Kyowa Kirin Co., Ltd.

Orchard Therapeutics IR Meeting

April 8, 2024

Event Summary

[Event Name]	Orchard Therapeutics IR Meeting	
[Date]	April 8, 2024	
[Number of Speakers]	2	
	Masashi Miyamoto	Representative Director, President, and Chief Executive Officer
	Bobby Gaspar	Chief Executive Officer, Orchard Therapeutics plc

Presentation

Nakamura: Before starting the meeting, I'd like to give you some housekeeping announcements. We will keep the names and your company names of those attending today for a certain period of time in-house as a list of participants of today's meeting. The contents of this meeting will be available on our website as an on-demand audio stream and transcript.

The information to be presented today contains forward-looking statements. Please be aware that there are various risks and uncertainties involved. Today's speakers are Masashi Miyamoto, President and CEO; and Bobby Gaspar, CEO of Orchard Therapeutics.

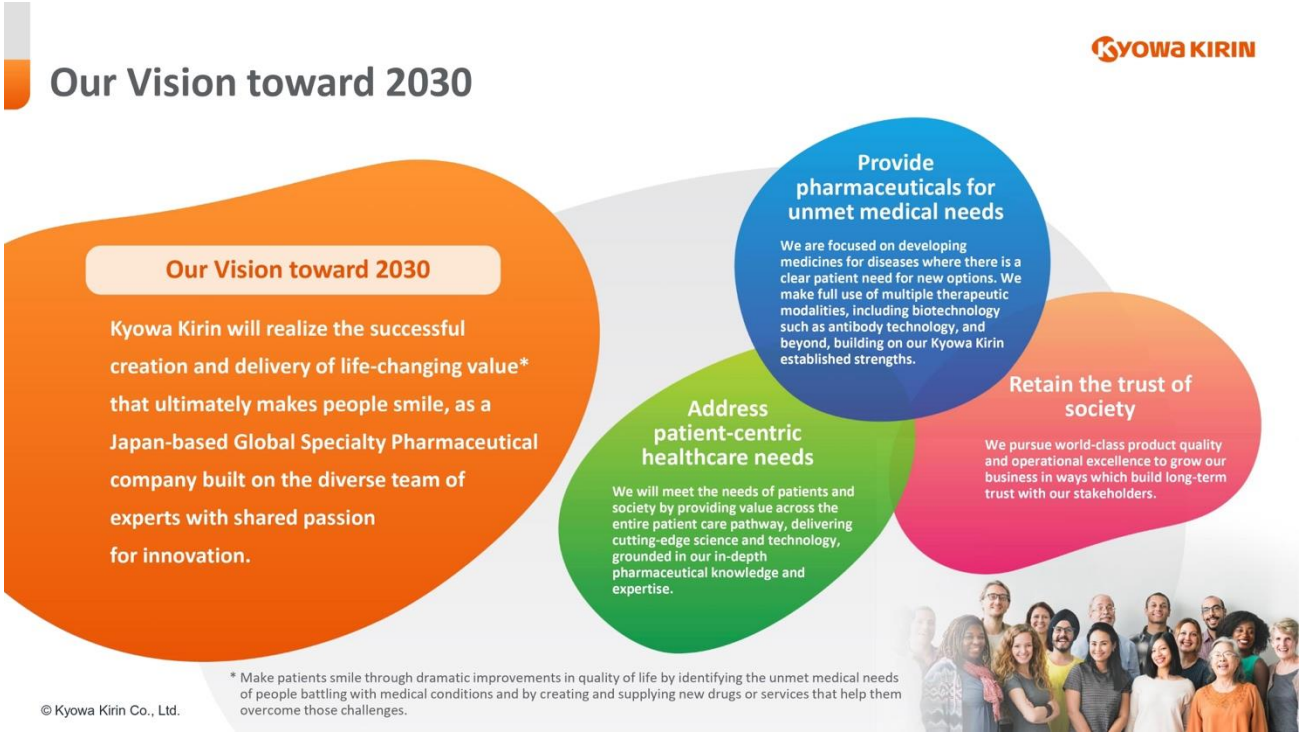
Bobby, could you turn on your microphone and your camera? Thank you. I am Nakamura from Corporate Communications, and I will be serving as your moderator today.

Today's meeting is scheduled up to 90 minutes. Miyamoto is going to make a presentation, and we will take questions from you. Please download the presentation materials from our IR website. Simultaneous interpretation will be available via Zoom. If you would like to listen to Mr. Gaspar's presentation with Japanese translation, please select the Japanese from the interpretation button at the bottom center of the screen. And if you want to listen to the English-translated version of Miyamoto’s presentation in Japanese, please select English. During the Q&A session, due to the system specifications, if you select Japanese, you may not be able to ask questions in English. Please make sure to ask your questions in Japanese. If you do not need an interpretation, please use the default setting of original voice. In the original setting, you may ask questions directly to Mr. Gaspar in English. Now, Miyamoto-san, please.

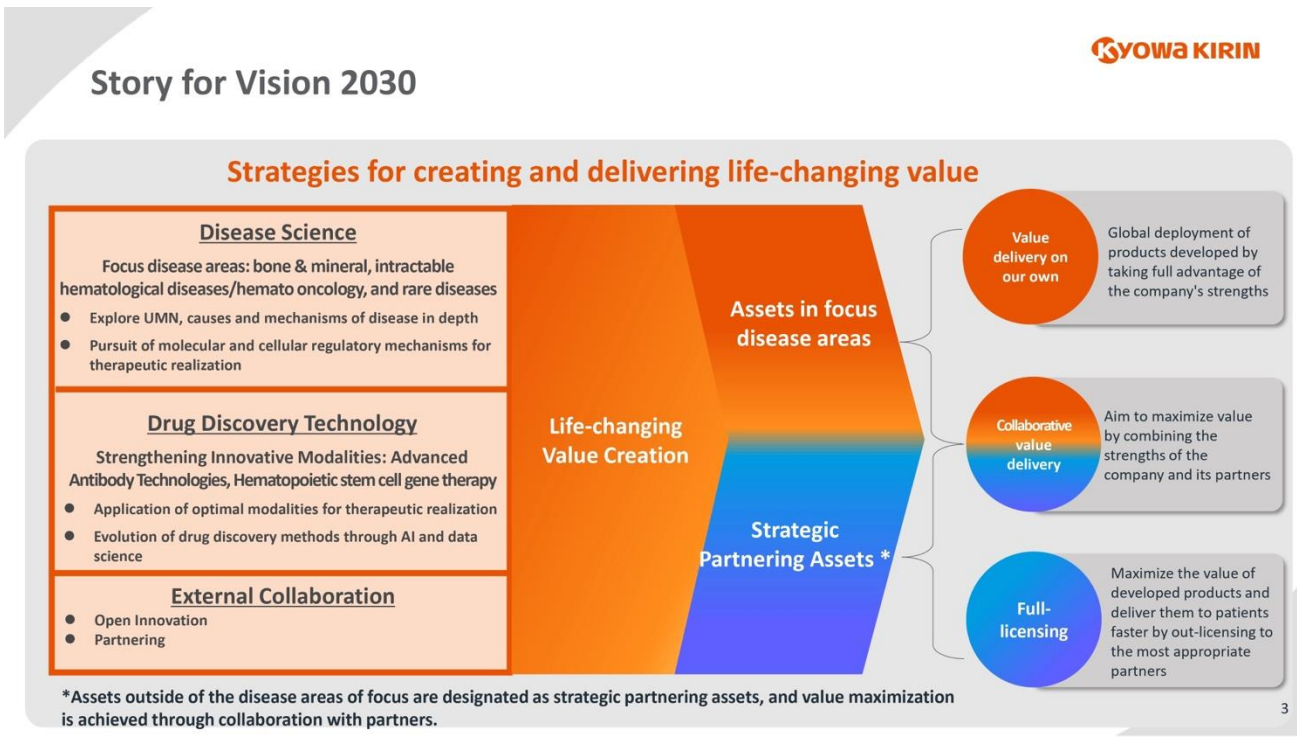
Miyamoto: Thank you for taking time out of your very busy schedule to attend this meeting today. In this meeting, I would like to explain Orchard Therapeutics, which we have acquired as of January this year. As you know, Orchard Therapeutics is a UK biotechnology company with an exceptional technology, hematopoietic stem cell gene therapy. In 2020, Libmeldy, which is based on this technology, was approved in Europe and it's already been used in eligible patients. And in March this year, Libmeldy was also approved by the US FDA under named Lenmeldy, and, in addition, next-in-line development pipeline is underway in clinical trials.

As shown in the agenda, I would like to first explain the reason why we have decided to welcome Orchard as a member of our team. And I would like to talk about the strategy, too. And then Bobby Gaspar, CEO of Orchard, will explain the HSC-GT technology and Libmeldy/Lenmeldy which is based on this technology and

also share some information about the pipeline currently under development. And finally, it will come back to me again. I will talk about the future plans of HSC-GT.

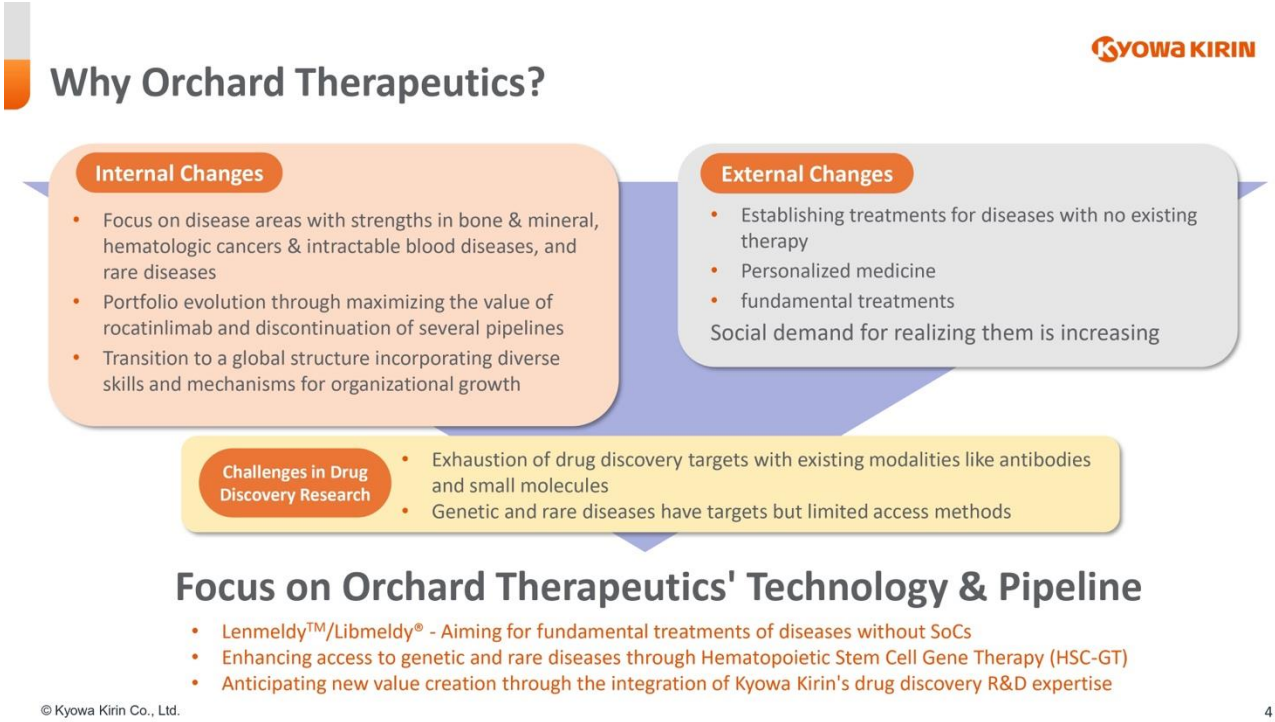


This is our vision for 2030. As a Japan-based Global Specialty Pharmaceutical company, we are committed to continuous creation of life-changing value that ultimately make people facing illness smiles. We decided to acquire Orchard because it is a company that perfectly fits this vision.



This is the story for Vision 2030, which we introduced at our earnings announcement in February this year. This is a clear statement of our strategy for creating and delivering life-changing value by increasing the

resolution of our vision toward 2030. In disease science, we defined the disease areas we will focus on, and in drug discovery technology, we will shift to innovative modalities, and we will also invite innovation from outside, and by making full of use all these, we will aim to create life-changing values. We would like to maximize the value obtained in this way by determining whether it is an asset that we should focus on or an asset that requires strategic partnering, and by adopting the appropriate strategy for each asset. In this story, we believe that Orchard joining us will not only provide us with a pipeline in the rare disease area, which is our focus, but will also strongly drive our shift to innovative modalities in drug discovery technology.



I would like to give you a more specific account of how it led to the acquisition.

As for our internal changes, with the global expansion of Crysvita and Poteligeo, bone and mineral, hematologic cancers and intractable blood diseases, and rare diseases are becoming our strength. During this period, there have also been changes in our portfolio, such as the discontinuation of late-stage development pipelines, while we sought to maximize the value of Rocatinlimab by starting a collaboration with Amgen. In addition, as our global structure evolves, we are transforming into an organization that can grow by incorporating a diverse range of skills and structures.

Looking outside, we see increasing societal demand for establishing treatments for diseases with no existing therapy and also there is a stronger demand for personalized medicine and fundamental treatments.

Looking at challenges in the current drug discovery research, exhaustion of drug targets in existing modalities such as antibodies and some molecules, is a problem. On the other hand, targets still exist for genetic and rare diseases, but access methods are limited.

In order to respond to these changes and resolve problems, we decided that we should focus on Orchard Therapeutics, which has an attractive technology and pipeline. HSC-GT is a technology that will significantly contribute to access in genetic or rare diseases, and Lenmeldy/Libmeldy is a therapy that aims to achieve fundamental cure for diseases for which there is currently no effective treatment. In addition, we believe that a combination of Orchard's and our research and development activities will enable us to pursue the creation of completely new values. Now, Orchard is part of our team, and we will be responding to the challenges and

the changing the environment we identified, and we will be realizing the 2030 vision. And we believe this is going to contribute to mid- to long-term growth.

Now, I would like to introduce Bobby Gaspar. He will be talking about the HSC gene therapy and the product and the company. And as you can see from this slide, he is the CEO. But also, he is a scientist and a medical doctor with a PhD. So from that perspective, he can talk about Orchard company as well as HSC-GT, which will provide a better understanding for the audience today about the significance of this acquisition. So, Bobby, it's your turn.

Gaspar*: Thank you, Miyamoto-san, and hello, everyone. I'm delighted to be here. I'm Bobby Gaspar, CEO and co-founder of Orchard Therapeutics. I'm delighted to join today's investor event to share more about our hematopoietic stem cell or HSC gene therapy platform.

It's been 75 days since Kyowa Kirin completed the acquisition of Orchard Therapeutics. And as we'll discuss in the next few slides, a lot of progress has already been made to help realize our shared vision of delivering life-changing value to patients in need.

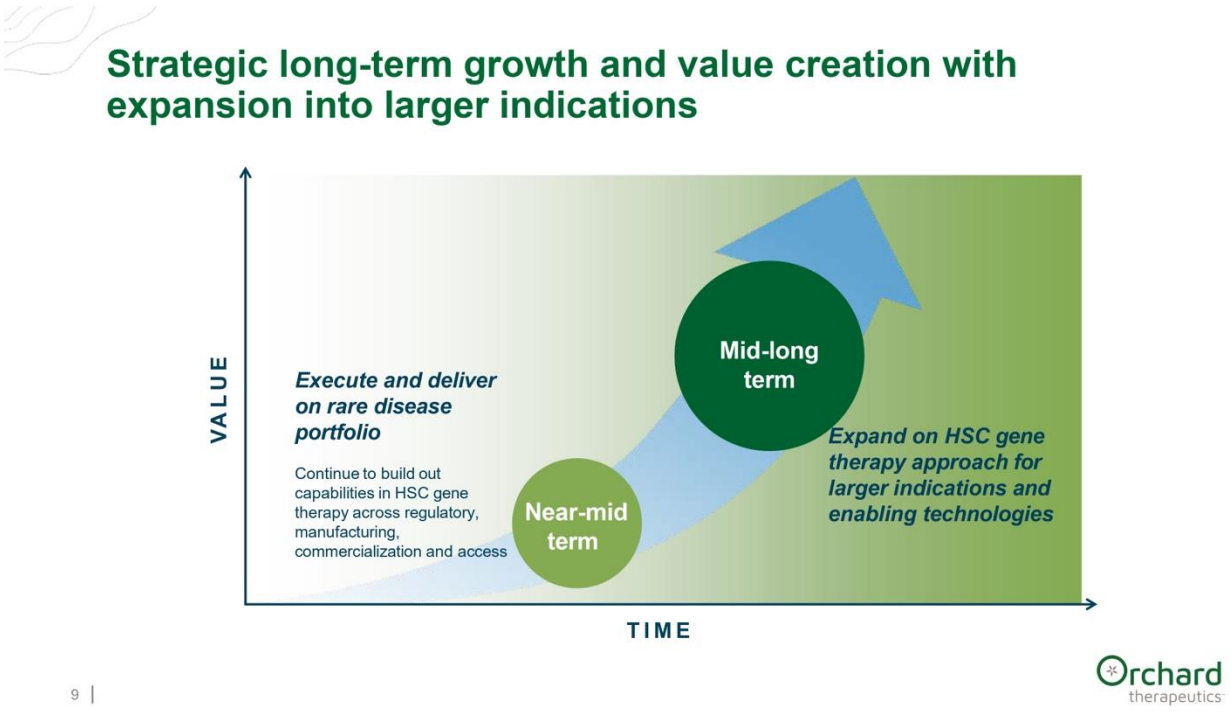
Today, we're going to focus on a few key areas. Firstly, we'll take a deeper look at the HSC gene therapy approach pioneered by Orchard Therapeutics. Next, we'll dive into our late-stage pipeline aimed at addressing devastating rare neurometabolic diseases. Finally, we'll share our plans to establish Orchard and Kyowa Kirin as a global gene therapy leader. Please, could we go to the next slide?

We aspire to end the devastation caused by genetic and other severe diseases through the curative potential of HSC gene therapy.

Orchard was founded in 2015 to end the devastation caused by severe genetic diseases through the curative potential of HSC gene therapy. The family photos on this slide help illustrate the potential impact of our approach. This is the story of Connie and Joe. You can see Connie, the little girl on the stretcher was born with a condition called metachromatic leukodystrophy or MLD. This is a devastating neurodegenerative disease where babies initially develop normally, but after a few years, they start to lose the ability to walk, to talk, and to interact with the world around them. Until Orchard's gene therapy, there was no treatment available for these children, just supportive and end-of-life care. By the time Connie was diagnosed, unfortunately, the disease had progressed too far for Connie to benefit from gene therapy. And tragically, since this photo was taken, our Connie has since passed away.

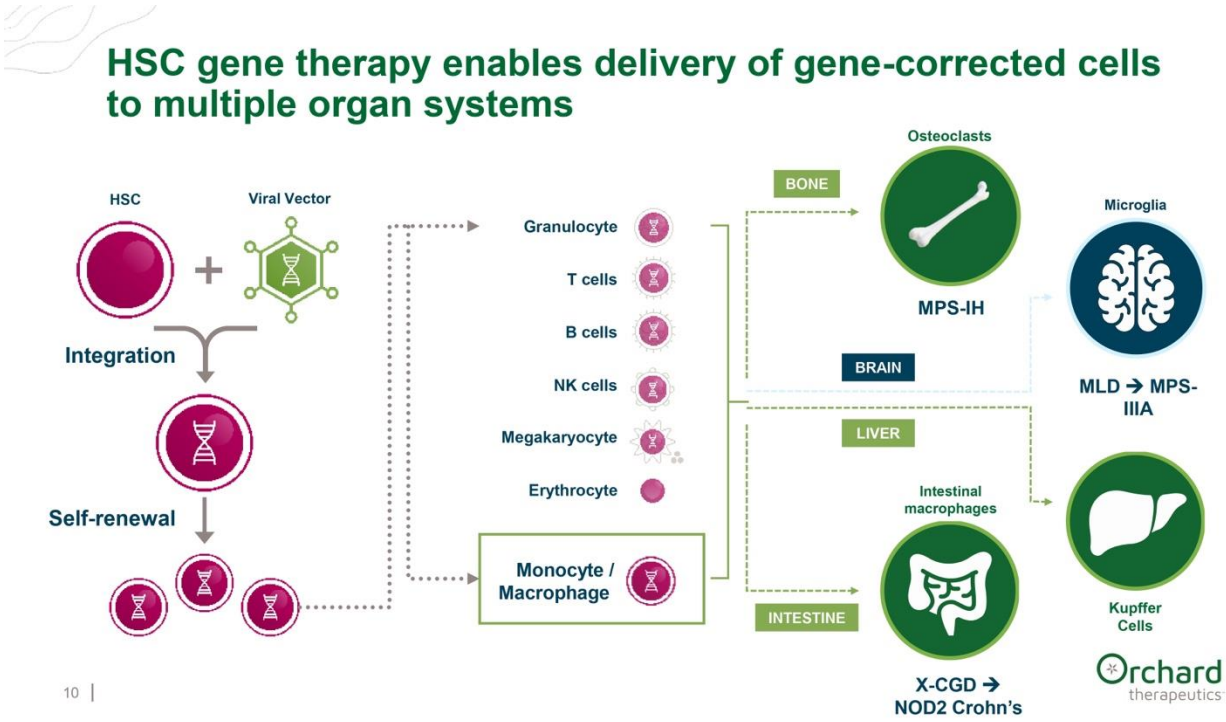
Her brother Joe sitting on the wall also has the same disease. He also has MLD. He has the same genetic mutation as Connie. He was diagnosed early because of Connie's illness, and he was able to receive HSC gene therapy as a toddler. The photo on the right is him five years later, five years later after a single administration of his gene-modified cells. And to this day, he continues to lead an essentially normal life, where he attends school, participates in sports, and plays with his friends with no signs or symptoms of the disease. And this underscores the impact of our approach to potentially transform the lives of patients.

Let's go to slide eight. Since our founding, Orchard has grown considerably. We've built a global presence with laboratories and offices at our London headquarters. We also have an established presence in Boston, comprising commercial, financial, and other supporting functions. Today, Orchard has approximately 170 employees with around 100 people in the UK, 40 in the US, and the remaining in other European countries where we have an established presence.



Please, slide nine. Thank you. We have a clear vision for the near and longer-term growth of Orchard. Over the near term, we will continue to execute and deliver on our rare disease portfolio by growing revenue in Europe and in the US, while we identify areas for geographic expansion and advance our next-in-line programs

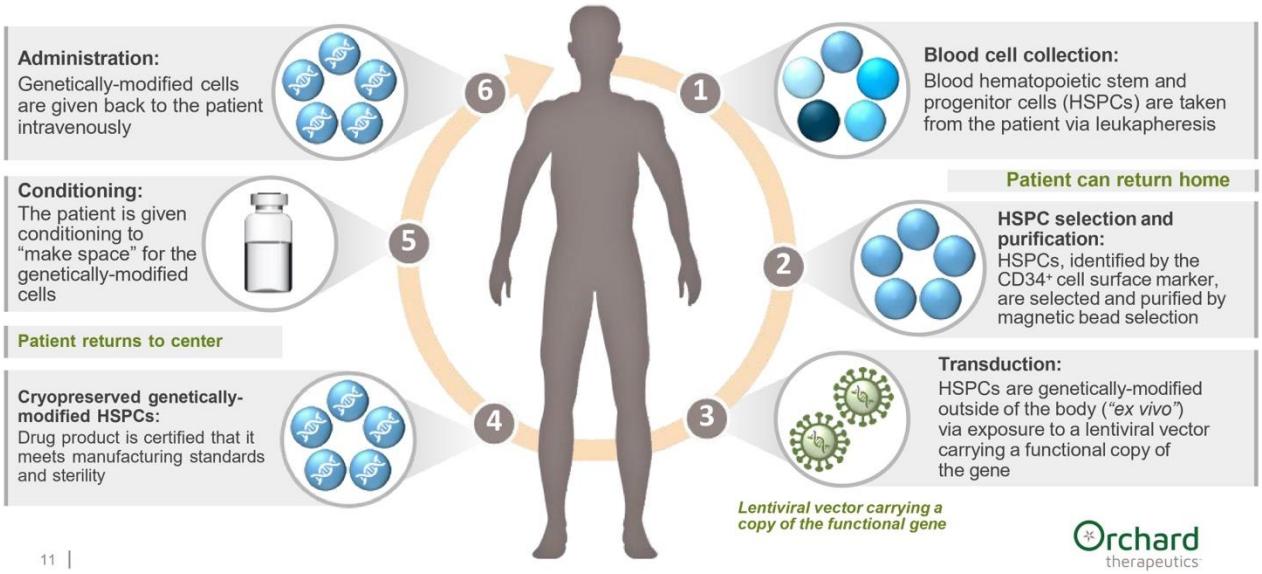
towards regulatory submissions. But we believe the HSC gene therapy approach has even greater potential, and we're working to apply our approach in more prevalent conditions, which will drive longer-term growth and sustainability.



Next slide, please. Now, let's talk a little bit about the science that makes our vision possible. In the approach pioneered by Orchard Therapeutics, we use a patient's own hematopoietic stem cells, which possess three characteristics that make them an ideal platform to address a number of genetic diseases, severe genetic diseases. First, we insert a working or a functional copy of the 40-gene into the cells using a lentiviral vector. The lentiviral vector integrates the therapeutic gene into the genome of the target cell. Essentially, this means it is hardwired into the genome so that when the cell divides, the genetic information is passed on to its progeny, which is a key differentiator compared to viral vectors used in other types of gene therapies.

Another important feature is that these gene-modified cells can self-renew. And it's through this process of integration and self-renewal that we can have a durable and long-term effect to potentially correct the underlying cause of disease with a single one-time treatment. Finally, HSCs can differentiate into multiple cell types, which enables us to address many different diseases. For example, HSCs give rise to cell types for monocytes or macrophages that can naturally migrate into many different tissues and organs, including across the blood-brain barrier to deliver therapeutic proteins and enzymes to the central nervous system. And this is why we can treat severe neurometabolic conditions like MLD and potentially, more prevalent neurodegenerative conditions. It also gives us the opportunity to address diseases of the gut and additional organ systems, not easily druggable using other therapeutic modalities.

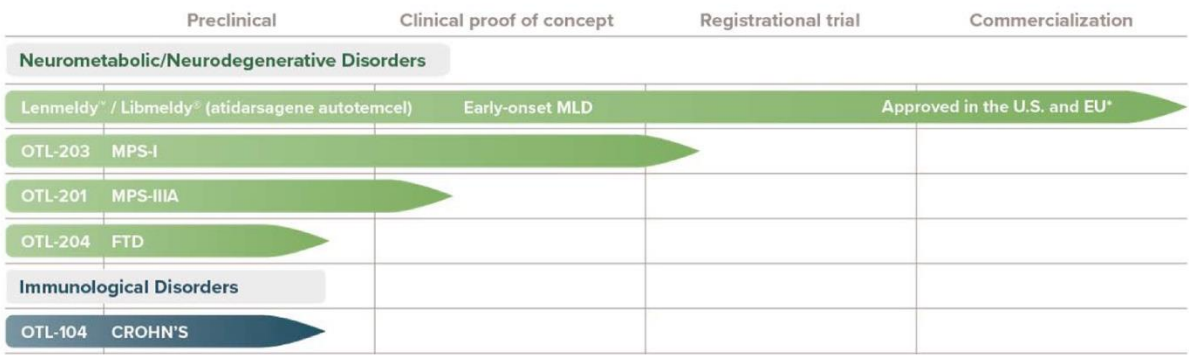
Autologous *ex vivo* gene therapy approach



Orchard therapeutics

Next slide, please. Here, we are outlined the treatment process. HSCs are first taken from the patient's bloodstream, using a process called apheresis, and then sent to our centralized manufacturing center in Milan in Italy. There, the cells are isolated and transduced with a virus that carries the new gene, creating gene-modified cells. The gene-corrected cells are then frozen or cryopreserved. They're tested for quality, released, and then shipped back to the treatment center where the patient is located. The patient undergoes chemotherapy before the modified cells are reinfused. On average, this process takes approximately five weeks from cell collection to reinfusion with some variability based on the treatment schedule. An important aspect is that cells are transported rather than the patient, enabling treatment at multiple sites in Europe and soon in the US, while cell manufacturing continues to occur at a single location.

Advancing a pipeline to address serious genetic diseases



*Lenmeldy™ is approved in the U.S. for the treatment of children with pre-symptomatic late infantile, pre-symptomatic early juvenile, or early symptomatic early juvenile metachromatic leukodystrophy (MLD). Libmeldy® is approved in the European Union, UK, Iceland, Switzerland, Liechtenstein and Norway.

Orchard therapeutics

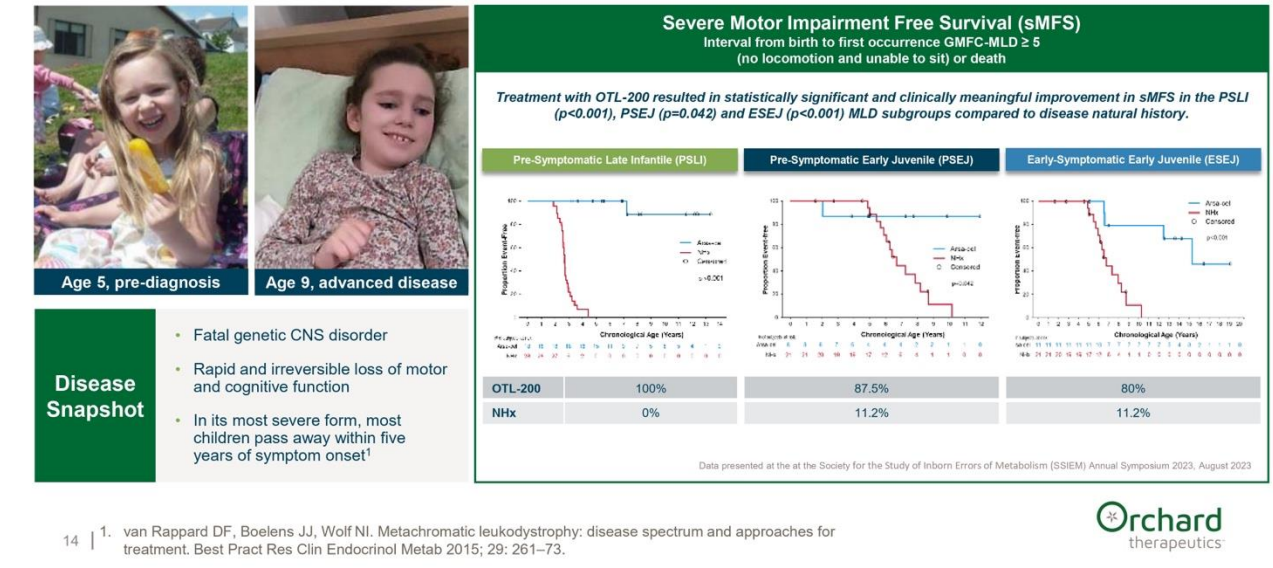
Let's go to the next slide. On this slide, we provide an overview of Orchard's portfolio and pipeline, which comprises Lenmeldy recently approved by the US FDA, and known as Libmeldy in Europe, where it has been successfully commercialized. We are also advancing two next-in-line programs for the treatment of another group of rare neurometabolic diseases, OTL-203 for MPS-I Hurler syndrome and OTL-201 or MPS-IIIA, also known a Sanfilippo syndrome type A. Earlier in our research pipeline, we are also exploring the potential of our approach to address genetic subsets of a common form of dementia and Crohn's disease. We're also endeavoring to create various functional cells using our approach in collaboration with Kyowa Kirin.

Strong operational execution already in 2024

Orchard therapeutics

Let's go to slide 13. Before we dive deeper into our late-stage neurometabolic pipeline, let's look at the operational success we've already achieved in 2024 across our portfolio. Importantly, last month, Lenmeldy was approved by the US FDA for the treatment of children with pre-symptomatic, late infantile, pre-symptomatic early juvenile or early symptomatic early juvenile, collectively referred to as early onset MLD. This momentous occasion was celebrated by the community as it opens up tremendous new possibilities for eligible children in the US. In anticipation of this milestone, we have already laid the foundation for launch success by building out our US field team. In addition, we continue to identify treatment-eligible patients in Europe through newborn screening and other disease education efforts, and we are on track to grow significantly YoY revenue in 2024.

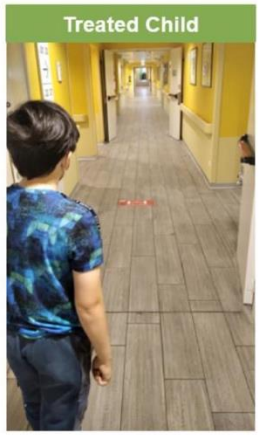
Moreover, we continue to execute on our geographic expansion following our agreement with the Beneluxa initiative on pharmaceutical policy, which enables reimbursed access to Libmeldy in several member countries, including Belgium, the Netherlands, and Ireland. Finally, we have successfully randomized the first patients in a registrational trial evaluating the efficacy and safety of OTL-203, our investigational HSC gene therapy in patients with MPS-I Hurler syndrome. This trial compares treatment with OTL-203 to the standard of care, which is allogeneic hematopoietic stem cell transplant, and this is expected to enroll 40 patients at sites across the US and in Europe.



Next slide, please. On this slide, we outlined the impact as observed in our clinical development program for Libmeldy, which is supported by more than 12 years of follow-up in the earliest treated patients. The graph on the left shows treatment with Lenmeldy significantly extended overall survival and resulted in the preservation of motor function and cognitive skills in most late infantile MLD patients past ages of which untreated patients share severe cognitive and motor impairment. These results are in the most severe form of the disease for which untreated patients typically pass away within five years of symptom onset. Lenmeldy also resulted in the preservation of motor function and cognitive skills in some early juvenile MLD patients, which is not expected when compared to untreated patients. But these are just the graphs.

All 7 surviving PSEJ patients maintained the ability to walk with normal performance for age (GMFC-MLD Level 0)

GMFC-MLD Level 6
3 years post-onset
8 years of age

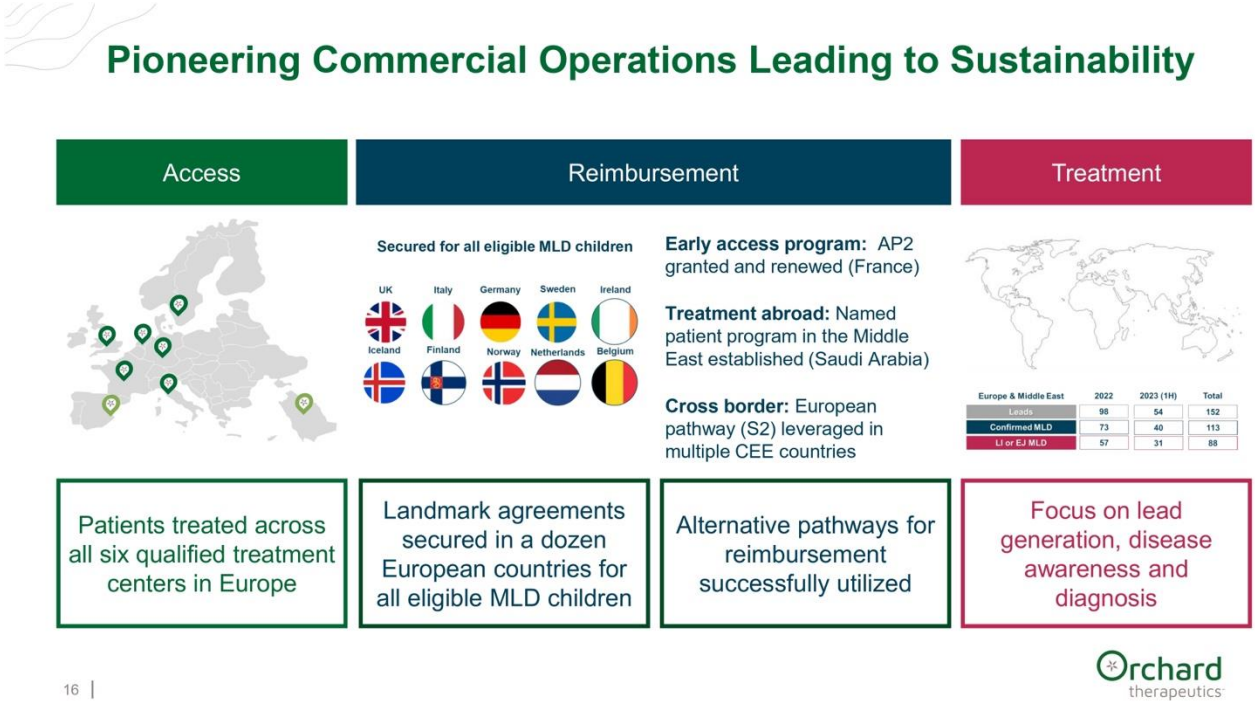


GMFC-MLD Level 0
8 years post-GT
12 years of age

Orchard therapeutics

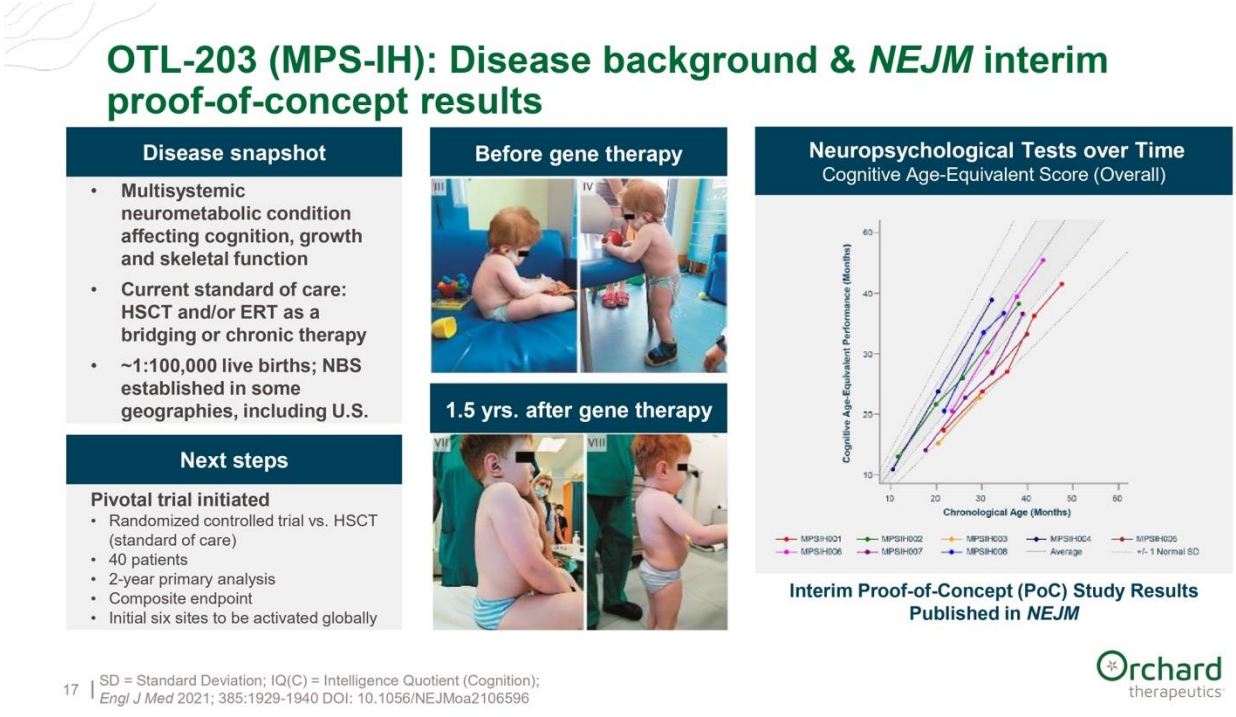
Let's go to slide 15. Here, in this slide, we actually see the drastically contrasting outcomes of two children with MLD and remember, these are siblings. So first video, please. So this is a video of Connie, who I mentioned at the beginning of the presentation, and was unfortunately diagnosed too late for treatment. She lost the ability to walk and move independently. And as we see, she's unable to sit up unassisted. She requires tube feeding. And sadly, she passed away not long after this video was taken.

Let's go to the second slide. This is her brother. He was pre-symptomatic early juvenile MLD, but he was treated with our gene therapy. This is him now eight years post-treatment, and he maintains the ability to run down the hallway and he can play with his friends, and it illustrates the potentially transformative impact of early intervention with gene therapy.



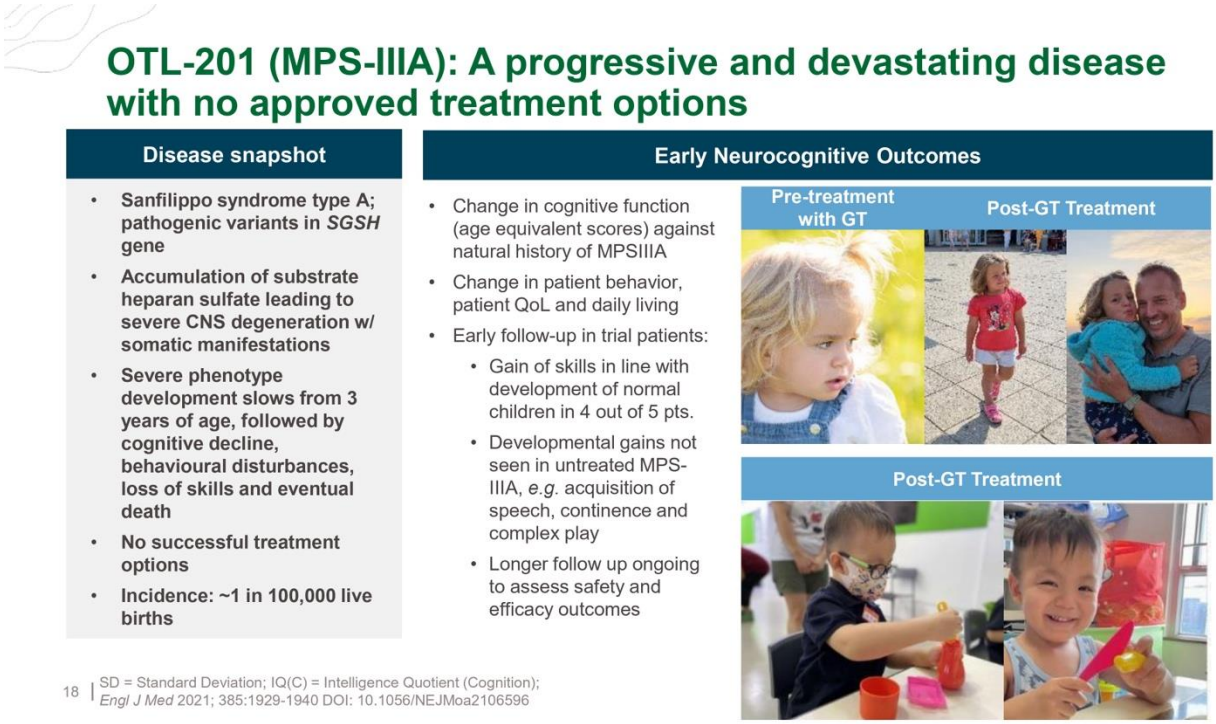
Let's go to slide 16. But the innovation we're delivering is not just limited to the clinical setting. With the approval in Europe and now in the US, our commercial and medical teams continue to work with members of the MLD KOL and patient community to identify, refer, and support treatment of eligible patients. We have made significant progress obtaining reimbursed access to Libmeldy in a dozen European countries and territories, including most recently in Beneluxa. Discussions are also ongoing in additional European countries to broaden reimbursement. In addition, we have been successful in expanding our commercial reach geographically through early access mechanisms in France, cross-border pathways in Eastern Europe, and treatment abroad programs in the Middle East, which are important growth drivers during this relatively early stage of our launch.

To date, we have now treated patients from six different countries on a commercial basis at all six qualified centers in Europe. As with many rare life-threatening pediatric diseases, early detection and diagnosis are key to ensuring the best possible outcome for patients. And Orchard Therapeutics supports efforts to expand newborn screening for diseases like MLD, which meet the Wilson and Jungner criteria. Currently, 10 prospective studies for MLD are active throughout the US, Europe, and the Middle East. With approximately 275,000 newborns screened as of March 31. The data from these studies provide critical evidence to support applications for universe screening of MLD in the US and around the world. Utilizing results from such studies, a multi-state older panel working group is finalizing a nomination to add MLD to the US recommended uniform screening panel or RUSP, a national guideline comprising a list of medical conditions for which the federal government recommends all newborns receive screening. States using RUSP to help them decide which conditions to include in their newborn screening panels. Based on current timelines and assumptions, Orchard Therapeutics expects the nomination will be submitted in mid-year 2024.

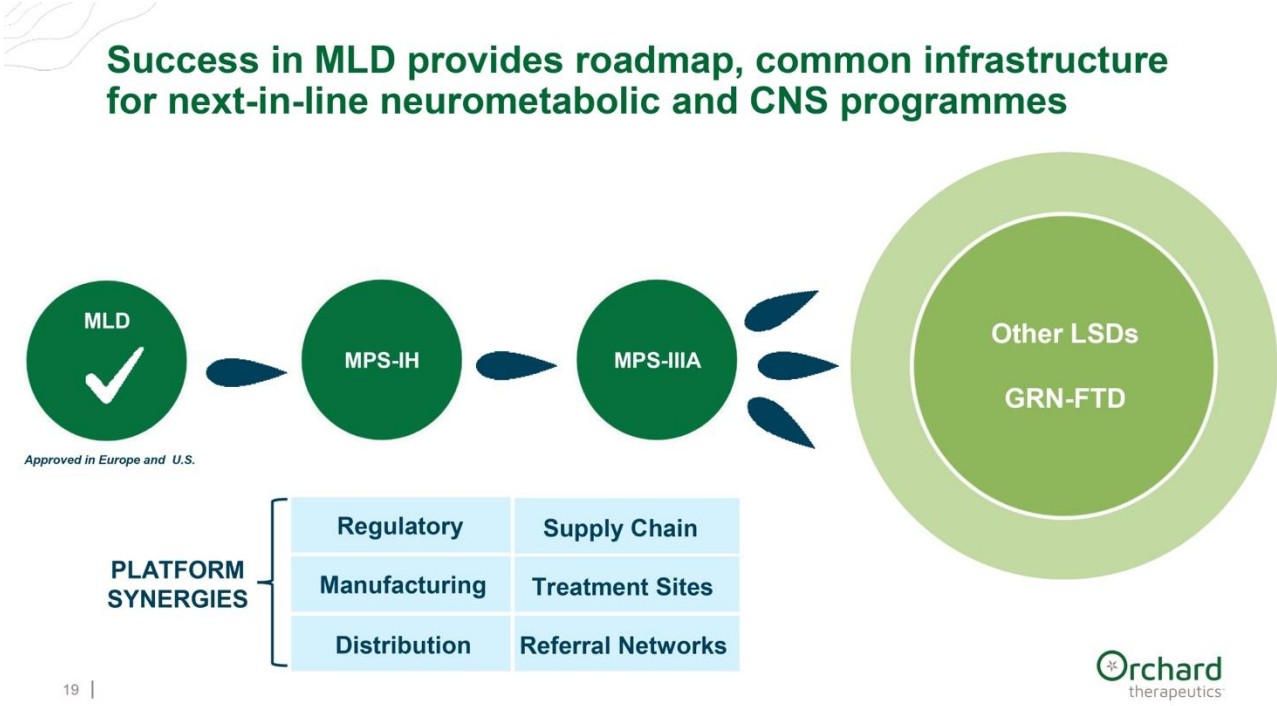


Next slide, please. Let's now turn our focus to Orchard's next-in-line programs for MPS, which is another group of rare, severe, multisystemic neurometabolic diseases. On this slide, we outline interim proof-of-concept results for OTL-203, an investigational HSC gene therapy in patients with MPS-I Hurler syndrome. MPS-I is a rare inherited neurometabolic disease caused by a deficiency of the IDUA lysosomal enzyme, which results in the accumulation of toxic levels of polysaccharides known as glycosaminoglycans, or GAGs, in multiple organs. Similar to MLD, MPS-I is estimated to occur globally in one in 100,000 live births. Approximately 60% of children born with MPS-I have the most severe subtype, MPS-IH, also called Hurler syndrome, and they rarely live past the age of 10 when untreated. Current treatment options for MPS-IH include allogeneic hematopoietic stem cell transplant and enzyme replacement therapy, both of which have significant limitations.

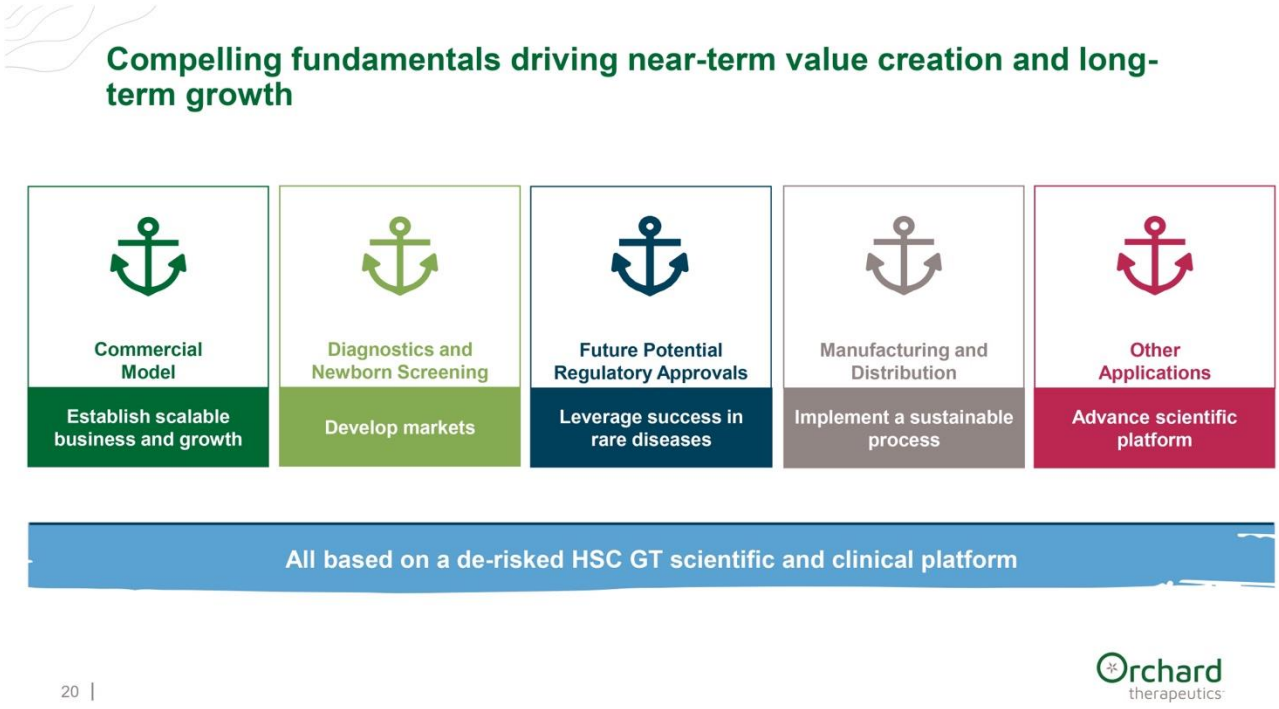
Interim results for our proof-of-concept study published in the New England Journal of Medicine showed all patients have super physiological IDUA enzyme activity with an associated sustained decrease in GAG levels and stable cognitive performance post-treatment. In addition, all treated children had progressed along expected growth percentiles of healthy children and exhibited longitudinal growth that was considered within the normal range adjusted for age and gender. In subsequent follow-up, study investigators have observed progressive acquisition of fine and gross motor skills as well as evidence of continued growth within normal range and improvements in skeletal health with a median follow-up of 3.78 years as of May 2023, the last presentation of updated results. Based on the strength of these data, we have initiated a registrational trial evaluating the efficacy and safety of OTL-203 compared to the standard of care with allogeneic hematopoietic stem cell transplant. The trial is expected to enroll 40 MPS-IH patients at sites across the US and Europe. Several enrolled patients have already been randomized and are beginning the treatment process.



Let's go to slide 18. We are also working on an investigational HSC gene therapy to address another form of MPS known as Sanfilippo syndrome type A. Children with MPS-IIIA are born with a mutation in the SGSH gene, which when healthy, helps the body breakdown the sugar molecule, heparan sulfate. The buildup of heparan sulfate in the brain and in other tissues leads to intellectual disability and the loss of motor function. MPS-IIIA represents another significant medical need, given there are no approved therapies and treatment with allogeneic HSCT has not been shown to be effective for this patient population. Interim results from an ongoing proof-of-concept study show that 4 out of 5 patients continue to gain cognitive skills in line with development in healthy children. Two patients were able to progress to a more advanced cognitive test known as the Kaufman scale, which has not been observed in natural history patients due to progression of disease and cognitive impairment. Evidence of developmental gains include the acquisition of speech, continence, and complex play requiring concentration, which are not seen in untreated MPS-IIIA natural history patients when this was also observed in treated patients. Patients enrolled in the ongoing proof-of-concept study will be followed for a minimum of three years, during which time we will continue to report additional biochemical and clinical outcomes.



Let's go to slide 19. Together, our pipeline continues to provide multiple opportunities for near-term data and inflection points. Moreover, they are all based on the same HSC gene therapy platform as Lenmeldy, providing a road map and common infrastructure to help us achieve scientific, clinical, regulatory, and commercial success.

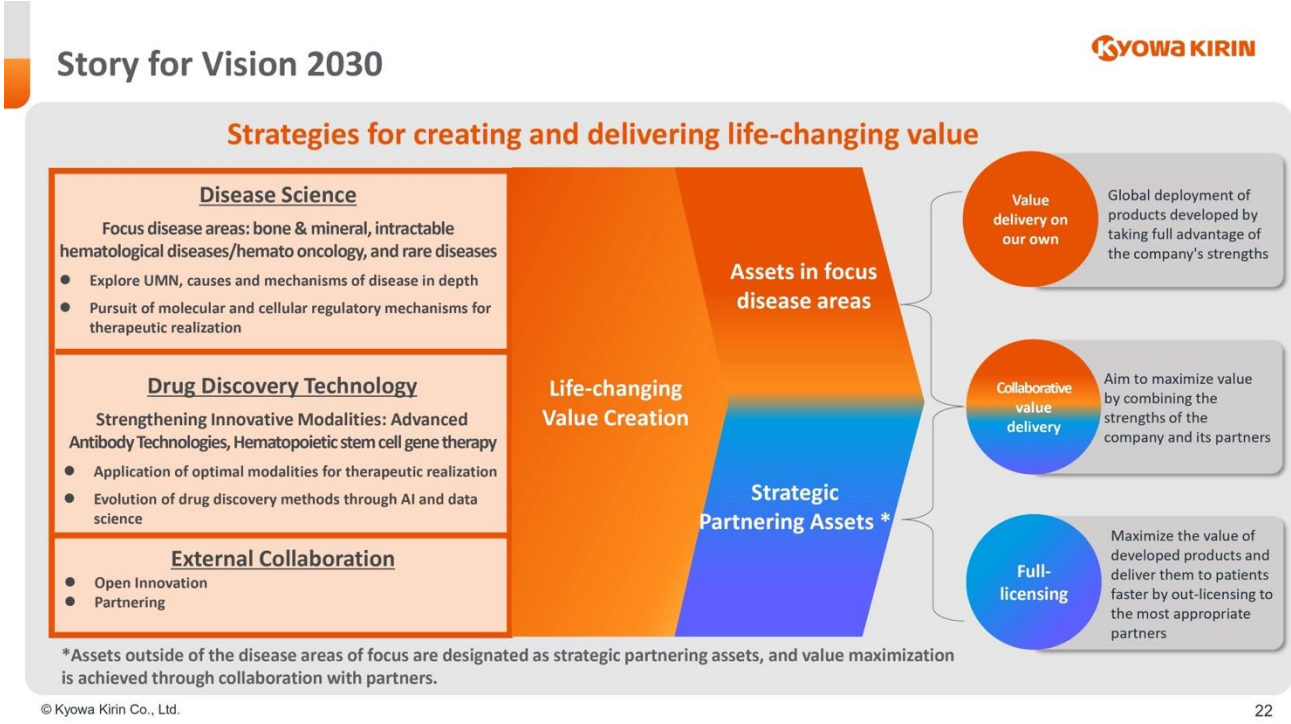


Next slide, please. We will close with the strategic anchors that will deliver value in the near term and position us for long-term growth. Following US approval, we will now work with our colleagues at Kyowa Kirin to determine geographic expansion plans for MLD, and we are on the path to further generate data that would support regulatory submissions in MPS-IH and MPS-IIIA. In parallel, we are advancing our commercial

infrastructure to identify more patients and continue to nurture a successful and sustainable commercial model. Looking ahead, we will apply our approach in more prevalent diseases where we believe HSC gene therapy has the potential to be scientifically and clinically differentiated.

Thank you for your attention. I will now turn the call back to Miyamoto-san to talk about how we are building the world's leading gene therapy company. Thank you.

Nakamura: Thank you for the great presentation, Bobby. Now, once again, Miyamoto would like to speak to you.



Miyamoto: Once again, I would like to share with you this slide. As you saw in the presentation of Orchard, at our acquisition of Orchard, we'll cover all of our focused therapeutic areas from R&D to market launch. In addition, it will make a deep contribution to the shift to innovative modalities in drug discovery technology and will make a significant contribution to our mid- to long-term growth.

Future HSC-GT related business

KYOWA KIRIN

Expansion of Lenmeldy™/Libmeldy® usage in EU and US

- US approval on March 18, 2024, followed by launch
- Ten prospective NBS* studies for MLD are active throughout the U.S., Europe and the Middle East, w/ ~275k newborns screened as of 31 March
- Projected revenue for FY2024: 4.5 billion yen

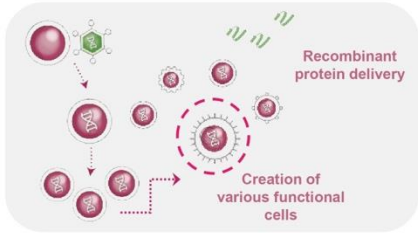
* Newborn screening

Steady progress in the current development pipeline

Code	Target disease	Status
OTL-203	MPS-IH (Hurler Syndrome)	Registrational study ongoing
OTL-201	MPS-IIIA (Sanfilippo Syndrome type A)	PoC study ongoing Planning for potential registrational study

Expanding into New Drug Discovery Technologies

- Fusion of our technology with HSC-GT: Recombinant protein delivery to sites typically difficult to reach
- Creation of functional cells utilizing the pluripotency of HSCs



Aiming for the successful creation and delivery of life-changing value through the integration of both companies' strengths

Finally, I would like to present our future plans. First of all, Lenmeldy/Libmeldy received the FDA approval last month and is now to be launched in the US. And as Bobby explained to you, currently, in the US, Europe, and the Middle East, 10 prospective newborn screening trials for MLD are ongoing. And as of the end of March this year, approximately 275,000 newborns have been screened. We aim to achieve revenue growth of JPY4.5 billion in this fiscal year. We will continue to study optimal methods to expand newborn screening geographically. We will also steadily advance the clinical trials of OTL-203 and OTL-201, either in progress or in preparation. This will further expand the potential of hematopoietic stem cell gene therapy.

In addition, we will work to realize new values by integrating Orchard's HSC-GT with our drug discovery technology. This is just one example at this point in time, but we are considering developments such as utilizing the pluripotency of hematopoietic stem cells for delivering recombinant proteins to normally hard-to-reach areas and for creating various types of functional cells. In the future, we will aim to generate life-changing values, not only through the progress of HSC-GT products, but also by integrating the strengths of both companies.

This concludes today's presentation.

Question & Answer

Moderator [M]: Now I would like to start taking questions.

Yamaguchi [Q]: Thank you. This is Yamaguchi from Citigroup. My first question. Orchard Therapeutics in MLD and some other technologies already commercialized. And I understand that the treatment is very effective. But the HSC technology is also done by other companies as well, Orchard is not the only company. So how does Orchard technology differ from other companies, technology- or manufacturing- or even patent-wise, can you please explain? That's my first question.

Miyamoto [M]: Thank you very much, Mr. Yamaguchi. I think Bobby can take this question. Bobby, the floor is yours.

Gaspar [A]*: Yeah. Thank you very much. So I think the first thing to say is there are not many companies that are working on the HSC gene therapy technology. So really, there is a company called Bluebird bio that has programs in beta thalassemia, sickle cell, and another different leukodystrophy called Adrenoleukodystrophy. There's a company called Rocket Therapeutics that also has HSC gene therapy for, again, different conditions. So although the technology is the same, the indications that we are working on are very different. And we have focused on our indications such as MLD, MPS-I, MPS-IIIA, and our earlier pipeline because we feel that there are the areas of greatest unmet need and where there are other very limited or no treatment options. So really, the differentiation is not on the technology per se, but on the indications. And we believe we are targeting some very important indications with a high level of unmet need.

In terms of the patents associated with this technology, the technology has evolved over a long period of time, and there are no technical patents that are associated. However, we do have a significant know-how that is related to Orchard. There is also, because these are rare diseases, there is orphan drug exclusivity that is granted by both the FDA and by the EMA as well and which gives us exclusive commercialization, especially for these pediatric diseases over a number of years. Also, I think because of the technicalities, the know-how, the time required, and the infrastructure required to develop these therapies and the length of the clinical trials, then it's very, very unlikely that any competitor will start to develop a program, for example, Lenmeldy/Libmeldy using the same technology.

Yamaguchi [Q]: Thank you very much. My second question is about your pipeline.

For OTL-203, OTL-201, I understand pretty well. But I think there are still many other diseases with unme medical needs actually in lysosomal storage disease. I understand there are limitations due to resources, but do you plan to expand HSC pipeline for LSD in the future? And if so, specifically, after Sanfilippo A, which ones do you intend to include in terms of LSD?

Miyamoto [M]: Thank you. I think I would like to ask Bobby first for his answer.

Gaspar [A]*: Okay. Thank you very much. And that's a very exciting question. As you can imagine, we've been able to demonstrate some really transformative changes in MLD. We're seeing it already in MPS-I. We're seeing it MPS-IIIA, using that same HSC gene therapy approach. And you're absolutely right. There is the potential to be able to take this to other lysosomal storage diseases where we understand the mechanism and where our HSC gene therapy has a unique ability to address the CNS and other organ systems.

Now, as a small biotech with limited resources previously, we had to be very, very focused on these programs we took forward. And so we had to confine ourselves to those three programs that we talked about. But I agree with you, there is the potential to expand this beyond these three to other lysosomal storage diseases.

And of course, I think this is one of the reasons why Kyowa Kirin and Miyamoto-san saw the potential of Orchard, but we could expand beyond what we currently have. And this is the subject of discussions internally. And so we can provide more news in the future.

Miyamoto [A]: Thank you, Bobby. And I would like to add. As Bobby has just explained, we believe that this treatment has great potential. And as you said, Mr. Yamaguchi, other LSDs could be targets as well. And the researchers already have a long list. So going forward, not only in research, but also development and commercial side from both sides, the teams need to get together and discuss as Kyowa Kirin team as a whole and decide to prioritize and push the program forward. As we mentioned in the R&D IR meeting at the end of last year, we can promote more quickly to clinical trials than the drug discovery in the past, with this technology. So we will try to run this quickly, and determine targets.

Yamaguchi [M]: Thank you. That's all for me.

Muraoka [Q]: Thank you. Libmeldy/Lenmeldy, concerning the potential of these products, I have a question. In the past, USD2.5 million was the assumption, and I think there was a chart shared with us, we're talking about USD1 billion or 500 million. And the price in the US this time is USD 4.25 million. I think, just simply speaking, double. So meaning that the expectation is now coming very close to USD2 billion. Is this interpretation correct? Or can you give us some supplemental explanation?

Miyamoto [A]: Thank you very much for your question. So I will ask Bobby later on to give more details. But yes, the unit price in the US is at a relatively high level. But overall, patient volumes and the actual commercial reach, well, I think those need to be taken into consideration. And I would like Bobby to explain how he thinks now.

Gaspar [A]*: Thank you, Miyamoto-san. And thank you for the question. I think when it comes to pricing, we have to concentrate and look at the value of the medicine and what the value of the medicine affords. Remember, in MLD, this is a severe devastating disease. These kids are born normally, but then lose all faculties and they will invariably die in the first decade or the second decade of life. And there is no treatment available, nothing at all, no disease-modifying therapies are available for these children. The disease has an enormous effect, not just on the child, but on the family, where the family often, because of 24-hour care that has to be provided, one parent has to stop working. There have to be changes to the house. The health care system is significantly impacted economically by the burden of this disease as children go in and out of hospital the whole time. And remember, with a single administration of gene-modified cells, we are taking away all of the burden, both emotional and economic burden, that is associated with the disease, not just for the child, but for the whole ecosystem around the child as well. And that is the value of this medicine.

Now independently to us, this medicine has been evaluated by independent bodies such as NICE, an HTA assessment body in the UK, and they gave Libmeldy more QALYs, more quality-adjusted life years than any other medicine that they have evaluated previously. And also ISO, which is another independent body in the US, when they evaluated Lenmeldy, as it is in the US, they recommended a price where it would have value that was higher than any other price that they had given for a previous medicine that they had evaluated. And they said it would be a value up to USD3.94 million. So you can see that the value of the medicine is extremely high because of the indication, because of the unmet need, the lack of any treatment so far and the value that this medicine affords.

Miyamoto [A]: And Bobby, Muraoka-san's question is, I think probably we would like to hear from you more about the total potential of the market. And well, previously, the unit price assumed was USD2.5 million. But now it's USD4.25 million unit price in the US then the market price is going to be much larger. Is that right? What is your global expectation of the total market?

Gaspar [A]*: Yeah. This is a disease where we have to find patients early. So at the moment, in the absence of newborn screening, it is finding children who are in the very early stages of disease in order to be treated. And also younger siblings of affected children who are pre-symptomatic. And so that is the population that we'll treat. Now, having got approval in the EU and in the US, this year, we anticipate approximately 14 children being treated with revenue of approximately USD35 million between the US and in the EU. But over time, as we increase awareness and importantly, as we increase newborn screening, we can expect that revenue to grow YoY. And ultimately, if we get to newborn screening, we believe there are approximately 40 children in the US, which would be eligible for treatment, another 50 or so children in Europe that would be eligible for treatment. So if you just take the number in the EU and in the US, you could imagine there'd be approximately 100 children that would be eligible for treatment. And that, with an average figure of USD3 million, would give you USD300 million as a yearly revenue. That's just in the EU and in the US. Now obviously, with the infrastructure that Kyowa Kirin has, we can think about geographic expansion, and we can think about going to other markets as well, which can capture greater revenue percentage.

Miyamoto [A]: Thank you very much, Bobby. So Muraoka-san, globally, if we can conduct newborn screening all across the globe, then it will be a very big number. But of course, it is not easy to achieve. So at least the EU and US, if we cover these two regions, then we'll be able to probably capture about 100 patients. That's the explanation. Thank you very much.

Muraoka [Q]: Thank you. And just let me assure you with Miyamoto-san, what we said USD3 billion that's probably, I think, the average of [USD]2.5 [million] and [USD]4.25 [million]. Is that right?

Gaspar [A]*: Correct. That's correct. That was an average figure, yeah, between the US price and the EU price.

Muraoka [Q]: Understood. Thank you very much. Another question I have. MLD treatment, after getting screening and let's say you have 40 patients or 50 patients each in a year. And this is a great treatment. And then even if that patient is eligible, are there any cases that a patient will not choose to get this treatment? Are there any such cases? And if so, what are the specific background conditions?

Miyamoto [A]: So thank you for your question. Are you asking that even diagnosis is given, then some patients may not receive the treatment? Or do you have any such patients who don't receive this HSC gene therapy? Or if any, what are those specific patients? What are the conditions of them? Bobby, please.

Gaspar [A]*: Yeah. So currently, the eligibility criteria are for late infantile patients and also the early juvenile patients. And in the early juvenile category, we can treat early symptomatic early juvenile patients. And so the only patients that fall outside of that are those patients that are too advanced to access therapy. And that's why early diagnosis is very important, and that's why we're working towards newborn screening. Now, when we get into the era of newborn screening, we anticipate that all patients will be identified. At birth, they'd be pre-symptomatic and then they would be eligible for Lenmeldy or Libmeldy.

I can't see a scenario where a family would refuse treatment or would not accept treatment because there's nothing else out there for this disease. There is no disease-modifying therapy. There is no other therapy available. It's only supportive or palliative care. So I anticipate that the vast majority of families would choose to be treated with gene therapy. Now obviously, there may be cultural or personal issues that may prevent some families from them wanting to undergo treatment. But that really is going to be a real minority. And the vast majority of families when faced with this diagnosis, will want a potentially life-saving treatment for their child.

Muraoka [M]: Understood. It's very clear. Thank you very much. Thank you. That's all.

Sakai [Q]: Thank you. I'm Sakai with UBS. I have two questions. MLD newborn screening. At what stage is Europe and the United States in terms of mandating the newborn screening? And if you do the test, I

understand this is gene panel genetic disease. So at the time of screening, I should think that most of the children will be diagnosed. Is that correct? Is that my correct understanding? Thank you.

MIyamoto [M]: Bobby, please take this question.

Gaspar [A]*: Okay. Thank you. Very happy to do that. So newborn screening has been a great passion of mine, both as a physician and now through Orchard. It is the way to be able to identify all of these patients early enough to be able to access therapy. Now there are very important criteria for newborn screening. And you can't have newborn screening when you don't have a therapy because why would you identify a child if you can't provide a treatment? So up until this point, there has been very little interest in newborn screening for MLD because there was no therapy available. But now that there is a therapy available, the physician community, the patient community has been very, very interested in putting forward newborn screening onto country panels.

And so we have been working with the stakeholders. We have been providing information, we've been providing support in order to initiate pilot studies. And from 2022 onwards, we have to now–so over a two-year period—we've screened through multiple different pilot studies over 275,000 babies across Germany, Belgium, Italy, France and other pilot studies, US as well. And in that period, we've actually identified five babies with MLD. 275,000 screened, five babies with MLD identified. And four of those babies with MLD have either received gene therapy or about to receive gene therapy as well.

So you can see that through newborn screening, we're already identifying children. The incidence is probably higher than we anticipated. We thought it was going to be one in 100,000. The current figures suggest something in the region of 50,000. But obviously, we'll have to screen more babies before we find exactly the true number. But what this will do is provide the information from these pilot studies to take to country-level agencies in order to implement national screening. So for example, in Germany, where the largest pilots have been undertaken, we'll be putting forward an application for national screening for MLD. And so again, in Europe, we expect to have a number of countries that will be screening universally for MLD. In fact, I think Norway will be the first country that will start screening all its babies for MLD. And as I say, there's an application that is going to Germany.

In the US, it's slightly different. And of course, we can only start that process now because there is an approved treatment now available in the US. We'll be putting forward an application to the RUSP, that's the Recommended Uniform Screening Panel, that is a federal body, that if accepted, will recommend that all states in the US should screen for MLD. Now, even before that, some states can pass legislation in order to screen for MLD. And so for example, the state of Illinois has already passed state legislation that was through KOL and patient advocacy that that state, Illinois, should screen for MLD. And we anticipate that maybe towards the end of this year, all babies in Illinois will be screened for MLD. There are also potentially state pilots where there will be a pilot study that we conducted statewide where screening can start. So you can see that even in advance of a RUSP nomination, all babies in a number of states could be screened for MLD. So that is where we— I mean, obviously, this will take some time, but there's a lot of impetus, there's a lot of interest, and there's a lot of momentum in establishing screening for MLD both in Europe and in the US.

The final, sorry, the second part of your question was about the type of test that was carried out. There's a number of tiers. The first tier is looking at the rise in sulfatides that could be done by mass spectrometry. Then there's an intermediate step, which looks at the level of the enzyme activity, which again can be done by mass spectrometry. But in order to make the definitive diagnosis, you have to do a genetic test. So usually, the first test is available after a few days and then the further testing before we get to confirmation will take a couple of weeks.

Sakai [Q]: I understand. Thank you. I have a follow-up question. So 40 in the US and 50 in the EU, newborn babies. I think you will see this number every year with MLD. And once the screening is widely spread, do you

think these two numbers, 40 and 50, will increase over time? Where do these numbers come from? What is the assumption behind numbers 40 and 50 for the US and Europe?

Miyamoto [M]: Thank you. Bobby, could you answer this question as well?

Gaspar [A]*: Yeah, yeah. No, I can answer that question. Firstly, the numbers come from a presumed incidence of the disease. And so we've used historical literature up until now. And so if you look at the historical literature, the incidence of MLD ranges anything from one in 50,000 to one in 250,000. And that's from different countries, different studies, and they're all retrospective studies. And so we've taken an average of one in 100,000 as the incidence figure. So that's where it's kind of the median of the various different studies lands at. So we've taken one in 100,000. Now, if you take one in 100,000, there are approximately four million newborns in the US per year and an incidence of one in 100,000 gives you 40 newborns per year with MLD. And similarly, there are approximately 5 million to 6 million newborns a lot across the EU. And again, 1 in 100,000 will give you 50 newborns in the EU per year. So that's where those numbers come from.

Now, the incidence, as our newborn screening studies are starting to show, may be higher than that. So we screened 275,000 babies, we found five babies with MLD. So I say, we're basing it on 1 in 100,000. If the true incidents through newborn screening are higher than that, that might reflect a higher incidence and a higher number of children eligible for treatment. It's a YoY figure. So it's about the number of babies that are born per year and the incidence, if it remains, will mean that it's that number every year that are diagnosed.

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

Wakao [Q]: Thank you. I'm Wakao, JPMorgan. I'd like to ask you a similar question. Having heard the discussion so far, in case the situation stabilized, you will find 50 patients in the EU and 40 patients in the US every year. On the other hand, in this year, regarding your market penetration in the US, is it better for us to assume that the start will be making a gradual ramp-up? I actually expected a quick ramp-up in the US because you have already launched this in the EU, however, the screening seems to take time.

I thought it would be a little difficult to expect some large scale of sales from the first year, is that correct? The sales figures themselves are shown in the company plan, but it would be helpful to know more about the view of this area.

Miyamoto [M]: Thank you, Mr. Wakao.

You mentioned that since the U.S. is also observing the situation in Europe, you expected the market penetration speed to be a bit faster. However, if screening is the key point, then you're asking whether this speed is not actually much faster compared to Europe, right? Bobby, please?

Gaspar [A]*: Yes, your observation is correct that it will be a slow increase. Because at the moment, as I say, there is no universal screening. There are only pilots that are available. So at the moment, we are dependent on identifying patients through two routes. The first is children who start to show early symptoms of MLD and are picked up by physicians. And they have to be picked up very early on. And so it's very important about disease awareness. It's a very rare disease. So physicians often have never encountered this disease. So we're- we have disease awareness programs that are ongoing. And the second route is if a child has already been diagnosed, and is unfortunately too late to be treated, then we screen family members or we ensure that physicians know to screen younger family members in order to see if any of these others can have MLD. So it's finding siblings of affected children.

So those are the two routes of identifying patients predominantly. And so that is why in the initial stages, in the absence of newborn screening, the number of patients we identified is well below the maximum that we

would expect to identify. Now, these efforts are ongoing and we're already gaining greater awareness amongst the MLD patient and physician community. So newborn screening will take time. But what I've experienced, and I was involved in screening for another condition, in Europe, for example, once a major country like Germany starts to screen, then other countries will start screening. It will expand very quickly. In the US, it's about getting states that can screen before the RUSP to start the screening. And then once a RUSP application has been successful and gets recommendation from the federal panel, then all states could start to screen relatively quickly. So this will not happen immediately, but over a few years, we expect newborn screening to start to increase both in states and at the country level in Europe, and then we will get to identifying as many of those babies as possible.

Wakao [Q]: Thank you. Understood. And my second question is about your pipeline. Having heard your presentation and discussion today, I have a impression that your future pipeline will be in the extension of those current pipelines Orchard researched and developed. And also, the presentation materials mentioned that you may integrate your technology with Kyowa's know-how assets and you'll be able to come up with something new. So, could you give us some concrete information like target disease? What will be expected as a result of integration of Kyowa Kirin and Orchard? And also, is it going to be for newborns? Because I think HSC-GTs are available not only for newborns, but also for adult patients.

Miyamoto [A]: Thank you for your question. I'd like to answer your question. Well, as you can see in this slide, we do have various ideas. I cannot disclose any specific items, but for instance, we'll be able to expect a delivery of the recombinant proteins to the site where usually the drug delivery is difficult. And also, as I explained today, a hematopoietic stem cell is a cell that has the ability to differentiate into various types of cells, and this technology can be used to insert genes into these cells from the outside, so there are many possibilities. Actually on the first contact with Orchard, our researchers had some ideas that they would like to try on the Orchard platform. Though that's the extent that I can talk today, but it is not limited for newborns as you pointed out, and there are, for instance, disease which will see the onset into adulthood or it is not limited to genetic diseases.

So currently, we do have plenty of ideas and we put them on the table and amongst researchers of Orchard and us, Kyowa Kirin, and also looking at all those ideas from the market side or commercial side, where we should prioritize. We are now trying to take this process, and I would like to take actions rather early. That's all.

Wakao [M]: I see. Thank you very much. When do you mean rather early?

Miyamoto [A]: Well maybe I was not expressing it in an appropriate way. In the case of conventional small molecule or monoclonal antibodies, the target disease is determined, then the target molecule is determined, and the capture antibodies such as agonists or antagonists for the target molecule are created. Then, we have to consider whether the antibody is really safe or not, and if it is an antibody, whether this antibody is really the right one, and then we have to consider the possibility of other antibodies, cell lines, etc. We believe that this technology can shorten these process considerably, so that the decision to go or no-go, to stop, or to change to the next one, can be made quickly.

Wakao [M]: Understood. Thank you very much.

Tsuzuki [Q]: Thank you. I have a question about the pipeline. OTL-201 Sanfilippo. In February, at the Congress, there was a presentation of our good results coming from the biomarker. And I understand that now this is in observation. But when will you start the pivotal study?

Miyamoto [M]: Thank you much for your question. Bobby, can you please respond to this question?

Gaspar [A]*: Sure. Thank you very much. So yes, we've seen some very exciting results coming from the MPS-IIIA OTL-201 study. I think you're referring to the World Symposium in February where the results were presented. And really, there was a lot of interest because 4 out of 5 patients are showing normal development, and they're getting at the ages at which you would start to see deterioration in the natural history population. So this is really very exciting for the community. It's the first time you're seeing this kind of outcome in MPS-IIIA patients. And it was not just about the composite function but also the other aspects of behavior, continence, acquisition of complex skills, and the ability of these patients to go on to more complex assessment of behavior as well.

So now, we've reached this proof-of-concept point, and we now have to plan for a pivotal study. And that's not just about talking to the regulators about the study design, but we also have to make some manufacturing changes as well. Currently, this is an investigator-sponsored study with vector and drug prod being made at academic centers, and that has to be transferred to the commercial setting. And so that will take some time for us to convert from academic manufacturer to commercially acceptable manufacturer as well. So those are the two important points before we go to start a pivotal study, the transfer to commercial manufacturing, and also to engage with the regulators to find the appropriate path for a pivotal study.

Tsuzuki [Q]: Thank you. Another question. Crohn's disease was mentioned in the presentation material from Orchard in the past. So what is the likelihood of you going into Crohn's disease?

Rather than going to Crohn’s disease, do you think you'll be walking on the synergy with Kyowa Kirin before you go into that? In other words, so are you really likely to go to Crohn’s disease or are you more likely to focus on development of new modality with Kyowa Kirin? Can you please organize my thoughts around that?

Miyamoto [A]: Thank you. I would like to respond to that first. This is Crohn's disease, but specifically a type of Crohn’s disease that can be treated with this technology. So as I have explained before, there are many ideas that we have. And these ideas will have to be discussed and prioritized as we move forward. So yes, there is possibility, and we will go into Crohn’s disease. There's also a possibility that we prioritize something else. So we cannot say one way or the other right now.

Tsuzuki [M]: I see. Thank you very much for your answer.

Haruta [Q]: Thank you. I'm Haruta, UBS Securities. I have one question. Mucopolysaccharidosis. I think the ERT is the main therapy. But I believe that for both Hurler syndrome and Sanfilippo syndrome, enzyme replacement therapies have already been developed that can, at least to some extent, cross the blood-brain barrier. Under such circumstances, your HSC gene therapy, if that's selected prior to the other therapies, what's the key? In the case of MLD, there are no other treatments available. However, if there are other treatments available, what is your gene therapy’s appealing point?

Miyamoto [A]: Well, thank you. Later on, I will ask Bobby to answer the question. But basically, efficacy over treatment, in the case of ERT, ERT cannot be finished just one time, but it has to be continued. But this HSC gene therapy is just one time. So Bobby, could you answer the question?

Gaspar [A]*: Yes. Thank you for the question. And I think the important thing here is about clinical need. Yes, there are ERTs available. But unfortunately, they are still associated with significant limitations. As Miyamoto-san said, they need to be given on a regular basis, so they're not potentially curative. But also they have significant limitations. So in MPS-I, for example, there is ERT that has been used for many, many years, but is associated with cognitive impairment because ERT cannot successfully cross the blood-brain barrier. It's also associated with significant skeletal problems as well. So it does not fully correct the different aspects of the disease.

Similarly, if you take other ERTs in MPS-III Hunter syndrome, you have the same problems there. It doesn't correct the cognitive problems. It doesn't correct the skeletal abnormalities. ERT is not available for MPS-IIIA. ERT in other conditions such as Pompe also has very significant abnormalities. But what we've been able to demonstrate with our HSC gene therapy is because the ability of these gene-modified cells to cross into the brain, to cross into the skeleton, to cross into all organ systems and deliver super physiological levels of enzyme in those organ systems, we are able to get complete correction of the target tissue and then correction of the clinical phenotype.

So MPS-I is the best example. The children that have been treated so far and the median follow-up, as I said, is over 3.5 years. They are showing normal cognitive function. You would expect significant deterioration from the current standard of care. They're showing remodeling of their skeleton, they're having normal growth, normal longitudinal growth, the abnormalities that were evident for disease have been corrected as a result of the gene therapy. So I think there is a unique property of gene-modified hematopoietic stem cells, the ability to engraft in these different organs through a natural process and the ability to deliver high levels of enzyme locally and correct target tissues. So we think this has a unique opportunity over and above ERT approaches.

Haruta [M]: Understood. Thank you very much.

Hashiguchi [Q]: Yes. This is Hashiguchi, Daiwa Securities. What about the durability of effect? I understand this is a single-dose administration. And maybe you don't have the data yet, but based on the past research, what can you do in terms of estimation of how long this effect will last? And also, if the effect wanes in the future, can anybody be re-administrated or only some of the patients can be re-administrated? What are your thoughts about this, please?

Miyamoto [M]: Mr. Hashiguchi, thank you for your question. This is definitely a question for Bobby.

Gaspar [A]*: Okay. Thank you very much. I'm very happy to take that question. My background is as an academic physician. So I've been working in this field for 30 years. I treated the first patient successfully at Great Ormond Street Hospital in 2001, over 20 years ago. And that was a boy with a genetic immune deficiency; was treated with HSC gene therapy. He has a fully corrected immune system over 20 years after the treatment was first given. And it all comes down to the detail on this slide here. The gene-modified cells, these HSCs, are capable of self-renewal. So once they have engrafted in the patient, they make new copies of themselves. There is a recurring pool of gene-modified cells that exists in the patient and exists potentially in that patient for their lifetime.

So we have seen in MLD, for example, the first patients were treated over 12 years ago, and there has been no waning of effect. We've been involved in trials of other HSC gene therapies for other diseases, immune deficiencies, where patients similarly were treated over 10 years ago, and they continue to have corrected immune systems. We continue to see the presence of gene-modified cells in the bone marrow, and there has been no waning of effect. And so although we can't say it because we don't have that follow-up, there are patients that are now being corrected from their disease for over a decade. And we think that they will potentially be corrected for a lifetime because of the engraftment of these gene-modified cells. We have to say potentially because we just haven't seen it for that long.

The other analogy that I will make is that of allogeneic bone marrow transplantation. So in allogeneic bone marrow transplantation, of course, you're taking somebody else's hematopoietic stem cells, and you're giving them to the patient. And the first allogeneic transplants were carried out in the late 1960s, early 1970s. And we know from that data that those individuals have on our 50 years after bone marrow transplant with the presence of those allogeneic hematopoietic stem cells. And so from these data, we can say that we can give a one-time treatment that has potentially a lifetime effect.

Hashiguchi [M]: Thank you very much. That's all for me.

Yamaguchi [Q]: Thank you. I'm asking the second time. Regarding screening, several points have been mentioned. And initially, you explained with the story of Connie and Joe. That's quite easy to understand. Without screening, the patient is already advanced at the time that the patient was identified. However, if you also screen the family members, then you may be able to identify the pre-symptomatic patients. Do you have such cases in many numbers? Or do you also identify patients without the screening? I mean that I'd like to understand better how you identify the patients.

Miyamoto [A]: Well, as Bobby explained, there are two patterns of identifying patients. And Bobby, could you give us a little more detail about how you identify the patients?

Gaspar [A]*: Yeah. Okay. So let me just go through the different ways in which patients can be identified. So firstly, there are patients that will present with certain symptoms. So they may start to stumble. The parents might notice that there is a loss of speech. There are some eye abnormalities that are associated with the disease. And so when they go and see a physician, a physician has to think about MLD and make the diagnosis. Now, if they do that early enough, early enough in the disease, of course, then that patient could become eligible for treatment. And so every year, we have a number of patients who have picked up because of the early symptomatology and are, therefore, treated. So that's one group of patients, but it requires the physician to make that link to MLD and to carry out the necessary test to identify MLD, and then they can be referred in order to be treated.

The second group of patients are patients where it's too late for those patients. They have advanced MLD. And then the physicians screen the younger children in that family. So increasingly, we are telling physicians, we're making patients aware of the fact that there is now a treatment available. And so if they've got a patient with MLD, even though it's too late for that patient, they should start screening younger family members, testing younger family members in order to see if one of them is now affected and then could benefit from the treatment. And that's what happened in the case of Connie and Joe here. And so again, every year, we have a number of patients who are diagnosed through that route. And the third group is now coming out of our newborn screening study. So our pilots are identifying patients as newborns. So those are the three groups, but over time, the group from newborn screening will start to be the majority group.

Yamaguchi [Q]: Okay. Understood. So I understand number three. What about the proportion of the number one and number two relatively speaking? Which is more frequently identified in patients?

Gaspar [A]*: I think it's roughly equal at the moment. It's roughly equal.

Yamaguchi [M]: Okay. Understood. Thank you very much.

Wakao [Q]: Thank you. I have one additional question.

Regarding MLD, it has become clear that it is better to diagnose and administer treatment early, before symptoms appear. It's understood that once MLD progresses, we can't expect much therapeutic effect. But what about OTL-203 and OTL-201, in the case of Hurler syndrome and Sanfilippo syndrome? Is it the same? In other words, for these as well, is it the case that if the treatment is not administered by a certain period, its effectiveness cannot be expected? Or if the patient is on ERT right now, can they be switched? And maybe 201 or 203 can be administered for treatment?

Moderator [M]: Thank you for your question. And Bobby, please answer.

Gaspar [A]*: Yeah, sure. So for OTL-203 for MPS-I, this is much more easily diagnosed than MLD because these children have some significant facial features that physicians can recognize. Also, there's already

newborn screening in place for MPS-I. So there are over 30— it's on the RUSP panel in the US, over 30 states already screened for MPS-I. There are initiatives in Europe as well. So it is much more frequently and better diagnosed than MLD for those reasons. And in now a proof-of-concept study, a number of patients— 7 of the 8 patients were already on ERT at the time that they were treated. So they've been established on ERT. They already had some features of the disease. And then the ERT was stopped, they were given gene therapy and none of those children had to go back on to ERT.

I'll just show you this picture here. This is a boy, and you can see him before gene therapy. And you could see the curvature of his back in the before gene therapy pictures, you can see the kind of rather hunched posture. And a year after gene therapy, you can see him sitting up straight and the curvature of the back has gone away because the ERT before gene therapy did not address the skeletal problems. You stop the ERT, you had gene therapy and now the skeletal problems have been resolved because of the bone remodeling that HSC gene therapy affords.

So you can switch patients from ERT into gene therapy. For MPS-IIIA, there is no ERT available. And for MPS-IIIA, again, it's about making a diagnosis very early, and we are already embarking on newborn screening studies for MPS-IIIA as well.

Wakao [M]: Very clear. Thank you very much.

Sakai [Q]: Thank you. The two of us are joining from the same company. But just one question to Miyamoto-san. Orchard appears to be quite an innovative company with technology, and we expect that Orchard will contribute to your business. At the same time, how will you be operating leveraging assets or technology of Orchard in your organization?

And we understand that you do not disclose Orchard as a single company's financial status. And if it's integrated with your Kyowa Kirin company, in terms of transparency, the transparency may come down. And so what is your policy or idea going forward regarding the disclosure of information and so on?

Miyamoto [A]: Thank you for your question.

As Bobby mentioned earlier, the most important thing to us is the technology. I often refer to this as the platform, because it encompasses everything from research to delivery to patients. This includes not only the technology itself but also the relationships with patients and with Key Opinion Leaders (KOLs). I believe that the entirety of what Orchard currently has is very important. And all those are supported by people. So together with the people of Orchard, how we can collaborate, making use of Orchard platform, not just maintaining their platform but even we try to evolve Orchard’s platform, I think that's the key.

And as I mentioned earlier, we do have lots of ideas. Moving forward, not only on the research side but also, of course, on the CMC side, or functions supporting them like PV or QA, we will be proceeding with the integration of each. In that sense, we won't be able to share with you the Orchard on the separated performance results in detail. However, as I explained, we also see value in the fact that the timeframe from ideation to actual clinical trials can be significantly shortened. When it comes to entering clinical stages or getting very close to them, we believe that we can inform you early on about the progress of such programs. In this regard, we believe that the time between "We have new technology, but please wait a bit longer until we can provide specific details" and actually being able to provide those details can be extremely short. So, we hope you can also look forward to that aspect as well. Did I answer your question?

Sakai [Q]: Well, so I think in a nutshell, you are saying that we should expect this integration. And Bobby Gaspar, is he going to be involved in the management? I mean, portfolio management and also he'll be involved in the management of Kyowa Kirin as well going forward?

Miyamoto [A]: Well, thank you. As Orchard, their reporting line is directly connected from Bobby to myself. And our ideas and Orchard's ideas will be discussed. And then we will discuss the prioritization. And of course, as a key member of that discussion, Bobby will be involved. So, in terms of Orchard's management and also overall R&D activation of Kyowa Kirin, he will be also joining as a team member.

Sakai [M]: Understood. Thank you very much.

Moderator [M]: Thank you very much, Sakai-san. So with this, we'd like to conclude the online IR meeting on Orchard.

[END]