisition, it is a little difficult to see the synergies, so I would like to know more about these synergies in more detail.

Also, in terms of revenue contribution, since you are going to make other acquisitions, is my understanding correct that this project is not something that will fit in there of revenue contribution in the short term? So can I assume that you will buy elsewhere and bring something that will contribute to short-term earnings?

Yamashita [A]: I would like to briefly introduce the business-based synergies part.

We are now doing business globally with Crysvita and Poteligeo, both of which also target diseases that have very few patients. We are not a large company, but we are developing this kind of business with a limited sales force and other resources, and I think this is one of our business models.

We focused a bit on the rare diseases that would fit in our model and selected the target of acquisition this time. In this venture business, there was a point earlier about the low evaluation of this area, but I think that Orchard alone is not strong enough to maximize the products, but if we join them, we will be able to increase sales and deliver treatments more quickly. We believe that we can do this without making major changes to our current style, and we believe that synergies can be created there.

Kawaguchi [A]: Regarding the profit contribution, this is not an acquisition intended to contribute to profits in the short term, but we believe that it will have a considerable impact on our profit contribution in the medium to long term and that it will contribute to improving shareholder value.

On the other hand, we will continue to consider the pipeline that has synergies with Crysvita or Poteligeo, which are our targets for strategic and growth investments.

Wakao [Q]: Thank you very much. Incidentally, should we not expect any synergy at this point between your company's basic research capability and a company that is involved in some way with your assets that can develop something in combination with them? As you just explained, the synergy is more in the area of sales.

Yamashita [A]: Yamashita will answer the question.

As I mentioned in my presentation, we are aiming for drugs that have life-changing value and can make breakthroughs, and I believe that you may see us focusing on such areas as antibody drugs in this context. In fact, we are in the research phase and are taking on a variety of challenges.

Among them, the blood stem cell-based modality, which I mentioned earlier, can enter the central nervous system, and it also has the property of delivering drugs to the central nervous system, which is something that other modalities cannot do. Therefore, we are looking at this case on the assumption that we will naturally consider combining the characteristics of this modality with our current research.

Wakao [M]: Thank you. That's all.

Sakai [Q]: This is Sakai from UBS Securities. Thank you very much.

Excuse me. This may miss the point, but why doesn't President Miyamoto attend this meeting? I am absolutely not saying that Mr. Kawaguchi and Mr. Yamashita are insufficient in the roles, but I believe that the President himself mentioned the importance of strategic investment at the last ESG presentation. If there is any reason for this, please let me know because I am a bit curious.

Yamashita [A]: Excuse me. It is our understanding that there is no particular reason. We have decided that it is appropriate to make this announcement at this time by both of us.

Sakai [Q]: It's not that you think this project is unimportant.

Yamashita [A]: That is not the case.

Sakai [Q]: I understand. I think people would be a little relieved if there was some kind of follow-up on this point at the next financial results briefing. This is my first point.

Secondly, you mentioned that it may be difficult to contribute to profits in the short term, but in the long term, it is an interesting technology, or perhaps the most advanced technology. However, I still think that we cannot evaluate the products you buy unless they make a reasonable contribution to profits or have an impact on your business performance.

In that sense, in Orchard's corporate presentation, there is a pie chart showing the size of the MLD market, and Mr. Yamashita mentioned that there are 90 patients among them, which multiplied by USD2.5 million would amount to about JPY30 billion. You see the value of this Libmeldy on that scale. Is this in terms of global?

Yamashita [A]: The figures you just mentioned are for a very small number of patients, about 90 patients in the US and Europe, where this treatment is actually approached. This is an extremely serious disease, so I think it is necessary to start up first in the US and Europe environment and quickly so that if such patients are born, we would definitely want to save all of them.

I also explained that we expect the drug price to be reasonable there, and our first goal is to focus on the areas I mentioned earlier.

Sakai [Q]: I'm not sure about European drug prices. If so, what is the average drug price in Europe now?

Kawaguchi [A]: The USD2.5 million figure shown here is about the average price of the drug, you can think of it that way.

Sakai [Q]: Does that mean the drug price in the US also will be USD2.5 million based on some estimates?

Kawaguchi [A]: This is only an assumption based on current performance in Europe.

Sakai [Q]: I understand. Also, PDUFA is coming up next year, and I understand that the US drug price will be a little different, so is my understanding correct that you calculated the product value and the acquisition price based on that assumption?

Kawaguchi [A]: The drug price used to calculate the acquisition price is, of course, based on our estimation. We are not able to answer how that compares to the USD2.5 million that has just been mentioned.

Sakai [M]: I see. Thank you very much.

Haruta [Q]: Thank you. This is Haruta from UBS Securities.

Regarding Libmeldy for MLD, you mentioned that it is the first drug, but as you mentioned, you also develop the pipeline for enzyme replacement therapies, I suppose.

On the other hand, in your explanation, you said that if your company was already the first to enter here in the market, it would be very difficult for subsequent companies to enter; however, considering the characteristics of gene therapy, I was wondering when the efficacy of gene therapy is reduced, enzyme replacement therapy would also come into use. Please let me know what I should do about understanding this one.

Yamashita [A]: Thank you for your question. As for MLD, I think there is less hope for a promising enzyme replacement therapy. As I mentioned earlier, we cannot save the most serious cases unless we target the central nervous system and treat them in the very early stages of life. In this context, I believe that this gene therapy is best suited for early detection, while it is a once-in-a-lifetime treatment.

As for development pipeline, there are certainly some that have already been used for enzyme replacement therapy. The unmetabolized substances have accumulated in the central nervous system, causing various disorders that have not yet been fully treated.

I believe that HSC-GT, which is being developed by Orchard, is expected to improve this situation, and is therefore highly superior to the existing enzyme replacement therapy. I think that this could be a standard therapy in the case of MLD, where there has been no treatment so far.

Haruta [Q]: Thank you very much. Incidentally, although some enzyme replacement therapy drugs are now available that can pass through the BBB, do you have any expectations or hypotheses that HSC-GT will be more effective in the central nervous system?

Yamashita [A]: It is difficult for us to comment on the details of enzyme replacement therapy that passes through the BBB, but it still needs to be administered frequently, and in general, I wonder if the rate at which it can pass is sufficient. I think that once gene therapy is done, it is difficult to talk about using other therapies if the results show that the treatment can be reliably cured without being bothered by such treatment.

We will have to wait and see the clinical results and the situation of other companies in the future, but we believe that HSC-GT has strong advantage.

Haruta [Q]: I understand. Thank you very much. If so, you mentioned that the existing pipeline is focused on lysosomal disease, but is this lysosome the best match for the area utilizing HSC-GT here? What do you think about other indications, you wrote you are going to focus on other organs, but what are they actually?

Yamashita [A]: Orchard is investigating several possibilities, including the brain and intestinal tract, as mentioned earlier, and other areas where HSC-GT may be the best treatment for serious genetic diseases. I think this will be the main focus of the study.

These three target lysosomal diseases in common, and they are consistent in terms of methodology, so once Libmeldy is established in MLD, it can be applied as it is for other pipelines. This is a great advantage.

We believe that such areas can be used to overlap as much as possible, even when used in other areas.

On the other hand, when it comes to adding new functions, there may be room for various research and development at the gene insertion stage. We will consider new possibilities in these areas again in the future.

Haruta [M]: I understand. Thank you very much.

Muraoka [Q]: Thank you very much. This is the second time to ask questions.

This was also written when I looked at 10-K, so maybe the answer is clear. My first thought was that a Priority Review Voucher could be gotten for this if the approval was acquired in March, and then the additional payment could be offset. However, when I read it carefully, it says that the voucher has to be transferred to GSK, and even if GSK says they don't need it, they will be distributed equally after the sale. Could you just explain how it would work for your company if you were to receive the voucher?

Kawaguchi [A]: My understanding is that the Libmeldy voucher will be transferred to GSK free of charge, so there will be no profit/loss impact on Orchard.

Muraoka [Q]: I see. Then, I wouldn't hold out too much hope for that. I understood.

Also, excuse me, I think this HSC-GT platform is interesting, but given the history of Orchard, it looks more like a company that is developing assets bought from GSK and others, rather than having the ability to create their drugs.

What I'm asking is, I was wondering if the ability of them to create the next fourth or fifth pipeline by themselves is not very promising, and if they just develop what they have and that's it. Is that a wrong understanding?

Yamashita [A]: Thank you for your question. I believe that GSK's involvement historically was a very important point in the process of creating a large platform here. In fact, some of the assets are actually being moved by Orchard, which has taken over some of the assets from that time.

However, even before GSK joined, these activities for HSC-GT were originally done by the founders of Orchard, and they went through various stages in the process of making it more successful.

Basically, Orchard has the spirit, technology, and basic skills enough to be the first in the world to succeed in this field, and to bring it to places where there are no such drugs available as soon as possible. The company is also putting considerable effort into new developments and is actually making considerable investments in research. Therefore, we do not see the power weakening as a result of the disconnection with GSK.

Muraoka [Q]: Thank you very much. Your immediate goal is USD250 million and 90 patients, but even so, they have already sold USD25 million in Europe alone in the last six months.* This is just about 90 patients and USD250 million; but I have a feeling that if you get approval in the US, it won't stop there. Is it better to see the number of waiting patients coming in at a much faster rate, resulting in a faster peak out? How should I interpret it?

*Orchard's Corporate Presentation (August 2023) lists cumulative net sales of $25,9M from the start of Libmeldy sales through the first half of 2023.

Yamashita [A]: I think we need to carefully examine these points from now on. One is that this is a one-time treatment, so how many patients will be seen each year? I still think the big challenge is to find out how and when such patients are currently being captured, and how to improve on that.

In some areas where the medical environment is well developed, the system may be used quickly, but in some areas, it may be difficult to reach such a situation. We are still not very optimistic about the situation.

Muraoka [Q]: Thank you very much. Sorry, it's taking you so long, but just one more question. Was this a one-on-one acquisition negotiated or were you competing with multiple firms?

Yamashita [A]: I will refrain from answering the details there.

Muraoka [M]: I understand. That's all. Thank you very much.

Wakao [Q]: I'm Wakao from JPMorgan.

I also think it is a good or even great thing that you were able to buy an already-approved modality. So, I'm trying to understand how great this modality is. I have done a little research in the past on gene therapy in general, and I think HSC-GT is a technology that has been around for quite some time.

So, I would like to know why, looking back in the past, others have failed, the product you have purchased this time had successfully launched.

The other thing is that I think you have an application with the FDA right now, and will it be something that has an AdCom regarding this drug? I would also like to confirm whether there are any potential risks that could be taken toward approval by the FDA.

Another thing I would like to know is that this is using patient cells, but I think that in the past this kind of thing has been considered for allogeneic cells as well. As for this modality, does it make any sense to do it with donor cells rather than from the patient?

Yamashita [M]: Thank you for your question. What was your first question?

Wakao [Q]: Historically, why the therapy didn't work well but only this drug is doing so well.

Yamashita [A]: As you say, there is talk that these blood stem cells can be used in various ways, and the concept of inserting genes into them and returning them to the body is not new itself, nor is the technology actually used here very new, it's just as you said.

However, I think it must have been very difficult to control the project at a practical level and bring it to fruition as a business.

We have been doing this kind of research for a long time, so there is nothing surprising about the experimental and technical aspects. However, we still need to find patients quickly, collect stem cells from a limited number of sources, and process and return them to the patients within a certain period of time. I still think it is a great infrastructure here to establish manufacturing processes while guaranteeing quality assurance in all of these processes.

Therefore, I assume that it would be quite difficult to actually do so, and that there have been many cases where the project has been abandoned.

Wakao [Q]: Is there any problem in developing this horizontally in other genes? Can you use that infrastructure as is?

Yamashita [A]: Other genes. Basically, I think we can already use that as well, including the so-called logistics here, where we take the cells from a patient, process them, and return them.

As I mentioned earlier, considering future development, if we modify the inserted gene or the lentivirus in various ways, it may be necessary to conduct another test to ensure various risks, including safety in that area. I have the image that it is necessary to make additional firm groundwork on such modified areas.

Wakao [Q]: I understand. What about the FDA? Do you need an AdCom?

Yamashita [A]: Basically, if the FDA is not able to fully evaluate the product on its own, I think they will need to hold an AdCom. This time, there have been no more serious problems, and with the various products having been successfully approved in Europe, I still think that the possibility of holding an AdCom is low in the normal sense of the word.

However, there are also cases where an AdCom is held to obtain various opinions on rare diseases from the viewpoint that they cannot be fully evaluated, so I am wondering if either of these could happen now.

Wakao [M]: I understand. That's all.

Moderator [M]: Thank you. This concludes today's online briefing on the conclusion of the agreement.

Thank you very much for joining us today, everyone. We would like to ask for your continued support for Kyowa Kirin.