



Kyowa Kirin Co., Ltd.

Q1 Financial Results Briefing for the Fiscal Year Ending December 2021

May 6, 2021

Event Summary

[Event Name]	Q1 Financial Results Briefing for the Fiscal Year Ending December 2021	
[Date]	May 6, 2021	
[Number of Speakers]	4	
	Takeyoshi Yamashita	Managing Executive Officer, Director, Corporate Strategy & Planning Department
	Motohiko Kawaguchi	Executive Officer, Director, Finance Department
	Yoshifumi Torii	Executive Officer, Vice President Head, R&D Division
	Tomohiro Sudo	Executive Officer, Director, Global Product Strategy Department

Presentation

Moderator: We will now hold a financial briefing conference call for Kyowa Kirin Co., Ltd. for the first quarter of the fiscal year ending December 2021.

Today's speakers are Takeyoshi Yamashita, Managing Executive Officer and Director of the Corporate Strategy & Planning Department. Motohiko Kawaguchi, Executive Officer and Director of the Finance Department. Yoshifumi Torii, Executive Officer and Director of the Research and Development Division. Tomohiro Sudo, Director of the Global Product Strategy Department.

I will now hand it over to Mr. Kawaguchi.

Summary of Q1 Results



(Billion Yen / Rounded)

	2020Q1 Results	2021Q1 Results	Changes	2021 Plans	Progresses
Revenue [Overseas Ratio]	77.3 [44%]	81.1 [50%]	+3.8 (+5%)	351.0 [54%]	23%
Gross Profit [Gross Profit Margin]	57.9 [75%]	58.7 [72%]	+0.8 (+1%)	270.0 [77%]	22%
SG&A [SG&A Ratio]	29.7 [38%]	31.7 [39%]	+1.9 (+7%)	141.0 [40%]	22%
R&D [R&D Ratio]	11.8 [15%]	12.2 [15%]	+0.4 (+3%)	65.0 [19%]	19%
Gain/Loss on Equity Method	4	6	+0.3 (+66%)	1.0	64%
Core Operating Profit [Core OP Margin]	16.8 [22%]	15.5 [19%]	-1.2 (-7%)	65.0 [19%]	24%
Profit	13.8	12.9	-0.9 (-7%)	50.0	26%

Kawaguchi: Thank you. First, slide 5. This is a summary of the financial results for the first quarter.

Compared to the same period last year, sales revenue increased by 5%, or JPY3.8 billion. Core operating income in the second line below was down 7%, or JPY1.2 billion. Quarterly profit, listed at the bottom, fell 7%, or JPY900 million.

I think some of you were a little surprised by the fact that core operating income fell. Although sales have increased by JPY3.8 billion, gross profit has only increased by JPY800 million. In other words, a temporary increase in the cost of goods sold in the first quarter is one of the reasons for the decline in profit.

There are special factors related to the elimination of unrealized income of inventories, which is a procedure for consolidated accounting. Our overseas subsidiaries have inventories of three global strategic products in the order of tens of billions of yen. The figure includes the internal income that we added when we sell to subsidiaries.

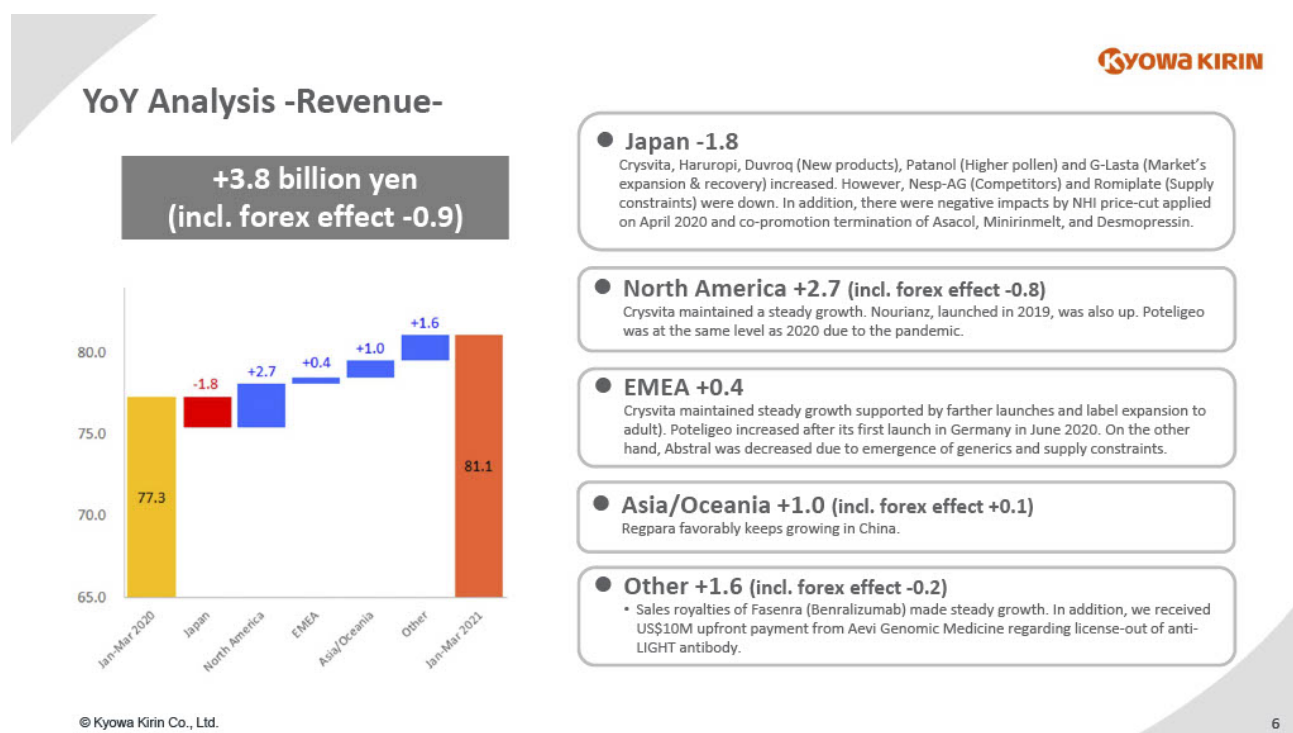
In the process of closing the consolidation, the cost of goods sold must be accounted for the purpose of erasing this. We used the exchange rate of JPY103.5 at the end of the previous fiscal year, but it shifted toward

a strong yen in this quarter. As a result, the amount of internal income to be erased will increase. Therefore, we are seeing compressed gross profit for the first quarter.

With regard to the overall progress toward the forecast, except for the cost of sales I mentioned just now, everything is progressing almost as expected.

With regard to sales revenue, global strategic products and benralizumab royalties are expected to grow further after 2Q. Regarding SG&A and R&D expenses, based on the trend that expenditure increases in the second half of the year, we would appreciate if you understood that progress towards the forecast is as expected.

In the full year, we aim to achieve a plan to increase income and profit.



Next is slide 6. This shows a breakdown of sales revenue by regional subsidiary. There have been no major changes in trends since the previous year.

In Japan, sales of new products are continuing to increase, led mainly by Crysvita. Beside the impact of the drug price revision in April 2020, there was succession of Asacol to Zeria Pharmaceutical, and Minirinmelt and Desmopressin to Ferring Pharmaceuticals. Sales of these by our company ended last spring, resulting in a decrease in sales of JPY1.8 billion.

In Europe and the United States, sales have increased due to the growth of Crysvita, Poteligeo and Nourianz. Regpara continues to be strong in China.

In the Other area, that includes technology license and contract manufacturing revenue, sales royalties of benralizumab and the USD10 million upfront payment for the anti-LIGHT antibody from US Aevi Genomic Medicine contributed to the increase.

Revenue of Major Items (Japan)

(Billion Yen / Rounded)

Item	2020Q1 Results	2021Q1 Results	Changes	Reasons	2021 Plans	Progresses
Nesp + Nesp-AG*1	7.4	6.5	-1.0 (-13%)		23.2	28%
Nesp	1.2	1.0	-0.2 (-19%)	Biosimilars' penetration	3.8	25%
Nesp-AG	6.3	5.5	-0.7 (-12%)		19.4	28%
Duvroq	—	0.2	+0.2 (—)	Launched in Aug 2020	4.0	4%
Regpara	1.0	0.7	-0.3 (-31%)		2.0	33%
Orkedia	2.0	2.1	+0.1 (+7%)		10.4	20%
G-Lasta	6.1	6.6	+0.5 (+8%)	Market's expansion & recovery	29.8	22%
Poteligeo	0.5	0.5	-0.0 (-3%)		2.0	24%
Rituximab BS	2.6	2.6	+0.1 (+2%)		11.5	23%
Romiplat	2.0	1.5	-0.5 (-24%)	Supply constraints (2020.6-2021.3)	8.7	17%
Allelock	3.0	2.9	-0.1 (-4%)		6.8	43%
Patanol	5.9	6.5	+0.6 (+11%)	Higher pollen	10.9	60%
Nourias	2.2	1.9	-0.3 (-14%)	Competitors' penetration	9.1	21%
Haruropi	0.1	0.6	+0.5 (+504%)	Launched in Dec 2019	4.6	12%
Crysvita	0.5	1.5	+1.0 (+182%)	Launched in Dec 2019	5.5	27%
Tech-licensing	0.3	0.6	+0.3 (+90%)		2.5	24%

*1 AG stands for Authorized Generic. Official product name is Darbepoetin Alfa [KKF]. Kyowa Kirin Frontier is a marketing authorization holder; Kyowa Kirin is a distributor.

I will now present the progress rate toward the full-year forecast by product. Please see slide 7.

First the progress for Nesp AG is 28%. This is generally according to plan given the drug-price revision in April lowering the drug price.

Duvroq is struggling with a 4% progress rate to full-year forecast. This is due to restrictions on a longer-term prescription under the coronavirus pandemic. We would like to continue steadily providing information so that we can recover from September onwards, when the restrictions are lifted.

Regarding Romiplat, progress is 17%. As described in the factors of YoY change section, demand has exceeded expectations, leading to supply constraints to distributors since June last year. The progress rate is low due to the impact of that. We have been able to resume regular shipments from this April, so we hope that we will gradually recover from here.

Allelock and Patanol have been progressing well, as pollen counts were higher than expected. Overall, progress is as planned.

Regarding Haruropi, progress is 12%. We believe this is due to restrictions on MR activities and outpatient appointments. As with Duvroq, we will actively utilize digital tools as well to continue our commitment to market penetration.

Revenue of Major Items (ex-Japan)

(Billion Yen / Rounded)

Item	2020Q1 Results	2021Q1 Results	Changes	Reasons	2021 Plans	Progresses
Crysvita	12.0	16.3	+4.3 (+36%)	[North America] Market penetration & Expanded indication (TIO)	77.2	21%
North America	9.2	11.7	+2.5 (+28%)	[EMEA] Farther launches & Expanded indication (Adult)		
EMEA	2.8	4.5	+1.8 (+64%)			
Poteligeo	2.9	3.2	+0.2 (+8%)	[North America] COVID-19	17.3	18%
North America	2.9	2.6	-0.3 (-11%)	[EMEA] Launched in Germany in Jun 2020 & Farther launches		
EMEA	—	0.6	+0.6 (—)			
Nourianz	0.4	1.0	+0.6 (+168%)	Market penetration	6.7	14%
Abstral	2.8	1.8	-1.0 (-35%)	Generic's penetration & Supply constraints	8.1	22%
Regpara	1.7	2.2	+0.5 (+31%)	Listed on Chinese NEDL*1 in Oct 2018	9.3	24%
Tech-licensing	3.1	4.9	+1.8 (+59%)	Growth of Fasenra & Upfront revenue of anti-LIGHT antibody license-out	23.7	21%
Benralizumab Royalty*2	2.7	3.8	+1.1 (+40%)			

*1 National Essential Drug List

*2 Sales royalties of Fasenra, marketed by AstraZeneca (Including our own estimation)

* Revenue from Early Access Program (EAP) are not included in revenue above.

Next is slide 8. This shows the overseas items.

Crysvita is on track in both Europe and the United States. As we anticipate further increases in sales in the future, 21% is roughly according to plan.

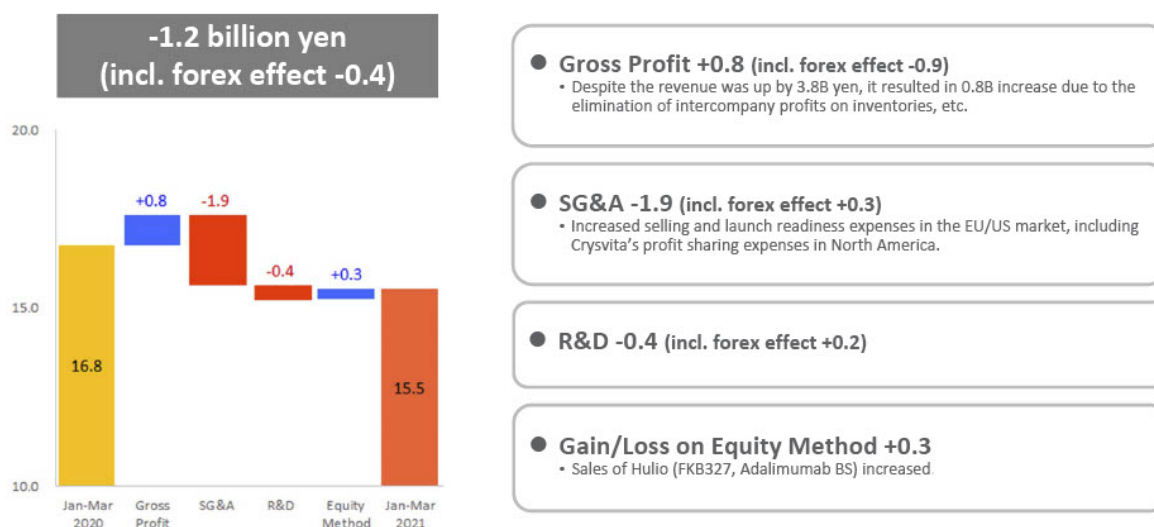
Poteligeo is at 18%, slightly behind progress. In the United States, guidelines on the interval between doses during the coronavirus pandemic continue to have an effect. In addition, we believe that bad weather in the south also had an impact in February. Price negotiations for reimbursement with authorities have been delayed in Europe due to the coronavirus pandemic.

Progress to the full-year forecast is 14% for Nourianz, but this is as planned.

As for Abstral, there was an unplanned shipment restriction, so progress is lagging, but we believe that it can be recovered in the full year.

In the technical revenue section, Fasenra's sales royalties are steadily progressing. Progress is as expected.

YoY Analysis -Core OP-



Slide 9 shows changes in core operating income.

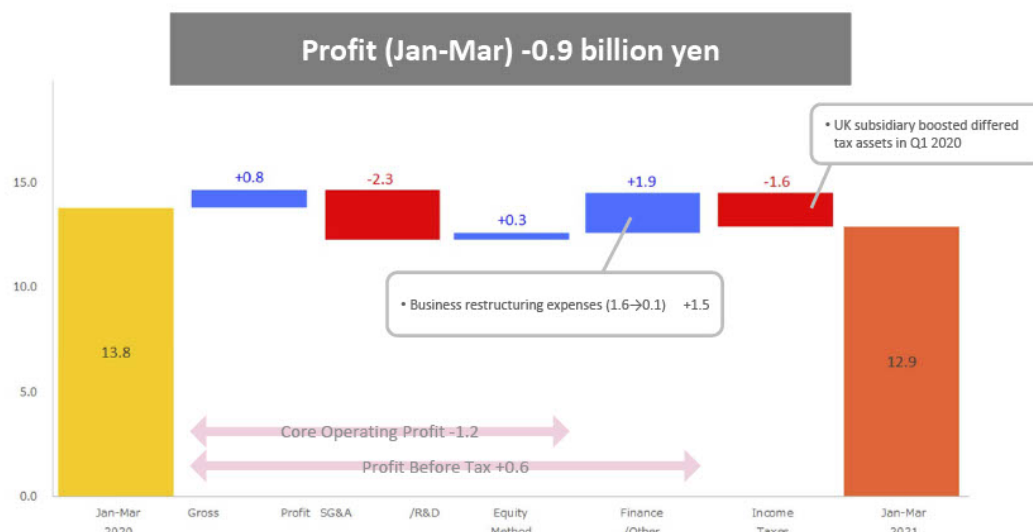
As explained at the beginning, gross profit increased JPY800 million despite an increase in sales revenue of JPY3.8 billion. This is due to erasure of unrealized profit on inventory.

SG&A expenses have increased by JPY1.9 billion, resulting in a decrease in profit. In addition to Crysvita's North American profit share, there is also an increase in the costs relating to launch of ME-401, and investment to strengthen the global base. Progress to the full-year forecast is 22%, but this is generally as expected.

Research and development expenses are comparable to the previous year, with an increase of JPY400 million. Progress is 19% toward the full-year forecast. As we released in April, 4 phase 3 trials were started for KK7791, or tenapanor. Additionally, increased costs relating to ME-401 are also anticipated.

With respect to equity method investment gains and losses, Hulio, a biosimilar of Humira, is progressing steadily with a plus of JPY300 million.

YoY Analysis -Profit-



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Finally, on page 10, I will present changes to the core operating income.

For financial and other revenue, there was an increase of JPY1.9 billion. This is mainly due to the fact that the cost of improving the business structure of EMEA, which was recorded last year, has reduced from JPY1.6 billion to almost 0.

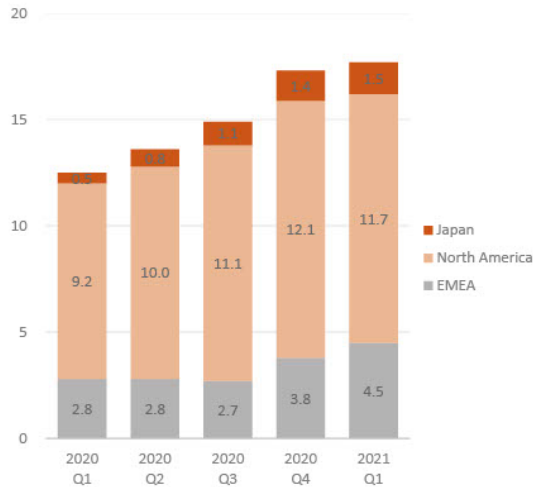
Regarding corporate income tax expenses, a transient accumulation of deferred tax assets in the UK subsidiary that covers EMEA due to a change in the UK tax rate led to reduced corporate tax costs last year. The figure returned to the regular base this year, resulting in a reduction of JPY1.6 billion.

I think some of YoY comparisons are a little difficult to understand, but progress is generally as planned against the full-year forecast.

This concludes the finance presentation.



(Billion Yen)



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Topics

- Steady sales in Japan, North America, and EMEA even under the influence of COVID-19.
- In EMEA, indications for adult were expanded in Luxembourg, Oman, Kuwait, and Qatar during the Q1 period.
- Sales in Germany are steadily increasing due to the expansion of the indication to adults.
- In China, following the approval for XLH in January, approved for TIO in March.

Launched Countries/Regions (XLH) as of March 31, 2021 Excluding South America Underlines: Pediatric and Adult

USA, Canada, Germany, Netherlands, Luxembourg, England, Wales, North Ireland, Slovakia, Sweden, Israel, UAE, Czech, Denmark, Italy, Japan, Norway, Bahrain, Scotland, Oman, Kuwait, Qatar, Romania, Slovenia, France, Finland, Estonia, Spain

Yamashita: Thank you. In this section, I will discuss the status of 3 global strategic products.

First, Crysvida. See page 12. The graph on the left shows sales revenue by region and by quarter.

Crysvida has been strong in Japan. At the end of last year, self-injection became possible. This may have contributed somewhat.

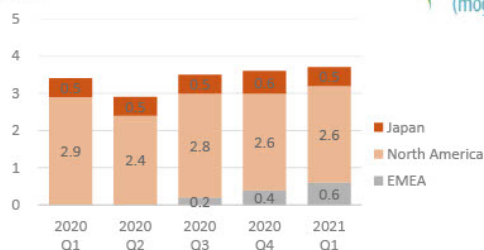
Self-injection is allowed in North America during the pandemic. This makes it possible for existing patients to continue treatment. Although the effects of the coronavirus pandemic still remain, new cases have also come in, and sales remain strong.

In EMEA, I think you can see the growth since last year's fourth quarter. It has been launched for adults in 4 countries: Luxembourg, Oman, Kuwait, and Qatar. Sales started in these markets in this quarter. There was no new launch for pediatric indication. Germany has been on track with the expansion of adult indications.

We have no sales yet for the Asia/Oceania region. In China, we have received XLH approval in January and TIO in March. Currently, we are proceeding with the procedure for release.

As of the end of March 2021, here are the countries where we have launched Crysvida for XLH. It is 28 countries and regions in total. It does not include South America. The 9 countries where both adult and child approval has been granted are shown underlined. Last time, Finland and Estonia were omitted, and sales in these countries started in the fourth quarter of 2020.

(Billion Yen)



POTELIGEO
(mogamulizumab)

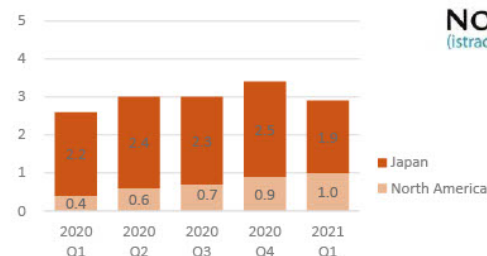
Topics

- Approved in Australia (Jan)
- Application for marketing authorization in Kuwait (Feb)
- Application for marketing authorization in Canada (March)

Launched Countries as of March 31, 2021

Japan, USA, Germany, Austria, Luxembourg, Italy

(Billion Yen)



NOURIANZ
(istradefylline) tablets

Topics

- Gradual improvement in call activity in North America impacted by COVID-19
- Ongoing review by EMA in Europe

Launched Countries as of March 31, 2021

Japan, USA

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Next is Poteligeo. Please see page 13.

Sales in Japan have remained strong, without major changes.

In the United States since last year, recommendations have been made to reduce the frequency of administration in relation to COVID-19. As a result, no growth in sales has been seen, and the situation seems static.

However, since vaccinations are continuing in the United States, we expect that the treatment environment will be restored and sales of Poteligeo will grow. In Canada, we applied for approval in March.

For Poteligeo in EMEA, more time is required to negotiate prices than expected in some countries due to the impact of the coronavirus pandemic. Following Germany, which launched in the second quarter of last year, we launched it in Italy in the first quarter this year. It is a gradual launch. In addition, in EMEA, we submitted an application for approval in Kuwait in February.

In Asia/Oceania, we gained approval in Australia in January. As of the end of March, Poteligeo has been launched in 6 countries.

Next is Nourianz.

Japan's market competition is intensifying, and Nourianz is also affected.

The United States has seen a decrease in the number of calls due to COVID-19, but there are signs of recovery. Yet, face-to-face meetings have not returned to their original level, but there has been a recovery in March compared to January and February.

Regarding Europe, the review process is continuing.

This concludes the commercial update.

Upcoming events: our Next-generation Strategic Products

✓ : Completed events from Jan 1 to May 6, 2021

Code generic name	Target disease	H1 2021	Mid-2021* ¹	H2 2021
KHK4083	Atopic dermatitis	P2b topline data ✓		P2b detailed data
KW-6356	Parkinson's disease			P2b detailed data
ME-401 Zandelisib	FL (3L, mono)	P2 LPI ✓		P2 topline data
	FL/MZL (2L, combo)		P3 FPI	
RTA 402 Bardoxolone methyl	Alport syndrome		MA (JP)	
	DKD			
	ADPKD	P3 FPI (JP) ✓		
KHK7791 Tenapanor	Hyperphosphatemia under maintenance dialysis	P3 FPI (JP) ✓		

*1 Events anticipated to be achieved around the end of the H1 2021 at present;

FPI: first patient in; LPI: last patient in; FL: follicular lymphoma; MZL: marginal zone lymphoma; ADPKD: autosomal dominant polycystic kidney disease; MA: marketing application

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Torii: Finally, I would like to give the R&D update.

Page 15 introduces the expected flow for next-generation strategic products in the near future.

The orange check mark indicates the events that have been completed from the beginning of the year until today. Today, we will briefly introduce the progress since the previous announcement of financial results.

First, we reported the top line data for Phase 2 trials in patients with moderate and severe atopic dermatitis on February 18 for KHK4083. More detailed data is scheduled to be presented in the annual academic conference. In addition, we will steadily prepare for the Phase 3 trial in response to the achievement of the main evaluation items for Phase 2.

For ME-401, we completed registration of the population to be analyzed for follicular lymphoma in the single-agent trial, the TIDAL Phase 2 trial. This was announced on April 14 jointly with MEI Pharma. The report of top-line data is scheduled for the fourth quarter of this year.

Finally, as released on April 13, regarding KHK7791, 4 Phase 3 clinical trials have begun in Japan for patients with hyperphosphatemia undergoing dialysis.

This concludes the R&D update.

Question & Answer

Moderator: Now I would like to move on to the Q&A session. I am very sorry, but I would like to limit speakers to 2 questions at a time. Thank you.

Yamaguchi: This is Yamaguchi from Citigroup Securities. Thank you. The first question is a follow-up regarding the unrealized profit.

I believe this has come up in the past other companies' cases also, but I understand the figure was decided based on the difference in exchange rate between the end of last December and the end of this March. I think that if you look at it across the full year, it will gradually fade depending on the state of exchange.

Although it is a technical issue, I think it can be considered that it remains to some extent throughout the year. In comparison with the Company's forecast, I wonder if this does not become a negative factor for the full year. That's the first question.

Kawaguchi: Yes. Thank you for your question. I will answer. I believe it is, but in this full year, even if this amount remains the same, as you say, the ratio will be diluted by a factor of 4. It diminishes in terms of profitability impact.

Then, the other point is that if the current yen depreciation level continues in the year, on the contrary, our foreign exchange sensitivity means a positive impact of JPY500 million given a drop of JPY1. In this way, I think that we will cover the negative factors as a whole.

In total, I think that it will not have such a big impact over the year, but the effect in the first quarter has been a little larger.

Yamaguchi: Understood. Second question. It's about KHK4083, regarding detailed data of the Phase 2b trial.

I have a recollection that you mentioned it was autumn before, but I think there are many conferences, whether in America or Europe, immunology or dermatology.

I believe the largest was postponed, but I was wondering if you could disclose at which academic society meeting you are aiming to present?

Torii: Yes. Thank you for your question. For now, we are preparing for presentation at the European Academy of Dermatology and Venereology, EADV, conference, which is scheduled to be held at the end of September this year.

Yamaguchi: I understand. Thank you. Those are all my questions.

Wakao: This is Wakao from JP Morgan Securities Japan. Thank you.

Please tell us about the status of Crysvita in Japan. There was a comment that self-administration also contributed, but it seems to be a very high progress rate for the full-year plan.

How is this first quarter performance going against the plan? Is it okay to think that the results so far are higher than expected? That's the first question.

Sudo: Yes. I would like to answer. As you said, I believe that sales of Crysvita in Japan are trending upward of the plan.

Although it has been on the market in the United States since 2018, it has just launched in the Japanese market, so there is still room to grow. JPY5.5 billion is the target for the year, but if we continue at this pace, I think that it will be higher.

Wakao: Thank you. The second question is about KHK4083, but I think it has been assumed that the KHK4083 has been developed in-house or alliances with other companies from the past. After obtaining the results of this phase 2b test, I would like to know about the strategy in this area right now. If you are going to co-develop with other companies, when will the alliance itself be concluded? Can you comment on the timeframe you are aiming for? Those are all my questions.

Sudo: I would like to answer. First of all, I think that it is still the most important thing to create a system that allows us to develop independently.

As you all know, this may be a very big market, so when it comes to maximizing the product value, there is the question of an alliance or something similar, and of course, this is not limited to KHK4083 alone. I always want to explore other possibilities.

Wakao: If you are going to make an alliance, can you tell me when you anticipate it will take place? I think the Phase 3 trial will also be initiated next year. Do you have any plans, for example, to create an alliance before the Phase 3 trial? Could you answer in those terms?

Sudo: Indeed. I couldn't give any specific timing, of course. If we find a good partner, a partner that meets the conditions, of course, it will go ahead, and if the partner does not meet the conditions, we are thinking based on the plan that we will develop firmly in our own company.

Wakao: I understand. Thank you.

Ueda: This is Ueda from Goldman Sachs Japan. Thank you. I would like to ask about the gross margin for the first point.

This was mentioned earlier. The effect of erasure of unrealized profit was discussed, but could you describe the degree of effect in terms of amount or gross margin ratio, on the first quarter results please?

Kawaguchi: It is quite difficult to explain the amount. Compared with the previous fiscal year, the figure is large, but it in terms of a ratio, about 2% in the first quarter; I think that's the impact. As I mentioned earlier, this denominator is only one quarter of sales, so in those terms it will be quite a big percentage impact. The fact that the effect of this denominator is diminished when seen over the fiscal year shows that it does not have such a big impact.

I'm sorry that the explanation is not very clear.

Ueda: No, thank you. In that case, I think there was a gross margin of 72.4% in the quarter, so it actually comes out at a rate of about 74%-75%. In this case, to some extent, against this gross margin forecast of 76.9% in the full year, is it possible to understand the progress as being as planned?

Kawaguchi: As you say, our best seasonal product in this first quarter has been Patanol. Approximately 60% of annual sales are in the first quarter, and this is a purchased product, so the profit margin is not so high.

Due to the product mix, the figures are a little lower in the first quarter, so we hope you understand that there is also a factor that aims to be close to 77% over the whole year.

Ueda: Thank you. I would like to ask about KHK4083.

When the top line results were published in February, I think there was a mention of exacerbation of atopic dermatitis being among the side effects.

What can be considered as the cause, and I would like to know whether the side effects of this could be the risks in future development, including whether or not it is manageable. I think it's hard to comment before the conference, but could you give us any hints about this?

Torii: Thank you for your question. It is not the case that effectiveness is observed in all patients, so in that sense there is a possibility that it can be ineffective or worse for some patients. In this regard, KOLs both in Japan and abroad are analyzing the data in detail, but we have confirmed that it will not be a major obstacle to our development of Phase 3 in the future. Those are all my answers.

Ueda: Thank you very much. That's all from me.

Sakai: This is Sakai from Credit Suisse Securities Japan. Thank you. Excuse me, I'm sorry for being a bit persistent, but at the beginning, regarding the inventory issue, Mr. Kawaguchi said there are tens of billions of yen in overseas inventory.

I think the inventory on your balance sheet is JPY55.1 billion at the end of the previous fiscal year.

Could you be a bit more specific about the scale of this figure? This is the first question.

Kawaguchi: Yes. Thank you for your question.

This 'tens of billions of yen' inventories are not inventories that we are purchasing from outside, but specifically inventory of our own global products: Crysvita, Poteligo, and so on.

In this case, the cost of manufacturing within our company is very low, so the actual amount of inventory after erasing by consolidation is small. Since this is manufactured in Japan, we are shipping with adding transfer price profit when shipping to the United States.

If we do so, the amount of inventory we have in the US affiliate looks big. Elimination of it is unrealized profit, and mostly, the profits are greater. As a result of erasing it, the inventory amount becomes small.

Then, where the amount to be erased is large, it comes out in the effect of the big foreign exchange loss I mentioned earlier. Does that make sense?

Sakai: After all, considering the COGs rate of approximately 20%, a significant portion of the profit is erased, right?

Kawaguchi: As you say.

Sakai: I understand. One more question, this may be a bit early, but I'd like to get an update on the status of TIO for Crysvita. Please let us know if you have any response, exchange of opinions with key opinion leaders, and/or any reactions.

Sudo: Indeed. I would like to answer. To be honest, we have yet to see any concrete response from the market. As for our expectation, I may have mentioned before, I believe that TIO can still be around 10% of the whole Crysvita market. However, we don't know the number of TIO patients. In the U.S., it has been just under a year since the additional approval in June last year, and we have seen a steady flow of patients. However, we have yet to see an acceleration in sales that meets our expectations.

The number of TIO patient in Japan is steadily increasing, and some are talking about a considerable number of patients in China. In the future, although this includes Europe and the United States, I think it is necessary to diagnose and solidly deliver care to TIO patients.

At the moment, we do not have a strong response yet, but we are making steady progress in penetrating the market.

Sakai: Then, TIO sales have been included in the figure of Crysvita for sure?

Sudo: Indeed. Of course.

Sakai: I understand. So, the details may come next time. Thank you so much.

Muraoka: Hello. This is Muraoka from Morgan Stanley MUFG Securities. Thank you.

Regarding Crysvita. The overseas part, outside the United States, also seems to be in good condition, but earlier, there was a mention of launch country count increasing. I believe there hasn't been a detailed breakdown of guidance, would it be correct to say that you are expecting it to come in above the forecast, as same as that of Japan? That is my first question.

Sudo: Indeed. In Europe, as you mentioned, the pediatric indication was first obtained, and after that, price negotiations were conducted at different times in different countries, and finally, the launch countries are almost lined up. In that sense, in Europe, we are finally at the complete starting point, in terms of treatment for children.

And, as another very important impact last year, we have obtained indications for adults. This is a very important market, starting from Germany.

These factors have given a big boost to the market from last year to the first half of this year, and I think that the trend of growth in Europe is probably going to continue in the future.

Muraoka: Excuse me. It's a bit of a repeat confirmation, but in that sense, is it okay to understand that you are expecting the forecast to go up?

Sudo: In fact, the impact of coronavirus is still very strong compared to the United States. In particular, in southern Europe there is a situation where most sales activities are not possible, so in that sense, there is no situation in which there is a big upward swing. Our expectations at the moment are as planned.

Muraoka: I understand. Thank you. My second question is about KHK4083. There has been a problem with the competing JAK inhibitors, and an IL-13 antibody has got a complete response letter, so competitors other than Dupi have a variety of problems or a weak effect.

In the present situation, which do you see as the biggest competitor to the OX40 drug? Or rather, which do you see as having the most similar profile? It would be helpful if you can tell me a little about that.

Torii: Thank you for your question.

Basically, different from Dupixent and so on, and JAK inhibitors, this KHK4083 is an antibody against OX40, a completely new mechanism. And this drug binds to OX40, which is present on T cells, which play an important role in this autoimmune disease.

Furthermore, by using our Potelligent technology to remove these cells, we can expect quite potent medicinal properties.

Even compared to Dupixent or others, I think there is a strong potential.

Muraoka: The fact that you can fight with Dupixent means that you can fight in the effectiveness part, right? Or, are you suggesting that, for example, the dose interval might also be large? Are you able to compete in effectiveness?

Torii: I am considering the design of phase 3, and I would like to discuss it again when it becomes possible to make a detailed presentation.

Muraoka: I understand. Those are all my questions. Thank you.

Tanaka: This is Tanaka from Mizuho Securities. The first question is about RTA 402, which wasn't mentioned today.

I think the filing was accepted in the United States for Alport syndrome, but I think it was written that there will be an AdCom, and I was wondering if there is any cause for concern there.

Reata has mentioned that there are patients from 30,000 to 60,000 in the United States, which is quite different from the 1,200 patients in Japan. Can you comment on this?

Torii: Yes. Thank you for your question. As for the Alport syndrome, as you asked right now, Reata filed in the US on March 1, and it was accepted on April 26. We are communicating with Reata, but they have not shown any concerns about the approval.

Regarding the difference in the number of patients, the details here are a bit unclear, but I still have not been able to grasp the actual situation in Japan in detail. There is a discussion about accuracy there, so I would like to continue investigating this part in the future. That's all from me.

Tanaka: I understand. Also, for the second point, it was mentioned that enrollment was completed for ME-401. As you wrote in your company's release, the figure for efficacy is 91 cases for follicular lymphoma. Is that sufficient to observe a difference?

Torii: Yes. As you say. Based on the data so far, there was a discussion with the FDA about the number of cases and various analysis considerations. The agreement was made for 91 cases for the analysis.

However, we do not end recruiting then since we want to collect additional safety data, so the entry itself will continue a little more.

Tanaka: The other MZL leaves 64 cases, and does this mean that the top line is at different times?

Torii: Yes. For now, the first patient in will be scheduled for the middle of 2021, so this will start later than the Follicular lymphoma.

Tanaka: I understand. Thank you very much.

Kohtani: This is Kohtani from Nomura Securities. Thank you. This question might be a little technical.

If you look at the disclosed data for KHK4083, three injections of 10 mg per kg once every 2 weeks in the phase 1 trial showed a reduction of 70% in the TARC score until 22 weeks later. The EASI score also decreased in the same way.

For dupilumab, there is no 3-dose data, so if you look at the results of the phase 1 trial of a single dose, there is only a 20% decrease even after about 10 weeks, and a result of 20% reduction with 300 mg subcutaneous injection, returning to its initial value after 57 days.

If you think that way, I think that the TARC is very sustained, given a normal antibody has a half-life of about 2 weeks. It is good to understand that this effect leads to the depletion of memory cells, and to see that these phenomena are occurring.

I think this mechanism will probably be validated when the results of this phase 2b trial come out. Is it okay to understand that such data will also be provided? This is the first question.

Torii: Yes. As you explained in your question, that is the case. We would like to report more details at EADV other than the top-line data, including biomarker movement if possible. That's all from me.

Kohtani: This is the second question, but my understanding is that the anti-OX40 drug is not just a drug for atopic dermatitis. It could be used for autoimmune diseases quite widely.

However, the level of evidence is not so strong, even if you are looking at GWAS, genome-wide associated analysis. After all, the odds ratio is around 1.4, so it is not that high.

Even if you look at other pathological evidence, you can certainly see the rise of OX40 in various conditions such as rheumatoid arthritis, but the evidence is still not that strong.

Which is significant for your company. Are you considering interactions for other autoimmune diseases after establishing effectiveness in the phase 3 trial with atopic dermatitis?

Or are you considering checking this at an earlier stage? A Phase 1 trial or something similar can be started earlier. What are your thoughts on this? This is the second question.

Torii: Yes. Thank you for your question. We are now considering all the options to maximize the value of this drug, as was mentioned earlier. So, rather than having finished the verification with atopic dermatitis, and then start considering other indications, we are already researching what indications are possible. I would like to continue these activities without waiting for the results of the phase 3 trial.

Kohtani: Is that activity only preclinical? Or would it include a clinical trial?

Torii: If there are effective results, including non-clinical, I would like to proceed to clinical early stages.

Kohtani: I understand. Thank you.

Hashiguchi: This is Hashiguchi from Daiwa Securities. Thank you.

The first is about the development of KHK4083. Various options are being considered for atopic dermatitis and other indications. What impact will this have on research and development costs?

In the midterm plan, I think there was guidance of actively investing from 18% to 20%. Was it about JPY400 billion in total? What kind of options were included in this estimate?

Including the change in possible future returns, to what extent do you think that your R&D costs may increase above this guidance?

Kawaguchi: Yes. I will answer this.

With regard to the premise of midterm spending of 18% to 20%, it is actually a concrete development plan from around 2021 through to 2023, and we plan to stick to that amount.

When it comes to around 2024 and 2025, we anticipate that sales will also increase, so we have leeway to increase R&D spending accordingly. As for KHK4083, the specifics of those options are not included in the forecast.

Even if any partnering would come up in the 2024 or 2025, the goal would be to increase profitability after aggressive R&D spending for the development of KHK4083.

Hashiguchi: In that sense, I guess there are still several options on the table.

As for the current prospect, is it correct to say that costs seem to fit within the frame you indicated for this medium-term plan?

Kawaguchi: Yes. At the moment, we would like to prioritize firmly and invest within that frame.

Hashiguchi: Thank you. The second point is about the reason for the difficulties with Duvroq. It was mentioned earlier that there is a restriction on long-term prescriptions.

At the time of the pre-launch, I think you mentioned as an advantage that the differentiating factor is that there are many forms, which makes dose adjustment easier.

However, the products of other companies that received approval after Duvroq do not list all of the approved forms, and the reason for narrowing down the list of forms seems to be that having multiple forms would make inventory management and dosage adjustment rather complicated.

I think companies coming later are looking at your situation, so it may seem that just having a lot of different doses available doesn't necessarily lead to positive results.

Can you tell us what you think about the sales outlook after the restriction to long-term prescription has been lifted?

Yamashita: Thank you, I will answer.

Currently, Duvroq is facing difficulties because of the restriction, as you mentioned. The long-term prescription is not available yet.

Conversely, if the long-term prescription were available, it would be possible to reduce the frequency of hospital visits, which is important during the coronavirus pandemic. I believe that for reasons such as this, being able to launch a long-term prescription is very beneficial. So, the current point is, I think that the impact of the coronavirus pandemic is large.

We cannot grasp at the moment the influence that having several different forms has.

In fact, we have a proven track record with Espo, Nesp, in that these have a very large number of forms. This is important in treating anemia.

In terms of relationships with other companies, I would like to look at the points you pointed out in the future. That's all from me.

Hashiguchi: Yes, thank you very much. That's all from me.

Yamaguchi: This is Yamaguchi from Citigroup. I'm sorry. Is it okay? A further question. Thank you.

The first is about tivozanib, as I think there was no update about it this time. Tivozanib for AMD. It looks the ongoing trial in Japan is compared with the placebo and is an oral medication trial comparing safety. Going into phase 2, will the route of administration of the drug be changed to eye drops when assessing effectiveness? Please tell me a little bit about the current formulation and future formulation.

Torii: Yes. Thank you for your question. This is listed on ClinicalTrials.gov, but now it is not oral, and in phase 1 it is tested as eye drops. It is being tested in healthy people and those with AMD.

Yamaguchi: I see. So, in the future, it will be tested as eye drops.

Torii: Yes. That's right.

Yamaguchi: I understand. Thank you. The second question is about another item that was not mentioned this time. There was a 2-by-2 Kyowa Kirin bispecific antibody series introduced at the R&D day meeting.

It's presumably hard to say how this will feature in this fiscal year or next fiscal year, but there was a mention to start a trial during this mid-term cycle. However, that is not very specific. Has anything more specific been decided, such as clinical trials in the next fiscal year, for example?

Torii: Thank you for your question. Now, we are preparing with the research department so that it can be put in clinical trials as soon as possible, so I would like to explain when it becomes possible to present it in more detail.

Yamaguchi: Can you be any more specific about timing now?

Torii: Indeed. I am afraid not.

Yamaguchi: I understand. Yes. Thank you. That's all from me. Excuse me.

Moderator: We will end the conference call here. Thank you very much for joining us today. Thank you for your support.

[END]