



Kyowa Kirin Co., Ltd.

Q1 Financial Results Briefing for the Fiscal Year Ending December 2023

May 10, 2023

Event Summary

[Event Name]	Q1 Financial Results Briefing for the Fiscal Year Ending December 2023	
[Date]	May 10, 2023	
[Number of Speakers]	4	
	Motohiko Kawaguchi	Managing Executive Officer, Head of Finance
	Yasuo Fujii	Managing Executive Officer, Head of Strategy
	Yoshifumi Torii	Executive Officer, Head of R&D
	Tomohiro Sudo	Executive Officer, Head of Global Product Strategy

Presentation

Moderator: We will now commence the teleconference for the Q1 financial results briefing for the fiscal year ending December 2023 of Kyowa Kirin Co., Ltd., which we announced at 3:30 PM today.

Before we begin the briefing, there are some points to note. Please understand that we will keep the names and company names of all participants on a list for a certain period within our company. Furthermore, the contents of this briefing will be made public on our website in the form of on-demand audio distribution and transcripts. We ask for your understanding and discretion in your remarks.

The content we will present today includes forward-looking statements. Please note that there are uncertainties due to various risks.

Today's speakers and those handling questions are Managing Executive Officer and Head of Finance, Motohiko Kawaguchi; Managing Executive Officer and Head of Strategy, Yasuo Fujii; Executive Officer and Head of R&D, Yoshifumi Torii; and Executive Officer and Head of Global Product Strategy, Tomohiro Sudo.

We plan for today's teleconference to last up to 90 minutes. After explaining the overall financial results, we will take questions from you. Please download the materials from our IR website.

Summary of Q1 Results

(Billion Yen / Rounded)

	2022Q1 Results	2023Q1 Results	Changes	2023 Revised Plans	Progresses
Revenue <i>[Overseas Ratio]</i>	87.8 <i>[58%]</i>	93.5 <i>[63%]</i>	+5.8 (+7%)	426.0 <i>[64%]</i>	22%
Gross Profit <i>[Gross Profit Margin]</i>	65.6 <i>[75%]</i>	74.6 <i>[80%]</i>	+9.0 (+14%)	326.0 <i>[77%]</i>	23%
SG&A <i>[SG&A Ratio]</i>	36.1 <i>[41%]</i>	41.8 <i>[45%]</i>	+5.7 (+16%)	162.0 <i>[38%]</i>	26%
R&D <i>[R&D Ratio]</i>	13.6 <i>[16%]</i>	16.6 <i>[18%]</i>	+3.0 (+22%)	79.0 <i>[19%]</i>	21%
Gain/Loss on Equity Method	1.4	0.8	-0.6 (-44%)	3.0	27%
Core Operating Profit <i>[Core OP Margin]</i>	17.3 <i>[20%]</i>	17.0 <i>[18%]</i>	-0.4 (-2%)	88.0 <i>[21%]</i>	19%
Profit	16.0	12.8	-3.3 (-20%)	76.0→70.0	18%

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Kawaguchi: Good afternoon, everyone. I am Kawaguchi, and I will explain the financial figures for Q1. Please refer to page five of the slides.

Firstly, compared to the same period last year, revenue increased by JPY5.8 billion, a 7% increase. Core operating profit decreased by JPY400 million, a 2% decrease, and quarterly profit decreased by JPY3.3 billion, a 20% decrease.

The decrease in core operating profit is mainly due to the increased cost of establishing our own direct sales system for Crysvita in North America. After the start of direct sales with our own sales force on April 27, our obligation to cover 50% of sales expenses spent by Ultragenyx will decrease. However, in Q1, we temporarily incurred doubly the sales and administrative expenses.

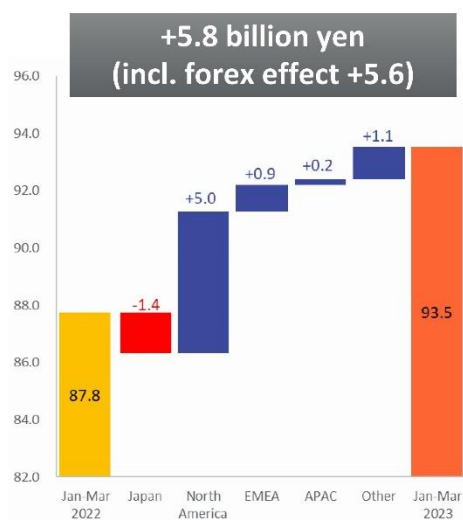
In addition, the quarterly profit decreased by 20% due to increased other expenses.

Regarding the full-year forecast, we decided to record an impairment loss of JPY8.3 billion in Q2 due to the discontinuation of development of RTA 402, which we will explain in more detail later. Consequently, we revised the current profit forecast down from JPY76 billion to JPY70 billion, a JPY6 billion downward revision.

Although the progress rate for revenue against the full-year forecast seems slightly low, Q1 tends to show this trend every year, and we are progressing generally within the planned range.

We continue to aim to achieve our full-year plan through sales growth centered on global strategic products and cost control.

YoY Analysis -Revenue-



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● Japan -1.4

Although Duvroq, Romipate, and Crysvita increased, revenue in Japan region decreased by 4% due mainly to negative impact by NHI price-cut in April 2022 and shrink in Nesp-AG and Allelock affected by competitive products.

● North America +5.0 (incl. forex effect +3.5)

Revenue in North America region increased by 24% with the growth of Crysvita(+19%), Poteligeo(+31%), and Nourianz(+46%).

● EMEA +0.9 (incl. forex effect +0.7)

Revenue in EMEA region increased by 6% with the growth of Crysvita(+27%), and Poteligeo(+60%).

● APAC +0.2 (incl. forex effect +0.5)

APAC revenue increased by 3% with the growth of Crysvita, and Nesp, while Gran was down due to the Chinese national tender system.

● Other +1.1 (incl. forex effect +0.9)

12% growth in the other revenue was due to the royalties of growing Fasenna (Benralizumab).

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Now, let me explain, starting with revenue compared to the previous year.

Please refer to page six. This is the regional breakdown of revenue.

In Japan, despite continued growth in Duvroq and Crysvita, primarily due to the impact of the NHI drug price-cut in April last year, Nesp-AG and Allelock saw a decrease in revenue, resulting in a 4% decrease in the Japan region.

Both North America and EMEA saw increases in revenue of 24% and 6%, respectively, thanks to the robust growth of global strategic products centered on Crysvita and the impact of a weaker yen.

APAC saw a decline in Gran due to being listed in the national tender system in some parts of China, but sales of Crysvita, which started in Australia last November, grew. Furthermore, with the tailwind of the exchange rate, it resulted in a 2% increase.

As for other revenue, the royalties from Fasenna continued to increase, resulting in a 12% increase in revenue.

Revenue of Major Items (Japan)

(Billion Yen / Rounded)

Item	2022Q1 Results	2023Q1 Results	Changes	Reasons	2023 Plans	Progresses
Nesp + Nesp-AG ¹	5.2	4.2	-1.0 (-20%)		16.6	25%
Nesp	0.8	0.8	-0.1 (-9%)	NHI price-cut & Biosimilars' penetration	2.8	27%
Nesp-AG	4.4	3.5	-1.0 (-22%)		13.8	25%
Duvroq	1.1	1.8	+0.7 (+65%)	Market penetration (Launched in Aug 2020)	7.8	23%
Orkedia	2.2	2.2	+0.0 (+1%)		11.2	20%
G-Lasta	7.1	7.0	-0.1 (-1%)		33.5	21%
Poteligeo	0.5	0.4	-0.0 (-6%)		2.0	22%
Rituximab BS	2.5	2.2	-0.3 (-14%)	NHI price-cut	8.7	25%
Romiplat	2.2	2.7	+0.5 (+23%)	Market penetration (New indication in 2019)	11.2	24%
Allelock	2.4	1.9	-0.5 (-19%)	NHI price-cut	4.7	42%
Nourias	1.8	1.7	-0.1 (-5%)		7.5	22%
Haruropi	0.8	0.9	+0.2 (+21%)	Market penetration (Launched in Dec 2019)	4.7	20%
Crysvita	2.0	2.3	+0.3 (+18%)	Market penetration (Launched in Dec 2019)	11.1	21%

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.

Now, please turn to page seven for the situation by product in Japan.

Nesp-AG has seen a decline in sales due to the NHI drug price-cut and competition, but it is progressing smoothly against the plan.

Duvroq continues to grow steadily and maintains the number one share within its class.

Allelock saw a decrease in revenue due to the NHI drug price-cut even though the amount of pollen dispersal was higher than expected.

Crysvita continues to grow steadily with an 18% increase compared to the previous year.

Revenue of Major Items (ex-Japan)

(Billion Yen / Rounded)

Item	2022Q1 Results	2023Q1 Results	Changes	Reasons	2023 Plans	Progresses
Crysvita	22.2	27.1	+4.9 (+22%)		138.0	20%
North America	15.8	18.8	+3.0 (+19%)	[North America] Market penetration [EMEA] Geographical expansion & Additional indication (Adult/TIO)		
EMEA	6.3	8.0	+1.7 (+27%)			
APAC	0.0	0.3	+0.2 (+726%)			
Poteligeo	4.2	5.8	+1.6 (+38%)		27.5	21%
North America	3.3	4.3	+1.0 (+31%)	[North America] Market penetration [EMEA] Geographical expansion & Market penetration	19.4	22%
EMEA	0.9	1.5	+0.6 (+60%)		8.0	19%
APAC	-	-	-		0.2	-
Nourianz	1.1	1.7	+0.5 (+46%)	Market penetration	7.5	22%
Nesp	1.9	2.2	+0.3 (+18%)		8.0	28%
Gran	2.1	1.4	-0.7 (-31%)	Listed on Chinese tender list	8.2	17%
Neulasta	1.7	1.3	-0.4 (-23%)		5.7	23%
Tech-licensing	7.7	8.9	+1.2 (+16%)	Growth of Fasenna	39.0	23%
Benralizumab Royalty ¹	4.7	5.7	+1.0 (+22%)			

¹ Sales royalties of Fasenna which has been marketed by AstraZeneca, including our own estimation.

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Next, please turn to page eight. This slide shows the situation with our major products overseas.

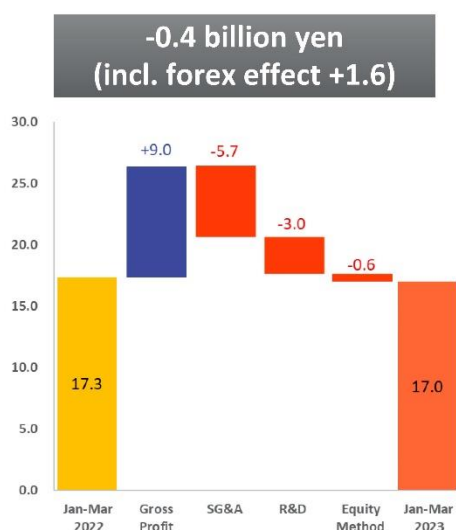
Firstly, Crysvita continued to grow, with a 22% increase in revenue compared to the same period last year.

Poteligeo also showed a strong growth of 38% compared to the same period last year. North America is doing well, and in EMEA, the expansion of countries where it is on the market and market penetration have progressed well, leading to increased revenue.

Nourianz is also steadily growing.

Tech-licensing progressed smoothly, with royalties from Fasenna (Benralizumab) contributing to a JPY1 billion increase in revenue.

YoY Analysis -Core OP-



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● Gross Profit +9.0 (incl. forex effect +5.2)

Increased in conjunction with JPY5.8B rise in revenue. Margin improved by 5% (75%→80%) due mainly to increased proportion of profitable "Global 3 brands" and tech-licensing revenue.

● SG&A -5.7 (incl. forex effect -2.6)

Increased in HR exp, etc by preparation for the transition of Crysvita commercial leadership role and investment in IT/Digital infrastructure and human resources for global business foundation, in addition to Crysvita profit sharing expenses for North America.

[HR exp -2.2 / Sales promotion -1.6 (incl. Crysvita profit sharing expenses -1.3)]

● R&D -3.0 (incl. forex effect -1.1)

Increased in clinical study costs of KHK4083.

● Gain/Loss on Equity Method -0.6

While revenue of Hulio (FKB327/Adalimumab biosimilar) increased, FKB's profit declined due to decrease in tax-accounting effect.

FKB; Fujifilm Kyowa Kirin Biologics Co., Ltd.

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Now, let's move on to page nine.

First, regarding gross profit, due to the growth of global products and improvements in product mix, the gross profit margin improved by 5%, resulting in an increase in gross profit of JPY9 billion.

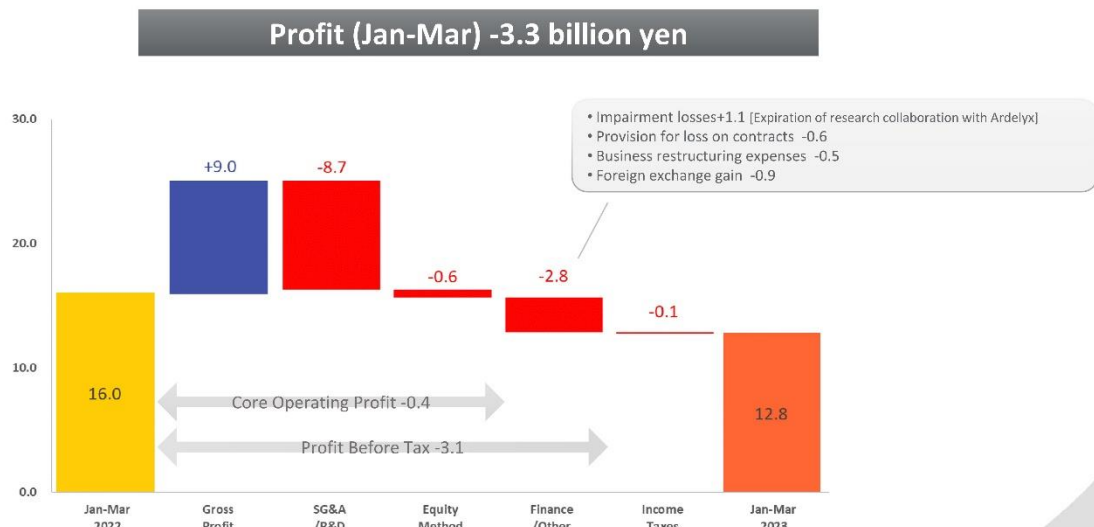
SG&A expenses increased by JPY5.7 billion. Of this, about JPY2.2 billion was due to increased costs, such as personnel expenses for starting up our own direct sales force of Crysvita in North America, as mentioned earlier. In addition, North American profit-sharing expenses increased by JPY1.3 billion due to increased sales of Crysvita. There was also an exchange rate impact of JPY2.6 billion.

R&D costs have increased by JPY3 billion due to the progress in development of KHK4083 and other pipelines. The exchange rate impact here is JPY1.1 billion.

The equity method gain/loss was a loss of JPY600 million. This is due to the impact of the additional booking of deferred tax assets at Fujifilm Kyowa Kirin Biologics in the same period last year.

As a result of these factors, core operating profit was down by JPY400 million.

YoY Analysis -Profit-



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Please turn to page 10. In this slide, I would like to introduce the portion below the core operating profit.

As indicated by the speech bubble, there is a JPY2.8 billion loss in finance and others.

We booked an impairment loss of JPY1.1 billion due to the expiration of our joint research contract with Ardelyx. In addition, the increase in contract loss provisions, business restructuring expenses, and the decrease in foreign exchange gain have become factors contributing to a total decrease of JPY2.8 billion.

As a result of these factors, the quarterly profit was JPY12.8 billion, a decrease of JPY3.3 billion compared to the same period last year.

That's all from me.

Sudo: Now, I would like to continue with an update on our commercial operations. I am Sudo, in charge of Global Product Strategy. Thank you for having me.

First, Crysvita, Poteligeo, and Nourianz, which we refer to as G3B, have now been on the global market for four years to five years. Thanks to you all, last year's G3B sales, which were launched in 2018, grew from about JPY20 billion to about eight times that, at JPY165.8 billion. In particular, we are witnessing strong global growth, especially with Crysvita at the center.

At the field level, various activities have led to the accumulation of experience and knowledge. Going forward, in addition to promoting individual product strategies, we plan to fully utilize the experience and knowledge we have gained so far to deliver value to more patients. We aim to further grow our business by enhancing field activities aimed at improving patient access.

With that in mind, we have included the subtitle "Coordinated Actions to Maximize the Patient Access to G3B" in this presentation.

2023 Key Actions

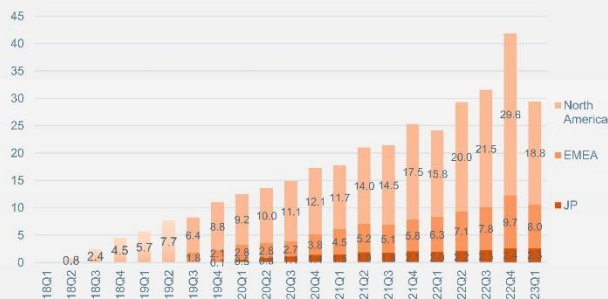
- North America:
Start own sales (Establish and start own operation of the direct sales force).
- EMEA:
Continue to focus on geographical & indication expansion.
- Japan:
Strengthen promotional activities centered by the dedicated personnel.

Q1 Topics

- North America:
• Establishment of own operation of the direct sales force progressed as planned.
• The number of patient enrollments in the treatment preparation stage increased steadily, despite a rebound sales from year-end load-up purchase by wholesales.
• Patient penetration rate in U.S.* : Pediatric XLH 39%, Adult XLH 11%
- EMEA:
• Launched in Italy, Romania, and Scotland for adult XLH
- Japan:
• Patient finding is progressing steadily.

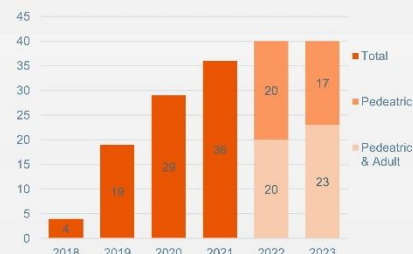
*Patient penetration rate in US is a rough estimate based on our calculations.

Sales Revenue (Billion Yen)



*Revenue from EAP (Early Access Program) is not included in sales until FY2022, and is included in sales from FY2023 onwards as it is insignificant in monetary terms.

Launched Countries / Regions (XLH)



*Excludes Latin America and Turkey, where Ultragenyx records sales.

Moving on to page 12, I would like to talk about Crysvita first.

Starting with our own sales initiative in North America, we have completed the establishment of our own direct sales force as planned, and as of April 27, we have started our own sales activities as per the contract. This is the point I would like to announce first. Over the next year, we will continue to collaborate with Ultragenyx to ensure our steady growth without losing the momentum we have built.

Next is the sales situation in North America. Looking at the graph on the left, it shows the sales revenue trend over the five years since we launched in 2018, but our sales revenue for this quarter appear to be significantly below the previous quarter.

We believe the reason for this is the pullback from the unexpected surge in wholesale buying at the end of 2022, in anticipation of price revisions from the beginning of the year. As I mentioned earlier, there was a larger-than-usual bulk purchase, so the pullback was also significant.

On the other hand, compared to the same period last year, we are seeing a 19% increase, confirming that we are continuing to grow steadily.

As of March, the penetration rate of Crysvita among patients with XLH in the US, based on our estimates, is at 39% for pediatric and 11% for adults.

There is also a step where we ask for a starting form to be filled out before starting treatment, and the number of these patients is also increasing steadily. We would like to continue to aggressively pursue activities aimed at penetrating the market.

Next is EMEA. In this quarter, we have achieved the expansion of the XLH adult indication in three regions: Italy, Romania, and Scotland. We would like to continue to firmly advance the expansion of markets and indications in the future. Regarding sales revenue, although they are below the previous quarter, like in the US, we are seeing steady growth compared to the same period last year.

In Japan as well, we are making progress roughly as planned, and we aim to further expand the market.

2023 Key Actions

- Strengthen promotional activities utilizing evidences including blood tumor data.
- Raise awareness of importance of blood testing among early-stage patients

Q1 Topics

- Continued promotional activities utilizing evidences including blood tumor data.
- Continued raise awareness of importance of earlier consultation with specialists and blood testing through the disease awareness website (PROBE IN CTCL).

* Revenue from EAP (Early Access Program) is not included in sales until FY2022, and is included in sales from FY2023 onwards as it is insignificant in monetary terms.

Sales Revenue (Billion Yen)



2023 Key Actions

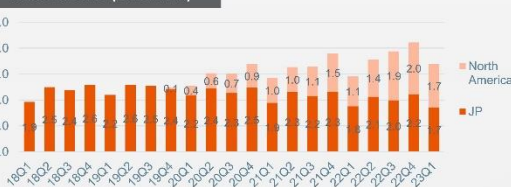
- Further instill importance of adenosine A_{2A} receptor antagonism in treating wearing-off.
- Strengthen field level activity through further collaboration and knowledge sharing between Japan and the US, and through maximizing available resources by utilizing effective approaches including digital.

Q1 Topics

- Established a social media channel in North America which stores all videos that has been created including mechanism of action of NOURIANZ, patient testimonial video and others.
- Implemented digital tool that provide standardized information (e.g., market access-related data) to field personnel.

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Sales Revenue (Billion Yen)



Moving on to the next page, let's talk about Poteligeo.

Sales revenue for the current quarter fell below the previous quarter but showed an increase of 31% in the US and 60% in Europe year on year, resulting in nearly meeting the planned sales revenue.

We want to continue to advance market penetration by enhancing our marketing activities using evidence, as well as working on activities to raise awareness of early visits to specialists and blood tests for early-stage patients.

Finally, we have Nourianz.

Although the sales revenue for this quarter was below the previous quarter, we believe we were able to achieve sales revenue roughly as planned. Sales revenue in the US has grown steadily, with a 46% increase year on year.

Through steady progress on the key actions we mentioned at the beginning of the year, we want to continue focusing on improving patient access through thorough field activities and continue our efforts.

That's all for the commercial update.

Upcoming Events: Main Development Pipeline Products

Code Generic Name	Events (Completed are in bold)	Timeline (Completed are in orange)
KHK4083/AMG 451 rocatinlimab	Atopic Dermatitis P3 Initiation	Dec. 2022
KHK4951 tivozanib	nAMD P1 LPO P2 Initiation	Aug. 2022 H2 2023
ME-401 zandelisib	Discontinuation of development in Japan	Disclosed May 2023
RTA 402 bardoxolone methyl	Discontinuation of development for AS, DKD, and ADPKD	Disclosed May 2023
KHK7791 tenapanor	Hyperphosphatemia under maintenance dialysis: Regulatory decision to be announced (JP)	H2 2023
KW-3357 antithrombin gamma (genetical recombination)	Preeclampsia P3 LPO Topline data	H2 2023 H2 2023

LPO: Last Patient Out; DKD: Diabetic Kidney Disease; AS: Alport Syndrome; ADPKD: Autosomal Dominant Polycystic Kidney Disease; nAMD: Neovascular age-related macular degeneration

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Torii: I'm Torii from the R&D Division. I will be providing updates related to R&D.

Please refer to page 15. Here, I will explain points of update regarding the news flow for the entire main development pipeline.

Firstly, ME-401, or zandelisib. Based on the results of Phase II trials in Japan and abroad, we have been discussing with the authorities toward an approval application. However, the PMDA has indicated that additional randomized controlled trials are necessary to dispel concerns about the safety of the entire class of PI3 kinase inhibitors to which zandelisib belongs.

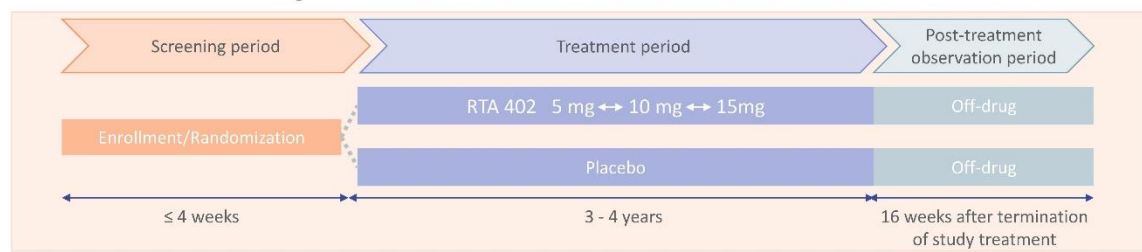
As a result, we have determined that it is difficult to apply for approval based on the results of the TIDAL and MIRAGE trials, which were single-arm Phase II trials and to conduct additional randomized controlled trials. We have therefore decided to discontinue the development of this product in Japan.

Next, regarding RTA 402. As we reported in the news release earlier, we have decided to discontinue the development of this drug after a detailed review of the top-line data from the Phase III trial for diabetic nephropathy, the AYAME trial. I will explain about this in the next slide.

Next, regarding KHK7791, which we applied for last year, we expect to have the results in H2.

Furthermore, for KW-3357, we plan to disclose top-line data after the final participant has completed their involvement (last patient out) of the Phase III trial for preeclampsia, which is scheduled for H2, aiming to do so within this year.

RTA 402 Ph3 study results



Primary Endpoint	Time to onset of a $\geq 30\%$ decrease in eGFR from baseline or ESRD	Meet the endpoint
Major Secondary Endpoint	Time to onset of a $\geq 40\%$ decrease in eGFR from baseline or ESRD	Meet the endpoint
Other Secondary Endpoints (Excerpt)	Time to onset of ESRD	No improving trend observed in the treatment group

- ◆ Primary and major secondary endpoints were significantly improved vs. placebo
 - ◆ In the course of the regulatory review for Alport Syndrome (AS) and others, in addition to "Decrease in eGFR," which was set in the primary and major secondary endpoints, "Time to onset of ESRD" became important. However, the improving trend of ESRD was not observed in the treatment group. Through discussions with KOLs and the regulatory authority in Japan, and after a thorough review of these results, Kyowa Kirin decided to discontinue the development of RTA 402.
 - Regarding Alport Syndrome, the existing regulatory application is scheduled to be withdrawn.
 - Our participation as In-Country Clinical Care-taker for the ongoing AS/ADPKD studies in Japan will end.
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Please refer to the next page. I will explain the top-line data results of the Phase III AYAME trial for diabetic kidney disease of RTA 402.

As shown on the slide, we confirmed that compared to the placebo, there was a significant improvement in the primary endpoint, which is a decrease of 30% or more in eGFR from the baseline, or the time until the onset of end-stage renal disease (ESRD), as well as the important secondary endpoint, which is a decrease of 40% or more in eGFR or the time to onset of ESRD.

However, in discussions with the authorities regarding the review of Alport syndrome (AS) for which we applied with this drug in 2021, in addition to "a decrease in eGFR" that we have been claiming, the importance of "time to onset of ESRD" has increased.

Therefore, when we evaluated the period until the onset of ESRD, excluding the part of eGFR, unfortunately, we found that there was no improvement trend in the active drug group.

Based on these results and a comprehensive judgment of the content of discussions with KOLs and the authority, we decided to discontinue the development of this drug. In addition, we will withdraw the application for approval for AS and plan to end our participation as In Country Clinical Care-taker in the ongoing trials for AS and ADPKD.

It is very regrettable for us to announce the discontinuation of the development of these two important products, but we would like to steadily progress our current development pipeline.

The Phase III ROCKET program of KHK4083 is currently proceeding with subject enrollment in cooperation with Amgen, and we also have KHK4951, which has a Phase II trial scheduled for this year, and our own bispecific antibody technology-based product aiming for clinical trials this year.

We will continue and strengthen our activities towards the successful creation and delivery of life-changing value.

Year-to-date Key News Flow

Category	Date	Headline	As of May 10, 2023
ESG	Mar 8	Kyowa Kirin Selected for a "Health & Productivity Stock" and awarded as a "Certified Health & Productivity Management Outstanding Organization"(White 500) (Japan)	
R&D	Mar 17	Presented New data from Phase 2b clinical study of Rocatinlimab in Atopic Dermatitis at the American Academy of Dermatology Annual Meeting 2023	
SCM	Mar 28	Completed construction of a new building at Ube Plant (Japan)	
ESG	Apr 6	Introduced RE100 renewable electricity to all purchased electricity at its two plants and three laboratories (Japan)	
SCM	Apr 7	Completed construction of a multipurpose facility relating to Quality Assurance (Q-Tower) at Takasaki Plant (Japan)	
R&D	Apr 27	Started collaboration in drug discovery technology with School of Life Science and Technology, Tokyo Institute of Technology (Japan)	
R&D	May 10	Announced Phase III Study Results of bardoxolone methyl (RTA 402) in Japan and Discontinuation of Development (Japan)	

ESG: environmental, social, and governance; LCM: lifecycle management; R&D: research and development; SCM: supply chain management

As ADVANZ PHARMA has announced on April 25, 2023, we have signed the agreement to transfer Kyowa Kirin International's rights for Tostran, established medicine brand, to ADVANZ PHARMA

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Fujii: Finally, I would like to share a few news updates for this term from the strategy division.

Please turn to page 18, where we have published news releases from our company since the beginning of the year.

On April 27, we announced a collaboration with School of Life Science and Technology, Tokyo Institute of Technology for research and development of drug discovery technology. This collaboration is a result of industry-academia cooperation under the cross-appointment system established by the Ministry of Economy, Trade, and Industry and the Ministry of Education, Culture, Sports, Science, and Technology. Our goal is to achieve the creation of Japan-based groundbreaking pharmaceuticals by combining the school's outstanding technology with our unique technology-driven drug discovery approach.

In addition, as mentioned in the footnotes, our company has entered into a contract to transfer the rights for Tostran, which is sold by Kyowa Kirin International, to ADVANZ PHARMA.

Furthermore, regarding the joint venture collaboration with Grünenthal comprising 13 established pharmaceutical brands in Europe announced in November last year, we had planned to transfer 51% of the joint venture company's shares in Q2, but we have changed this to August, so I would like to report this as well.

That concludes our presentation for today.

Question & Answer

Moderator [M]: We will now proceed to the question-and-answer session.

Yamaguchi [M]: This is Yamaguchi from Citigroup. Thank you.

My first question is related to the RTA 402 trial results, which are detailed on page 16 of the presentation.

Normally, my understanding is that if both the primary and major secondary endpoints are achieved, the drug will be approved. However, in the Alport syndrome case, the time of ESRD onset seems to have become a critical additional factor. Given the lack of improvement trend in ESRD in the treatment group, it appears to have altered the trajectory toward drug approval. As a result, you decided to halt RTA 402's development.

There seems to be significant external dissatisfaction over this. I'm wondering if there were any possible negotiation avenues that could have been explored?

Torii [A]: Yamaguchi-san, thank you for your question. We saw the top-line data in early April, and since then, we've been in discussions with KOLs and regulatory authorities over the past month.

Historically, eGFR has been recognized as a surrogate endpoint in relevant guidelines. When we initiated the AYAME trial, we agreed with the authority to start the trial with the composite of eGFR and ESRD as endpoints.

However, as you may know, this drug is intended to increase eGFR. Since the MOA was not clear in some areas, the discussion of whether this was truly improving kidney function in the true sense of the word, or whether it was only apparent, was a topic of discussion in discussions with the authority from the beginning.

Separately, as you pointed out, after we applied for Alport syndrome, this part became more highlighted as the drug was further discussed during that review process.

In terms of ESRD, that means the endpoint excluding eGFR I mentioned earlier, the trial was not designed to show a statistically significant difference, so we didn't originally expect that. At that time, however, there was some hope that the trend would be the direction of improvement. Unfortunately, the results moved in the opposite direction. Furthermore, after reviewing a variety of parameters, which we currently undisclosed, we concluded it would be difficult to continue in the current state.

We, Kyowa Kirin, had no choice but to decide that it was appropriate to cancel the program based on the results of our discussions with KOL, not only considering the views of the authorities.

Yamaguchi [Q]: I see. Thank you.

For the second question, just a simple response is fine, but you mentioned that the timing with Grünenthal has shifted. I think this has caused a temporary profit increase of about JPY10 billion in the earnings forecast. Does this mean that what should have been included in Q2 will be included in Q3, and the balance of earnings on a quarterly basis will change a bit?

Fujii [A]: Yamaguchi-san, thank you for your question. As you understand, what was scheduled for Q2 will now be in Q3.

Yamaguchi [M]: I see. Thank you. That's all.

Wakao [Q]: I'm Wakao from JPMorgan Securities Japan. First, I'd like to ask about RTA 402, though it may be less important to ask since the development has been discontinued.

In this trial, you had patients in stages G3 and G4. If we look at patients by stage, quite a few people in G4 have moved toward ESRD, and people in G3, who are originally in G3, seem to have seen increased eGFR. So, when viewed by stage, does it mean that it worked for people in G3, but not for those in G4?

It seems like eGFR increased but ESRD was not reached. I would like to understand this better, so could you provide some comments or explanations?

Torii [A]: Wakao-san, thank you for your question. While we will disclose the details in future conference presentations or papers, some patient groups show long-term improvements in eGFR.

Therefore, we did discuss with the authorities about focusing on a certain population and whether we could demonstrate this benefit there. However, to demonstrate this, if we were to prove events up to ESRD, it would require a considerable amount and duration of effort. It was therefore judged that it would not be feasible to actually implement this, and that was taken into account in deciding to discontinue development.

Wakao [Q]: I see. My second question is about strategic investments. Before discontinuation of RTA 402's development, zandelisib's US development had also been discontinued, and I feel that the development pipeline products before KHK4083 has become quite thin.

I'm not sure if it's correct to say "filling the gap" until KHK4083, but should we expect you to become more aggressive in introducing products that can contribute to revenue before KHK4083 sales, considering the results this time?

Please also tell us if we can expect changes in introduction activities or the like due to this discontinuation of development.

Fujii [A]: Wakao-san, thank you for your question. This is Fujii from the strategy division. We are working on further enhancing our pipeline as one of our top management priorities.

The President himself has a strong will in this regard, and organizationally, we have incorporated the business development department into the strategy division from April. Also, the Head of the Business Development Department has become the Head of the Strategy Division, which is aimed at accelerating our activities.

The President himself confirmed the progress report of the introduction project frequently, and if there are candidate projects, the person in charge of the project and the top management gather flexibly to discuss the introduction projects, so that timely decisions can be made.

While we have been examining multiple projects, it's not often that we find ones with sufficient potential at the stages we target, or in the territories and fields that we focus on. Unfortunately, we have yet to finalize the introduction of any of these projects. However, we are continuing, and will continue, to work diligently on these potential activities.

We aim to decide on an introduction within this year. We will conduct thorough due diligence to assess the potential of candidate projects, and we are committed to introducing cases that allow us to confidently fulfill our accountability for the investment to you. That's all.

Wakao [M]: Thank you. I understand very well. That's all from me.

Muraoka [M]: This is Muraoka from Morgan Stanley.

First, regarding Crysvita, I believe the point was that it has been going smoothly since April 27. After transitioning to a direct sales system, I imagine there are various internal milestones. However, for those of us on the outside looking in, apart from sales, if there is anything else we should be looking at to confirm that things are going smoothly, I would appreciate it if you could let us know.

Also, I hope you continue to update us regularly on this, but are there any areas of concern you have?

Sudo [A]: Thank you, Muraoka-san. I, Sudo, will answer your question. Setting KPIs is quite difficult, but the most important thing for us when considering this transition was not to cause any inconvenience to patients currently receiving treatment and their physicians.

In that sense, the first thing we are focusing on is ensuring our patient services, which we call a hub, operate smoothly to avoid causing any inconvenience to patients and to prevent any negative feedback from doctors.

Specifically, it's difficult to explain anything other than sales, but for example, in terms of hospital coverage, we have segmented it into several parts. Rather than reducing this during the transition, we are aiming to cover it more broadly, and according to our KPIs, we are achieving this.

Furthermore, although it may not be possible to announce it every quarter, the number of patients is another indicator. This includes the number of patients found, whether the starting forms I mentioned earlier are being completed properly, and whether they are ultimately transitioning to treatment. I think these three numbers of patients will be a significant indicator.

Incidentally, although it dropped significantly in Q1 compared to Q4, I also mentioned the inventory effects before. When we look at the actual trends among patients, the number of starting forms and findings is higher than last year and exceeds the number we targeted for the first quarter.

There were slightly fewer patients who transitioned to treatment, but overall, we have started to track our KPIs smoothly. We started transferring some functions in October last year, and it is in a state of transition.

Muraoka [Q]: Thank you. By the way, for the next quarter, can we expect good numbers due to a rebound from the pullback in the previous quarter's figures?

Sudo [A]: Yes, I have high expectations myself. Some figures came out in March and April, and there is quite a recovery trend, so I would appreciate it if you could look forward to and wait for it.

Muraoka [Q]: Thank you. One more thing. It's about the acquisition of new pipelines. Cash is at JPY340 billion and is increasing steadily, but deal sizes are also getting larger when looking at other companies. So, is it within your scope to use about JPY300 billion yen in one shot, or are you considering doing multiple deals of about half or a third of this size?

Your answer might be it's case by case, but could you tell me what your thinking is?

Kawaguchi [A]: Thank you for your question. I, Kawaguchi, will answer.

To conclude, as you said, it will be on a case-by-case basis, and we will have to look at each case carefully. However, as a total financial discipline, our primary consideration is within the range of net cash, so the scale would be about JPY300 billion, but whether it's for multiple deals or a single one would depend on the case.

Furthermore, if we decide to invest, of course we could consider using our borrowing position. However, as a standard, it would be appropriate in terms of financial discipline to keep it within the range of our net cash.

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

Kohtani [M]: I'm Kohtani from Nomura Securities.

I'm also interested in RTA 402, slide 16. I had very high hopes, so I think the results are very disappointing. For future learning, I would like to ask, in the end, this seems to have been hyperfiltration.

This is because the eGFR has improved, but honestly, the intraglomerular pressure is just increasing. As you say, if ESRD is progressing, then perhaps we should consider it as hyperfiltration.

What I would like to ask, and I don't know if you can answer this, is whether the amount of albumin in the urine has increased. If this has increased, I think it would clearly indicate a direction toward hyperfiltration, but could you say anything about that? That's my first point.

Torii [A]: Thank you for your question, Kohtani-san. While I would ask you to wait for the details to be presented at an upcoming academic conference or in a paper, regarding hyperfiltration, in our various discussions with KOL doctors, we have received comments that hyperfiltration could be ruled out from the AYAME trial, so we do not consider it as such.

If it were hyperfiltration, it would put a lot of strain on the kidneys, and with long-term administration of three to four years as in this case, the eGFR would drop rapidly, but we have not observed such an event, so we understand it not to be hyperfiltration. That's all.

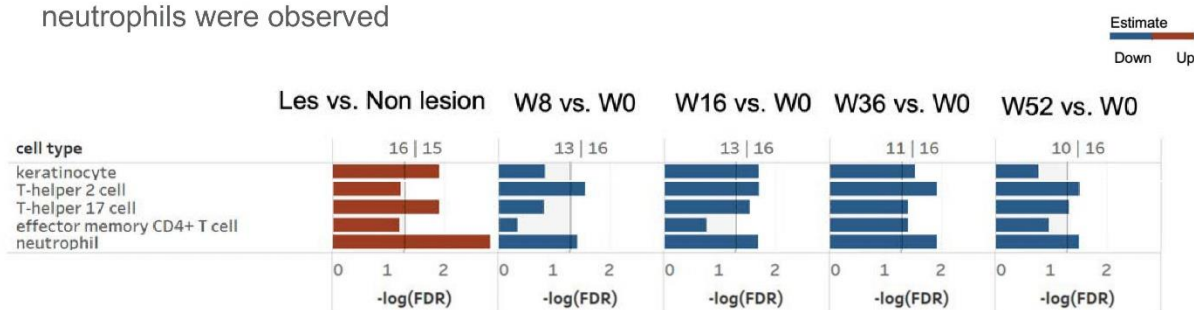
Kohtani [Q]: In the explanation at the conference, will there be any speculation about what the MOA of RTA 402 was?

Torii [A]: We've been researching this for many years, including non-clinical studies, but we haven't yet arrived at a clear answer, so there is a possibility that we may remain in the realm of speculation.



Transcriptome Deconvolution Analysis (Microarray Analysis): Differential Cell Contribution

- Significant decreases in keratinocytes, key immune cells (Th2/Th17 cells), and neutrophils were observed



Differential cell contribution analysis between AD lesion and non-lesion samples at baseline, and between before (W0) and after (W8, W16, W36, and W52) KHK4083 treatment in lesion samples. Bar lengths indicate the significance level ($-\log_{10}(\text{FDR})$) of each comparison, while the bar color represents the direction (red=increase in cell levels in disease or in post-treatment samples; blue=decrease in these samples). The vertical lines indicate an FDR cutoff of 0.05. At the top of each graph, the number of samples participating in each comparison is indicated.

AD, atopic dermatitis; FDR, false discovery rate; Th, T-helper; W, week

31st EADV congress, 7-10 September 2022.

Kohtani [Q]: Understood. The second point is about slide 23. I have not seen this before, but I want to understand its meaning.

Perhaps this figure shows that if the blue bar line goes to the right of where the vertical line is drawn, it is a statistically significant phenomenon, and that the immune cell system is very low until 36 weeks, when the administration continues.

What I wanted to ask is, I believe that the main point of 4083 is the reduction of effector memory CD4-positive T cells, and until the 36th week, they were significantly reduced and started to recover when stopped. Probably, if this continues, CD4-positive T cells will return, and the disease will relapse. Is that the correct understanding? Can we think of it like that?

Torii [A]: This system itself has quite a bit of variation, so it's difficult to draw clear conclusions. On the 36th week, there is what you mentioned, but on the 52nd week, there are parts that are further to the left, so it's difficult to have a definite interpretation without more data.

Kohtani [Q]: Honestly, what I'm most afraid of, though afraid may not be the right word, is the concern about whether it can completely cure the disease. Especially looking at slide 22, TARC hasn't come back at all, has it?

Torii [A]: Yes, compared to other drugs, the drug has a persistence of effect, so in a way, we take that as a positive.

Kohtani [Q]: Understood. Everyone seems to think your company doesn't have much of a pipeline, so I'll add that the Regulgent bispecific antibodies are scheduled to enter clinical trials this term, that hasn't changed, has it?

Torii [A]: Yes, the members of both projects are currently working toward that goal.

Kohtani [Q]: You explained before that it's not a T-cell engager, but I forgot about it, so I want to ask again, does it have a mechanism not to cause something like cytokine release syndrome? This is the last question.

Torii [A]: The answer to this question falls under product details, so we would appreciate it if you could wait until the start of the projects.

Kohtani [M]: Understood. Thank you.

Ueda [Q]: This is Ueda from Goldman Sachs Japan. I would like to ask about the impact of the discontinuation of RTA 402 and ME-401, which were positioned as your next-generation strategic products.

How should we view the impact on the medium-term plan that you currently have out and the effect on performance, including future R&D expenses?

Kawaguchi [A]: Thank you for your question. Regarding the impact on revenue of the medium-term plan, the final year of the plan is 2025, and in terms of incorporating these two drugs, first, we weren't expecting significant sales from them, and second, we incorporated them based on the probability-adjusted sales and profit, so it won't have a huge impact. Thus, the impact won't be significant.

As for R&D expenses, for both RTA 402 and ME-401 in this term, they're near the end of their development, so the amount isn't large. Regarding RTA 402, we've spent a certain amount of R&D expenses until April, and we can't stop this trial immediately, so closing costs will be incurred toward the end of the trial. Although there will be a certain amount of unspent expenses, it won't cause a significant upside to the performance. I hope that answers your question.

Ueda [Q]: Thank you. My second point is about the progress of SG&A expenses.

Compared to typical years, I think the progress rate of your SG&A expenses for Q1 of this term is high. Could I confirm that this is according to plan?

Kawaguchi [A]: Yes, to give you the conclusion first, that is correct. One special factor for this term is that until April, the profit share cost of the gross profit with Ultragenyx is included in the SG&A expenses. However, this switches to sales royalties from April 27 and moves to cost of sales. When considered on an annual basis, that amount will be a factor in the decrease in SG&A expenses in H2.

This year, in addition to this change, the transfer preparation costs and 50% of the Ultragenyx SG&A expenses I mentioned in my explanation is also going to be put in the Q1 SG&A.

Due to these factors, the progress of Q1 may appear higher than usual, but all of this is incorporated into the plan, so it is progressing as planned.

Ueda [M]: I understand. Thank you very much. That's all from me.

Hashiguchi [Q]: This is Hashiguchi from Daiwa Securities. Thank you for your time. I think the sales of G-Lasta are progressing at a rate lower than your full-year forecast, and it seems weak compared to the quarterly performance of the previous term. How should we understand the factors behind this? Could you also comment on the current penetration level of BodyPod, which was launched in December last year?

Fujii [A]: Thank you for your question, Hashiguchi-san. This is Fujii from the strategy division. As you pointed out, the current situation is that the progress is a bit slower than we expected. We think it will gradually penetrate the market from here. That's all for my response.

Hashiguchi [Q]: How do you view the reason for the slower than expected progress?

Fujii [A]: Well, the current situation is that we haven't been able to fully analyze the confirmed factors. Some factors are being raised as possibilities, but we haven't been able to do an analysis that definitively says this is the cause at this stage.

Hashiguchi [Q]: Can you provide any quantitative information about the current situation, like how much has been switched over?

Fujii [A]: At this time, we would like to keep this information undisclosed. Thank you for your understanding.

Hashiguchi [Q]: Understood. The second point is about the disclosure of data on tivozanib for age-related macular degeneration. I remember that you presented a summary at last year's R&D briefing and mentioned that a more organized disclosure or paper would be released. If there's a specific timeframe for that, could you share it?

Torii [A]: Thank you for your question, Hashiguchi-san. Although the exact timing has not yet been determined, we are currently preparing with the goal of releasing it within this year. That's all.

Hashiguchi [M]: Thank you. That's all from me.

Moderator [M]: Thank you. Alright, it seems there are no further questions, so we will conclude the teleconference for Q1 earnings for the fiscal year ending December 2023.