Kyowa Kirin Co., Ltd.

Joint Development and Commercial Agreement of KHK4083 with Amgen

June 1, 2021

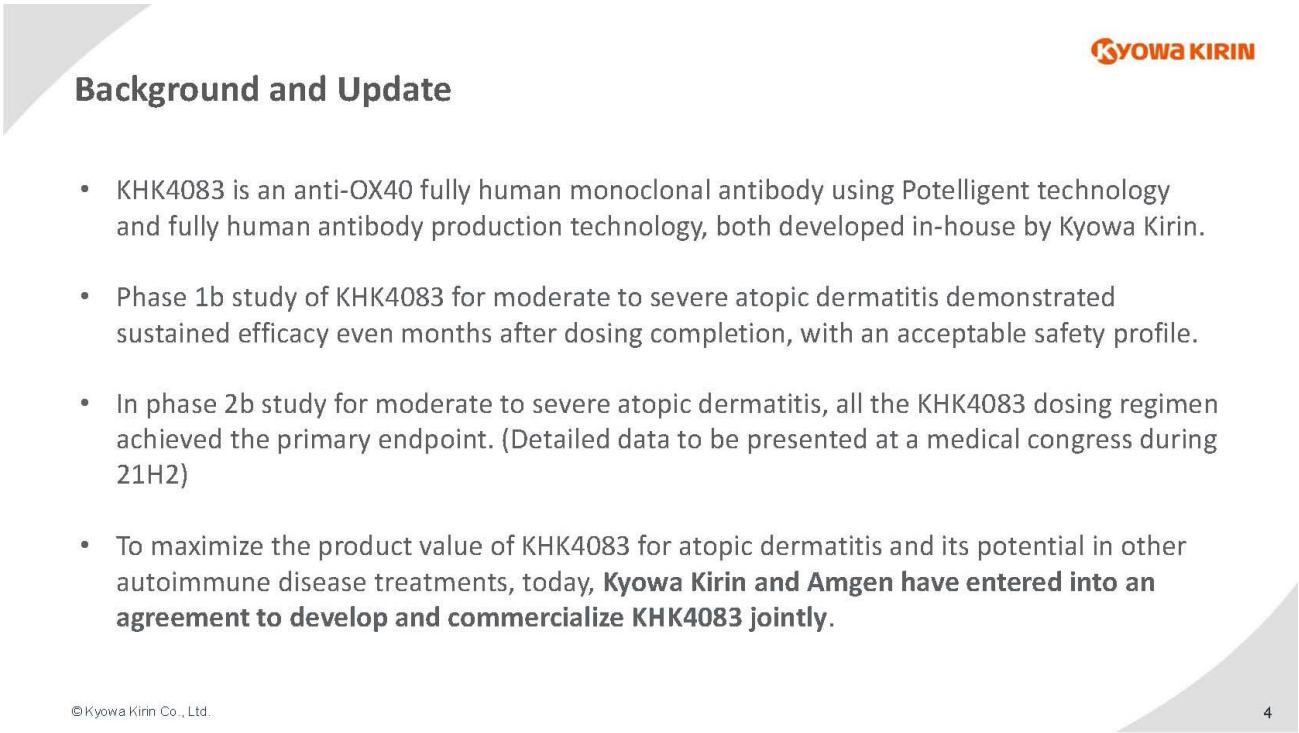
Event Summary

[Event Name]	Joint Development and Commercial Agreement of KHK4083 with Amgen	
[Date]	June 1, 2021	
[Number of Speakers]	5	
	Takeyoshi Yamashita	Managing Executive Officer, Director, Corporate Strategy & Planning
	Tomohiro Sudo	Executive Officer, Director of Global Product Strategy
	Yoshifumi Torii	Executive Officer, Vice President, Head of R&D
	Motohiko Kawaguchi	Executive Officer, Director of Finance
	Yasuo Fujii	Executive Officer, Director of Business Development

Presentation

Moderator: We will now hold the conference call.

I will now introduce today's speakers. Takeyoshi Yamashita, Managing Executive Officer and Director of Corporate Strategy Planning. Tomohiro Sudo, Executive Officer, Director of Global Product Strategy. Yoshifumi Torii, Executive Officer, Head of R&D. Motohiko Kawaguchi, Executive Officer, Director of Finance. Yasuo Fujii, Executive Officer and Director of Business Development.



Yamashita: Hello. Thank you very much for your participation at such a short notice. We are pleased to announce the signing of an agreement with Amgen for the joint development and commercialization of KHK4083, as released at 5:00 PM today.

Please see page 4.

KHK4083 is a fully human monoclonal antibody targeting OX40 that was created by Kyowa Kirin using our Potelligent and human antibody production technologies.

In a Phase 1 study in patients with moderate to severe atopic dermatitis, the drug showed a sustained improvement in clinical symptoms for several months after the end of treatment. We have also confirmed the acceptable safety profile of the drug.

In the subsequent Phase 2b study, all KHK4083 arms were able to meet the primary endpoint. As for the detailed test results, we would like to report them at the EADV to be held from the end of September, as we mentioned at the recent financial results briefing.

In order to maximize the value of KHK4083 as a potential treatment for atopic dermatitis, as well as other autoimmune diseases, we have entered into an agreement with Amgen to develop and commercialize the drug jointly.

KYOWA KIRIN

Development and Commercial Conditions

	US	Europe and Asia (ex. JP)	JP
Development	• Amgen leads development • Share development cost	• Amgen leads development • Share development cost	• Kyowa Kirin leads development
Commercialization	• Amgen commercializes and books sales • Kyowa Kirin co-promotes and shares cost	• Amgen commercializes and books sales • Kyowa Kirin has opt-in rights for co-promotion	• Kyowa Kirin commercializes and books sales
Sales Royalties	• Double-digit royalty to Kyowa Kirin	• Double-digit royalty to Kyowa Kirin	
Commercial supply	• Amgen supplies	• Amgen supplies	• Kyowa Kirin supplies

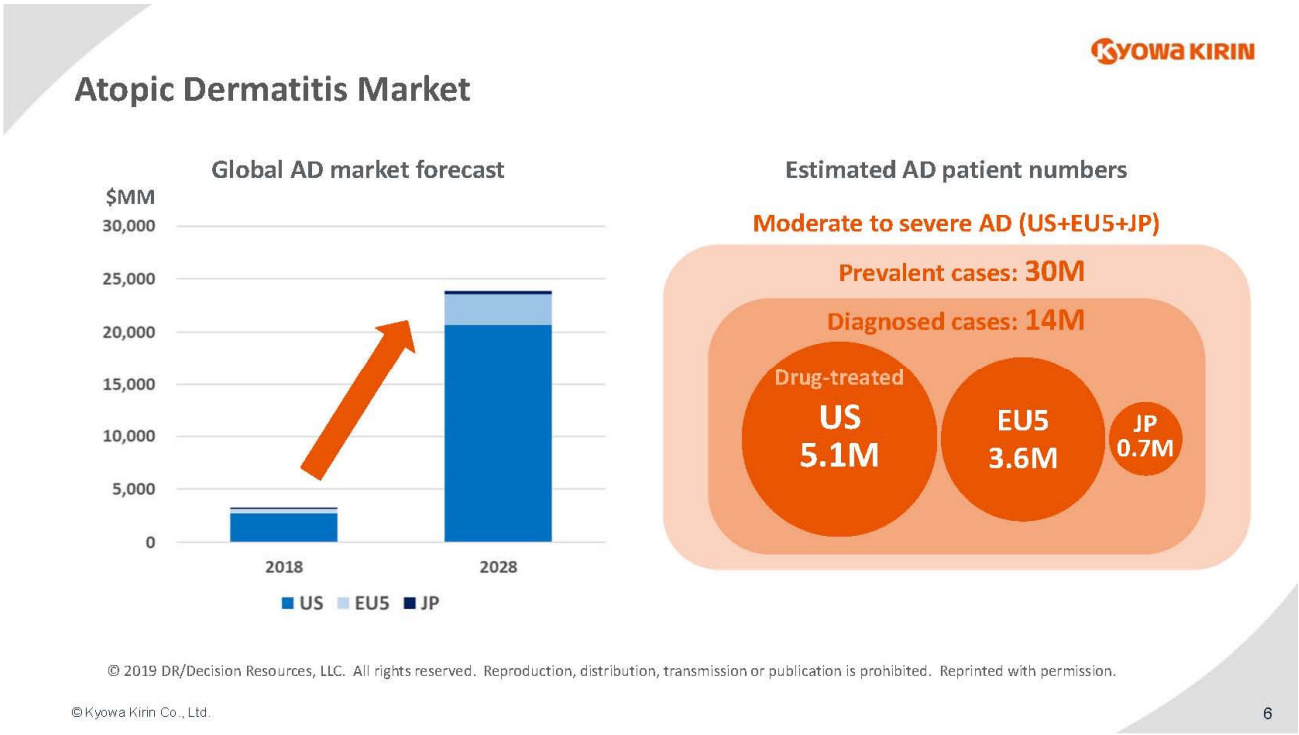
Amgen will make a $400 million up-front payment to Kyowa Kirin and future contingent milestone payments potentially worth up to an additional $850 million, as well as royalty payments on future global sales.

Please see page 5. The following is a summary of the various terms and conditions for development and marketing in this agreement.

First of all, in terms of development, Amgen will lead the clinical trials in regions other than Japan, while we will lead the clinical trials in Japan. Development costs outside Japan will be split between the 2 companies.

As for commercialization, in Japan, Kyowa Kirin will record sales and conduct promotional activities. In the US, Amgen will record sales, and both companies will conduct promotional activities and split the costs. In addition, outside of Japan, royalties as a double-digit percentage of sales will be paid to us.

The agreement will provide us an upfront payment of USD400 million and subsequent regulatory approval and sales milestone payments of up to a total of USD850 million.



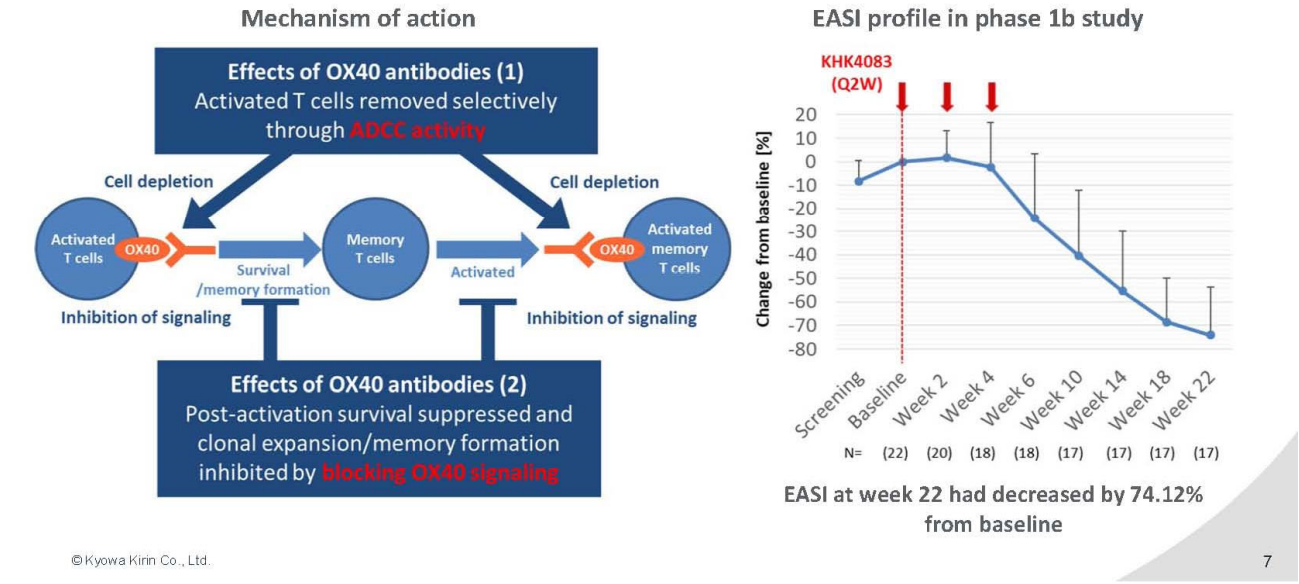
Please see page 6. The following is an overview of the atopic dermatitis therapeutics market.

The graph on the left shows the forecast for atopic dermatitis therapeutics market across the United States, EU5 and Japan.

The figure on the right shows the size of the population of patients with moderate to severe atopic dermatitis who could be treated with biologics, by region.

At present, several compounds are being developed for the treatment of atopic dermatitis, and we are aware that the competitive environment will be intense.

However, we recognize that this is a highly significant market to enter, as multiple treatment options are expected to be available in clinical settings, with patients able to choose a medication according to their changing symptoms.



Please see page 7.

KHK4083 is an antibody that targets OX40 and has enhanced ADCC activity through our Potelligent technology. It is expected to efficiently eliminate activated T cells expressing OX40 and inhibit the formation of memory T cells.

In addition, as shown in the graph on the right, a study we conducted have suggested that the clinical effects of the drug are sufficient and sustained over the long term.

By collaborating with Amgen who has an advantage in the field of inflammatory diseases, we will accelerate the development of this drug while making the most of its capabilities.

We will further focus on providing therapeutic drugs that can contribute to improving the QOL of patients with atopic dermatitis as quickly as possible.

Based on the attractive mechanism of action and activity of the drug, we will continue to explore the possibility of applying the drug not only to atopic dermatitis but also to other autoimmune diseases, with the aim of further enhancing the value of the drug.

This concludes my presentation. Thank you very much for your attention.

Question & Answer

Moderator: I would now like to move on to the Q&A session.

Yamaguchi: This is Yamaguchi from Citigroup Japan. The first question is about the upfront payment of USD400 million. Can you tell us first how this will be treated in accounting terms, and how it will be treated in terms of P&L?

Kawaguchi: Thank you for your question, Mr. Yamaguchi. As for the upfront payment of USD400 million, we are still in discussion with the auditing firm, so we cannot say anything definite, but as a matter of company policy, we do not plan to post it as a one-time revenue.

The basic idea is that revenue is recognized over a certain period of time in accordance with the fulfillment of performance obligations related to the contract, for example, development cooperation. Therefore, we are now receiving confirmation from the audit firm that we will record the revenue as deferred income over the period of the performance obligation. As for the period of the performance obligation, we are not able to provide a definitive answer at this time.

Yamaguchi: I understand. So, USD400 million, plus the remaining USD450 million, will give a total of USD850 million. That figure will be divided. I think the timing will be different, though.

Kawaguchi: There is a milestone of USD850 million in addition to the USD400 million. However, the USD850 million is the maximum, so it is not a definite figure.

Yamaguchi: Including the upfront payment, that gives USD1.25 billion.

Kawaguchi: That's right. As you say.

Yamaguchi: Thank you very much. My second question is about royalties. A double-digit percentage was mentioned. Regarding commercialization, you receive a copromotion fee and split costs. In that sense, is it correct that the profit is also shared among each location for the US, Europe, Asia, and maybe Japan?

Kawaguchi: This deal is not about profit sharing, but rather a royalty system based on sales. However, as you pointed out, in the US, promotion costs are shared on a 50-50 basis, so naturally the royalty rate takes this into account. Outside of the US, Kyowa Kirin does not pay for sales costs, so the royalty rate for that part of the business is different from that of the US. Does that answer your question?

Yamaguchi: Thank you very much. Is it the case that royalties will be higher in the US due to shared cost of promotion being factored in?

Kawaguchi: I believe that’s correct.

Yamaguchi: Thank you very much. That's all.

Wakao: Hello. This is Wakao from JP Morgan Securities. Thank you. First, in order to understand the value of this deal, I would like to ask some more detailed questions. Can you tell us how much the expected peak sales would be if you were to go it alone, and how much the expected peak sales are through this alliance? Naturally, peak sales will be greater than if your company acted independently, and I think this difference will allow us to see the value of this deal more clearly. This is the first question.

Sudo: Indeed. Thank you, Mr. Wakao. First of all, I would like to refrain from discussing peak sales here, as it relates to the performance of the drug in the future. However, the point I would like to make is that the market for atopic dermatitis alone is very large and the competition is intense, so we expect that peak sales will increase with Amgen as a collaborator.

In addition, in terms of LCM, it will be necessary to have an expanded development plan and a corresponding production and promotional structure, so in total, peak sales will increase. We made this decision because we thought that it would be more beneficial for Kyowa Kirin under these conditions than going it alone. That's all.

Wakao: Thank you very much. Understood. Next, I would like to talk about the development that you just mentioned. In the past, you told us that the timing of the launch would be in 2025 or 2026, but I would like to know if there is any change in the timing of the launch as a result of this collaboration.

Also, if possible, please tell us when the plan for the expansion of indications will be revealed, and when such additional indications will be launched on the market.

Sudo: First of all, we don't expect any major changes in development timeline at this point. We are going to start discussing the details of Phase 3 trial design with Amgen, and as we have reported before, we are still planning to launch the product in 2025 to 2026 for atopic dermatitis.

As for LCM, we also have not yet started concrete discussions with Amgen. However, since this area is very expansive for both companies, we are talking with a hope to start the discussion and studies for LCM as soon as possible.

Wakao: Thank you very much. That's all.

Muraoka: Hello, this is Muraoka from Morgan Stanley MUFG Securities. Thank you. I understand that it is difficult for you to give details about the contract conditions related to royalties, but in order to quantitatively evaluate the impact on stock prices, I would like to know more about it. My understanding is that you receive royalties from sales in the US, which essentially include co-promotion fees. Is that correct?

As a result, for example, with the Crysvita profit sharing scheme in the US, your OP margin for KHK4083 is comparable to the OP margin your company is currently earning on US Crysvita? The sales are booked at Amgen, so there may be differences, but is it correct that the operating margin on the final US sales is comparable to Crysvita for your company?

Kawaguchi: Thank you for your question. First of all, I am sorry to say that we cannot disclose the details of the contract. We can only disclose that the figure is in the 2-digit range. However, we feel that in contract discussions, the potential of KHK4083 has been fully evaluated.

The first point is that we have been able to agree on a quite satisfying rate compared to similar deals that we have been able to identify, as well as deals that we have done in the past few years.

Also, compared to the royalty rate when the product is completely out-licensed, the royalty rate in this case is duly considered with the condition that we bear one-half of development costs and US sales costs. In that sense, we are fully satisfied with the rate.

The comparison with Ultragenyx's conditions is a little more specific, so I am afraid I am unable to comment on the specifics here. Thank you.

Muraoka: Understood. By the way, just a clarification on the word choice in Japanese: is it correct to say that the split for development and sales costs will be 50-50?

Kawaguchi: I believe that is correct. In terms of terminology.

Muraoka: Understood. Thank you. The second question is about the future addition of indications for inflammatory diseases.

I know that UC was not so good. As for asthma, Amgen has an anti-TSLP antibody for asthma, so it may be difficult to consider this. From a business point of view, after having removed such indications, that may leave niche conditions such as SLE. Is it indeed the case that asthma would be ruled out because of concerns about competition?

Torii: I'm Torii, in charge of research and development. Thank you for your question. As Mr. Sudo mentioned earlier, we have not yet started full-fledged discussion on how to expand the indications as LCM. First of all, we are now focusing to develop for atopic dermatitis as fast as possible.

As mentioned in the press release, Amgen has an affiliate company, deCODE Genomics, that has a lot of expertise in this area, so we will be utilizing that data and information as well. We are still working on the specifics of how we can show our competitiveness.

Muraoka: Is it correct to say that even in areas where there is business competition, if the product is good enough, Amgen will not refuse?

Torii: Indeed. Given that the target is OX40, it has a mechanism that is different from other existing drugs such as Dupixent, so even if there are existing drugs or competitors, if there is an opportunity, we would like to go for it proactively.

Muraoka: Understood. Thank you. That's all.

Arai: This is Arai from BofA Securities. Thank you very much. The first question is about the opt-in rights for co-promotion in Europe and Asia. What kind of decision-making process will be there to decide whether or not to exercise this right? How does that change the royalty rate? I would like to ask you about this point first.

Sudo: Thank you for your question. As you can imagine, at this time, this is an opt-in, so there is no definite agreement between the 2 companies. We will consider this matter based on the future situation of our company. I would like to refrain from saying when, but that is our current position.

Also, I understand that there is no change in the royalty rate, regardless of whether we exercise the right. If Mr. Fujii can give us some comments on this, I would like to ask him to do so.

Fujii: Thank you very much for your question, Mr. Arai. I'm Fujii from Business Development. As Mr. Sudo mentioned, there is no change in the royalty rates in Europe and Asia. I hope you understand that there will be no change regardless of whether we participate in co-promotion or not.

Arai: Sorry, this is a follow-up. So, what will be the benefit of exercising the opt-in right of co-promotion? I'm sorry, my understanding is not up to par.

Sudo: This product will become a very important product for Kyowa Kirin in the future. Especially after 2025 and beyond 2030, we anticipate that we will contribute together through co-promotion in terms of how to make global contributions in the future. I hope you understand that our desire is to contribute in the form of co-promotion, if necessary, to achieve our vision.

Arai: I understand. Thank you. The second question is about the breakdown of the milestone payment. I believe this would apply to both development and sales milestones, but could you tell us how they will be broken down? I am referring to the USD850 million figure.

Kawaguchi: This USD850 million figure includes 2 elements: the first is development milestones associated with regulatory approval. In addition, we have set certain milestones for sales achievement, but the breakdown of these milestones is not disclosed.

Arai: I understand. Thank you. That's all.

Ueda: This is Ueda from Goldman Sachs Japan. Thank you. The first point is that I would like to get some more hints about how the decision was made at Amgen. I wonder if Amgen made a decision based on the detailed data from Phase 2, which has not been disclosed yet.

Also, could you tell us what you think Amgen appreciated about your company that led to the agreement?

Fujii: Thank you for your question, Mr. Ueda. We disclosed almost all our current data to Amgen for their evaluation of the drug. I believe that Amgen has come to the conclusion that it is as potent as they thought it was and then we were able to conclude the contract on that basis. That's all.

Ueda: Thank you very much. Secondly, I would like to ask about sales and costs. In terms of sales, is there any revenue other than royalties, such as export sales from your company? Additionally, in the area of research and development expenses, could you tell us whether or not the agreement to split the expenses 50-50 will have any impact on the outlook in the mid-term plan?

Kawaguchi: Thank you for your question. In terms of sales, Amgen will be supplying the products in this case, so there will be no sales of APIs or anything like that. I think what we will receive are sales royalties, upfront payments, and milestone payments. Could you repeat the last part of your question?

Ueda: What is the effect on R&D expenses forecast that was presented in the mid-term plan?

Kawaguchi: Of course, we did not anticipate in the mid-term plan that we would be sharing development costs, so I think that part of the budget will be lower. We are going to jointly go over the development plan, so we will be able to examine the development costs again and make a plan for the future. That's all.

Ueda: Understood. Thank you very much. That is all.

Sakai: Thank you. This is Sakai from Credit Suisse Securities Japan. I know there are a lot of questions right now, but on the first page of the release, in the third paragraph, the bottom sentence, there is a statement that Amgen will also consider the possibility of further developing KHK4083 by utilizing the proprietary data of its subsidiary, deCODE Genetics. So, I think that's a good point. When I read this, it seems to me that your company has already disclosed the data to the other side, and Amgen is fully convinced, and is considering its future development plan.

In the past, we have received answers such as "we will consider it in the future," or "we will consider various indications in the future." From what I read, it sounds like you have already had in-depth discussions and have given Amgen the so-called opt-in right for future development. That seems like quite a change from your previous stance, doesn’t it?

Sudo: Thank you for your question. We haven't actually talked about the specifics of this case at all yet. I understand that Amgen's intention here is to use genetic data in order to find more appropriate patients to target in the future, and that Amgen has the database to do so. I understand that Amgen has that database and they want to use it.

At this point, with the information we have, I think it's safe to say that the conversation about approaches using genetic data will start from scratch.

Sakai: Is it correct to understand that this is only referring to atopic disease?

Sudo: No, I understand that the wording is intended to include a wide range of LCMs, not only for atopic dermatitis but also for other diseases for which there is a possibility of treatment, as was mentioned in the previous question.

Sakai: Understood. Thank you. As for the future development of Crysvita in the US, I think Crysvita will be back in your hands in 2023. I believe there was mention of strengthening sales abilities and infrastructure in the US. After that, if KHK4083 were developed independently, it would have seemed natural to expect further expansion in the US. However, with this deal, the US is Amgen's territory.

I think both parties have found the best partner here, and I don't think Amgen would betray Kyowa Kirin. It seems to me that your company's future strategy in the US will be a little difficult if you only sell Crysvita. Do you have a vision for the future of the project?

Sudo: Thank you very much. This is a very important question. This is one of the reasons behind our decision to partner with Amgen. As you mentioned, Crysvita promotion will return to us in the spring of 2023. Naturally, this is going to be a very large drug, and the entire company will be working together to promote it. In addition, the drug will still be growing towards 2024 and 2025, so we will be putting in a lot of effort.

At the same time, sales of Poteligeo and Istradefylline, the other 2 of our so-called Global 3 products, will be very important in the US, so it is very important for us to keep working to firmly establish this sales function.

Also, as you know, our company also has plans for KW-6356 and ME-401. We hope ME-401 will be 2023, if all goes according to plan. The other compound, KW-6356, will be launched in 2025 or later, so it will be very important to build a sales system in the US as well, and there will be a lot of work involved.

In this context, we have KHK4083, where we will be competing in a very large market. We think that working with Amgen is the best way to maximize the drug and deliver the value of the drug. In terms of the sales system, we have decided that this is a good balance.

Sakai: Understood. Thank you.

Tanaka: This is Tanaka from Mizuho Securities. Thank you very much. My first question is about the milestones. You mentioned that the milestones are for the approval and the sales of the product. Regarding LCM, will there be separate payments?

Kawaguchi: With regard to the development milestones associated with the approval by the pharmaceutical affairs bodies, they are set only for the current indication of atopic dermatitis, and for the other indications, there are no specific conditions set for each indication in this contract.

Tanaka: So, if a new indication is developed, we can assume that milestones will be set separately?

Kawaguchi: Within the current contract, options would be, for example, sales added to sales royalties, but please understand that I am not able to disclose the details here.

Tanaka: Understood.

Kawaguchi: Please appreciate that this has not been decided at this time.

Tanaka: It is only decided for atopic dermatitis.

Kawaguchi: That's right.

Tanaka: Understood. Secondly, I think the field of dermatology is a very specialized area. It is mentioned in the release that Amgen sells the medication Otezla for psoriasis.

Other than that, I don't think the company has a very strong presence in the field of dermatology. Of course, I understand that the relationship between your company and Amgen has existed for a very long time. How did you reach the conclusion that they were the best partner to market in the dermatology field? Please let us know if you have considered other companies.

Sudo: Thank you for your question. This was also a very important decision point for us. You mentioned Otezla, but I believe Amgen has 5 or 6 other drugs, including Enbrel. As for scale, about 30% of Amgen's sales for 2020 were in the field of dermatology.

Specifically, Enbrel, which I just mentioned, is the largest, but there is also Otezla. Amgen is currently working on biosimilars, so total sales in dermatology are about USD7.2 billion.

On the other hand, in terms of sales, global expansion is extremely important, and Amgen has a presence in North America, Europe, other regions, Japan, and Asia. They have launched their products in about 100 countries.

We are also working in the field of dermatology, and we will make good use of Amgen's broad sales network to deliver this drug as quickly as possible. This is one of the reasons why we decided to work with Amgen.

Tanaka: Did you consider other companies?

Sudo: We conducted broad and comprehensive research. We cast a very wide net for our initial analysis.

Tanaka: Understood. Thank you very much.

Kohtani: Hello. This is Kohtani from Nomura Securities. First of all, what seems to be the biggest feature of this deal is that this upfront payment is unusually large. USD400 million. I'm looking at similar examples, but they are usually in the double digits. This is for other compounds at the Phase 2b stage. I would like to know what I can read from that.

I would like to know if this is because of competition or because the data from Phase 2b is very promising. Anything at all you can say about this would be helpful. This is not a cancer drug, so there is still a big risk that it will fail in Phase 3. Amgen, a world class company, puts up USD400 million upfront, and if it fails, the whole thing goes to zero. Could you please explain the background of why Amgen took such a big risk?

Fujii: Thank you for your question, Mr. Kohtani. As was mentioned in a previous answer, in discussions with Amgen we disclosed all of the necessary Phase 2 data. In the process, Amgen came up with a variety of comprehensive economic conditions and this is the amount of money that was offered from them at that time. I'm afraid the only way to get a solid answer would be to ask Amgen, but from my understanding, Amgen saw the potential of this drug, and that is why the price was set at this level. Thank you.

Kohtani: As far as your company is concerned, it is correct that this upfront payment is higher than the previous similar cases, right?

Fujii: Well, similar examples are considered to be for reference only. Each drug is different, and this time, we have a collaboration agreement. There are various parameters involved, so figures for other drugs can only ever be a reference. Even with this in mind, we do not believe the conditions of this contract were so out of the ordinary. Thank you.

Kohtani: Understood. The second question is that the most important point has been missing until now. Will the collaboration with Amgen speed up the pace and gain success rate of the expansion of OX40 antibody indications? deCODE genetics is a company that has been working on the genome data in Iceland or somewhere for quite long time, so they have a lot of capability in genetic analysis.

The problem with OX40 is that there is a lot of pathological evidence, but to be honest, the genetic evidence is a little weak. Perhaps there was 1 deficient reported case, right? A patient, or rather, 1 person who did not have OX40, who had leishmaniasis. However, since it is only one case, the genetic evidence is weak, and I think it is quite important that this deCODE genetics comes on board. Can you tell me what role deCODE genetics plays in this?

Torii: Thank you for your question, Mr. Kohtani. As I mentioned earlier, we are still in the process of studying the specific expansion of indications. However, as you mentioned, the information provided by deCODE genetics is not limited to atopic dermatitis, and we are hoping that it will be a very powerful tool for efficiently and quickly expanding the indications for other diseases.

I'd like to repeat what I said earlier: while giving first priority to the smooth development of atopic dermatitis, I would like to collaborate and consider maximizing the value of this drug by expanding its indications in parallel.

Kohtani: Understood. I'm sorry, but I have just 1 more question. I understand that your company will receive something that takes into account sales and development costs. They make the formulations, so your company has to buy them, right?

However, if Potelligent technology is used to for formulation, it is very complicated to calculate the cost of purchasing the formulation. As for purchasing the cost of APIs from Amgen, is that something we don't have to think much about?

Kawaguchi: Thank you for your question. In this case, Amgen will manufacture the product and we will not purchase it, but Amgen will sell it, so there will be no cost burden. We will receive royalties for sales.

Other than that, we have a scheme in which we share the cost of US sales.

Kohtani: Thank you very much.

Yamaguchi: This is Yamaguchi from Citigroup again. A further question about the relationship with Amgen. I think it's important to maintain the mutual commitment to development with Amgen. Of course, I understand that Amgen is one of the companies that you have historically been familiar with.

On the other hand, they are a very large company, so there is always the risk that they will get ahead of themselves or fall short of their commitments, as we have seen in the past. I would appreciate it if you could tell me how you are trying to control that area.

Yamashita: Thank you very much for your question, Mr. Yamaguchi. As you pointed out, we have had a good relationship with Amgen, and we consider this to be a relationship of trust. Communication between top management of both companies is good. We have a positive outlook.

While there is always the possibility of conflicting ideas as projects move forward, I am confident that we can discuss any issues as they arise in the Joint Steering Committee as we move forward with the development and launch of the product. Basically, decisions will be made by mutual agreement between the 2 companies, and we believe that there will be no major discrepancies.

Yamaguchi: Thank you very much. Thank you.

Moderator: As there are no further questions, this concludes the conference call regarding the agreement with Amgen for the co-development and commercialization of KHK4083.

Thank you very much for taking time out of your busy schedules to join us today. Thank you for your continued support of Kyowa Kirin.

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