



Kyowa Kirin Co., Ltd.

Q3 Financial Results Briefing for the Fiscal Year Ending December 2022

November 4, 2022

Event Summary

[Event Name]	Q3 Financial Results Briefing for the Fiscal Year Ending December 2022	
[Date]	November 4, 2022	
[Number of Speakers]	4	
	Takeyoshi Yamashita	Managing Executive Officer, Head of Strategy
	Motohiko Kawaguchi	Managing Executive Officer, Head of Finance
	Yoshifumi Torii	Executive Officer, Head of R&D
	Tomohiro Sudo	Executive Officer, Head of Global Product Strategy

Presentation

Moderator: We will now begin a conference call to discuss the financial results for Kyowa Kirin for the Q3 of the fiscal year ending December 31, 2022. The results were announced at 15:30 today.

Please note the following prior to the start of the conference call. Please be advised that the names and company names of all participants in this conference call will be kept on record at our company for a certain period of time. Please note that the content of this meeting will be available on our website as an on-demand audio stream and transcript.

Today's speakers are Dr. Takeyoshi Yamashita, Managing Executive Officer, Strategy; Motohiko Kawaguchi, Managing Executive Officer, Finance; Dr. Yoshifumi Torii, Executive Officer, R&D; and Tomohiro Sudo, Global Product Strategy.

Today's conference call is scheduled for a maximum of 90 minutes. After presenting the overall financial results, we will take your questions.

Summary of Q3 Results



(Billion Yen / Rounded)

	2021Q3 Results	2022Q3 Results	Changes	2022 Revised Plans	Progresses
Revenue <i>[Overseas Ratio]</i>	254.0 <i>[53%]</i>	283.8 <i>[61%]</i>	+29.8 (+12%)	400.0 <i>[62%]</i>	71%
Gross Profit <i>[Gross Profit Margin]</i>	189.9 <i>[75%]</i>	219.6 <i>[77%]</i>	+29.8 (+16%)	312.0 <i>[78%]</i>	70%
SG&A <i>[SG&A Ratio]</i>	104.1 <i>[41%]</i>	117.3 <i>[41%]</i>	+13.2 (+13%)	172.0 <i>[43%]</i>	68%
R&D <i>[R&D Ratio]</i>	40.2 <i>[16%]</i>	44.1 <i>[16%]</i>	+3.9 (+10%)	67.0 <i>[17%]</i>	66%
Gain/Loss on Equity Method	1.3	2.6	+1.3 (+103%)	4.0	66%
Core Operating Profit <i>[Core OP Margin]</i>	46.8 <i>[18%]</i>	60.9 <i>[21%]</i>	+14.0 (+30%)	77.0 <i>[19%]</i>	79%
Profit	32.9	49.2	+16.3 (+50%)	63.0	78%

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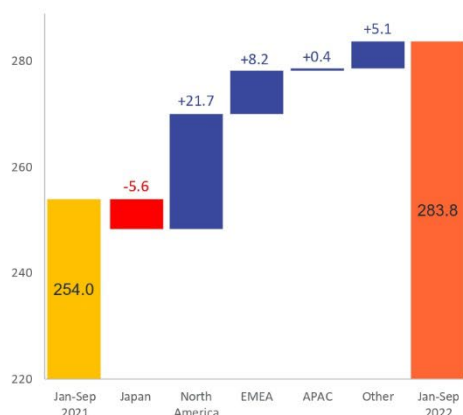
Kawaguchi: I will now present the financial results for Q3. Please see slide five.

First of all, net sales increased YoY by 12% to JPY29.8 billion. Core operating profit increased by 30% to JPY14 billion, and quarterly profit increased by 50% to JPY16.3 billion. We saw a significant increase in both sales and profit following Q2.

As for the percentage of progress toward the full-year forecast revised in Q2, sales revenue is at 71%. Core operating profit and quarterly profit are progressing steadily at 79% and 78%, respectively, partly due to unused cost trends.

YoY Analysis -Revenue-

**+29.8 billion yen
(incl. forex effect +18.7)**



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● Japan -5.6

Although Duvroq, Romiplat, G-Lasta, and Crysvita increased, revenue in Japan region decreased by 5% due mainly to negative impact by NHI price-cut in April 2021 & April 2022 and shrink in Patanol for which generic products entered the market last December.

● North America +21.7 (incl. forex effect +10.7)

Revenue in North America region increased by 40% with the growth of Crysvita, Poteligeo, and Nourianz.

● EMEA +8.2 (incl. forex effect +3.4)

Growth of Crysvita and Poteligeo contributed to the 21% increase in EMEA region, although Abstral fell due to generic products' penetration.

● APAC +0.4 (incl. forex effect +2.2)

APAC revenue increased by 2% with the growth of Gran, Nespi, Neulasta, etc, while Regpara was down due to the Chinese national tender system.

● Other +5.1 (incl. forex effect +2.5)

22% growth in the other revenue was due to the deferred revenue of USD400M upfront payment from KHK4083 partnership, that was initiated from last July, and royalties of growing Fasentra (Benralizumab).

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I will now explain the year-on-year comparisons, starting with sales revenue. See slide six.

This is a breakdown of sales revenue by region.

First, in Japan, sales declined 5% YoY due to the impact of NHI price revisions in April last year and this April, as well as a significant decline in sales of Patanol, for which generic version were launched in December last year.

For both North America and EMEA, sales increased significantly by 40% and 21%, respectively. This was thanks to solid growth of global strategic products, especially Crysvita, as well as the impact of the yen's depreciation.

In Asia, sales increased 2%, as growth in other products such as Gran and foreign exchange effects offset the decline in sales of Regpara, which was affected by the national tender system in China last October.

As for others, in addition to the continued increase in royalties from Fasentra, there was an upfront payment of USD400 million for KHK4083, which we began to recognize deferred revenue last July. This resulted in a 22% increase in overall other revenue.

Revenue of Major Items (Japan)

(Billion Yen / Rounded)

Item	2021Q3 Results	2022Q3 Results	Changes	Reasons	2022 Rev. Plans	Progresses
Nesp + Nesp-AG ¹	19.6	15.7	-3.9 (-20%)		20.7	76%
Nesp	2.9	2.5	-0.4 (-14%)	NHI price-cut & Biosimilars' penetration	3.3	76%
Nesp-AG	16.7	13.2	-3.5 (-21%)		17.4	76%
Duvroq	1.4	4.4	+3.1 (+226%)	Market penetration (Launched in Aug 2020)	5.9	75%
Regpara	2.1	1.7	-0.5 (-23%)		2.0	83%
Orkedia	7.1	7.5	+0.4 (+5%)		10.4	72%
G-Lasta	21.2	22.7	+1.5 (+7%)	Market's recovery & penetration	31.5	72%
Poteligeo	1.5	1.5	+0.0 (+0%)		2.0	73%
Rituximab BS	8.1	7.6	-0.5 (-6%)	NHI price-cut	10.3	73%
Romiplat	4.9	7.5	+2.6 (+53%)	Recovery from supply constraints from Jun 2020 through Mar 2021	10.0	75%
Allelock	6.3	4.8	-1.5 (-24%)	Generics' penetration & NHI price-cut	5.6	85%
Patanol	9.2	2.4	-6.8 (-74%)	Generics entered in Dec 2021	3.0	81%
Nourias	6.4	5.9	-0.5 (-8%)	Competitors' penetration	8.1	72%
Haruropi	2.2	2.8	+0.6 (+29%)	Market penetration (Launched in Dec 2019)	4.1	68%
Crysvita	5.1	6.4	+1.3 (+24%)	Market penetration (Launched in Dec 2019)	9.2	69%
Tech-licensing	1.5	0.5	-0.9 (-63%)	Deferred process of FKB ² -related upfront revenue completed	0.9	59%

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.

² FKB stands for Fujifilm Kyowa Kirin Biologics Co., Ltd.

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Please continue to page seven.

This is the situation for major products in Japan. Nesp AG continues to see its market share decline slightly since shipment adjustments of its biosimilars are lifted. Progress against the revised full-year forecast is solid at 76%.

Sales of Duvroq continue to grow steadily and the product maintains the number one market share within its class.

Sales of Allelock and Patanol have declined significantly due to the penetration of generics and NHI price revisions.

Sales of Crysvita continue to grow steadily, but as of the end of Q3, progress toward the full-year forecast was 69%. Starting in October, dedicated Crysvita staff will be assigned to each branch to further focus on finding patients.

Revenue of Major Items (ex-Japan)

(Billion Yen / Rounded)

Item	2021Q3 Results	2022Q3 Results	Changes	Reasons	2022 Rev. Plans	Progresses
Crysvita	55.1	78.7	+23.7 (+43%)	[North America] Market penetration [EMEA] Geographical expansion & Additional indication (Adult/TIO) [APAC] Launched in China	116.2	68%
North America	40.3	57.4	+17.1 (+42%)			
EMEA	14.8	21.2	+6.5 (+44%)			
APAC	0.0	0.1	+0.1 (—)			
Poteligeo	11.0	16.1	+5.1 (+47%)	[North America] Market penetration [EMEA] Geographical expansion & Market penetration	23.6	68%
North America	9.2	12.6	+3.4 (+37%)		18.1	69%
EMEA	1.8	3.5	+1.7 (+96%)		5.5	64%
Nourianz	3.1	4.5	+1.4 (+46%)	Market penetration	6.1	73%
Abstral	6.3	5.4	-0.9 (-14%)	Generic's penetration	7.2	74%
Regpara	6.7	2.9	-3.8 (-57%)	Listed on Chinese tender list ¹ in Oct 2021	3.8	77%
Tech-licensing	16.4	23.3	+6.8 (+42%)	Deferred revenue of KHK4083 upfront payment (July 2021-) & Growth of Fasenra	35.0	67%
Benralizumab Royalty ²	11.7	15.4	+3.6 (+31%)			

¹ Volume-Based Procurement (VBP) program that has been introduced since 2018 for reducing healthcare cost in China. A few companies are selected as a supplier through a tender, while their drug prices dramatically drop down.

² Sales royalties of Fasenra which has been marketed by AstraZeneca, including our own estimation.

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

Next, page eight. Here is the status of major overseas products.

Sales of Crysvita continue to grow strongly, up 43% YoY. We have heard that patient recruitment is progressing steadily, and we hope to achieve our full-year plan, taking into account year-end demand in Q4 and the impact of the yen's depreciation.

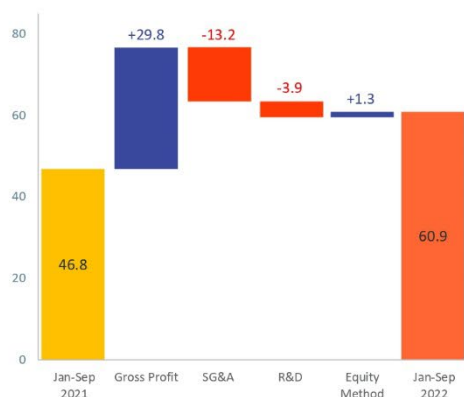
Poteligeo also showed strong growth of 47% YoY. Progress in EMEA is lagging slightly, but like Crysvita, we are aiming to achieve our full-year plan here as well.

As for Nourianz, although it has not lived up to pre-launch expectations, it continues to grow steadily at 46% YoY.

As for technology revenue, we started to recognize deferred revenue for KHK4083 in July last year, so six months of deferred revenue contributed to the increase in revenue. In addition, royalties for benralizumab also progressed favorably with an increase of JPY3.6 billion in revenue.

YoY Analysis -Core OP-

**+14.0 billion yen
(incl. forex effect +6.7)**



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● Gross Profit +29.8 (incl. forex effect +16.6)

Increased in conjunction with JPY29.8B rise in revenue. Margin improved by 2% (75%→77%) because there was a big negative impact related to elimination of intercompany profits on inventories last year.

● SG&A -13.2 (incl. forex effect -7.4)

Increased by aggressive investment in IT/Digital infrastructure and human resources for the maximization of the global 3 brands (G3B) and the early consolidation of global business foundation, in addition to Crysvida profit sharing expenses for North America.

[Labor -7.7 / Sales promotion -5.3 (incl. Crysvida profit sharing expenses -6.3) / Depreciation & Amortization +0.4 / Other -0.5]

● R&D -3.9 (incl. forex effect -2.6)

Clinical study costs of KHK4083 and ME-401 increased.

● Gain/Loss on Equity Method +1.3

FKB recorded additional deferred tax asset.

FKB; Fujifilm Kyowa Kirin Biologics Co., Ltd.

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Now please turn to page nine. This is an analysis of core operating profit.

Gross profit increased by the same amount, JPY29.8 billion, due to the JPY29.8 billion increase in sales revenue. The gross margin improved by 2%, due to the dying of foreign exchange effects related to the elimination of unrealized income and an increase in the percentage of global product sales.

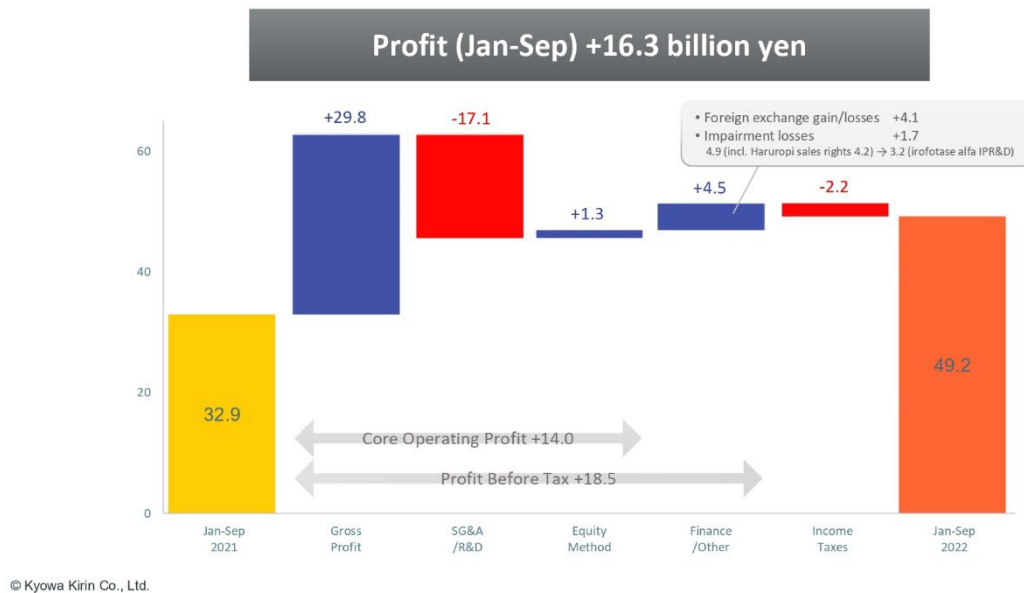
Sales, general and administrative expenses increased by JPY13.2 billion. The main breakdown is a JPY7.7 billion increase in personnel expenses and a JPY6.3 billion increase in profit-sharing expenses in North America due to the increase in Crysvida's sales.

R&D expenses increased by JPY3.9 billion due to increased development costs for KHK4083 and ME-401.

Equity in earnings of affiliates was positive JPY1.3 billion. As introduced in Q1, this is due to the additional recognition of deferred tax assets at Fujifilm Kyowa Kirin Biologics.

As a result, core operating profit increased by JPY14 billion. Excluding the effect of foreign exchange, the increase in profit was JPY7.3 billion in real terms.

YoY Analysis -Profit-

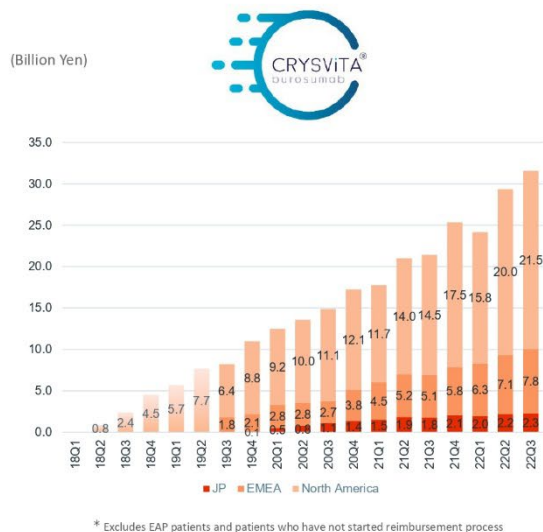


Page 10, please. In this slide, I would like to touch on a breakdown of post-core operating profit.

The balloon is showing a positive figure of JPY4.5 billion in the area of financial and other income and expenses. The main reason is the positive effect of JPY4.1 billion on foreign exchange gains/losses due to the weaker yen.

In Q3, impairment losses on intangible assets related to ilofotase alfa, which was in-licensed from AM-Pharma last September, specifically upfront payments and milestone payments, were recorded, but they were JPY1.7 billion less than the impairment losses on Haruopi and other assets recorded in the same period of the previous year. This resulted in a total increase of JPY4.5 billion.

As a result, quarterly profit increased YoY by JPY16.3 billion, or 50%, to JPY49.2 billion. That is all from me.



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2022 Key Actions & Q3 Topics

2022 Key Actions

- North America: Initiate full-scale preparation for transfer of commercialization planned in spring 2023.
- EMEA: Continue to focus on geographical & indication expansion. TIO review completed.

Q3 Topics

- North America: Amended the contract with Ultragenyx for specifying the transition scheme. Finalize training of field personnel to start customer outreach in Q4.
- EMEA: Received additional approval for TIO indication from the European Commission and started commercialization.
- Japan: Dedicated personnel is assigned to each branch.

Launched Countries/Regions as of Sep 30, 2022

Excluding Latin America

Underlines: Pediatric and Adult / Bolded types: New launches in Q3 2022

2018	<u>USA</u> , <u>Germany</u> , <u>Netherlands</u> , <u>Luxembourg</u>
2019	<u>Canada</u> , <u>England</u> , <u>Wales</u> , <u>Northern Ireland</u> , <u>Slovakia</u> , <u>Sweden</u> , <u>Israel</u> , <u>UAE</u> , <u>Czech</u> , <u>Denmark</u> , <u>Italy</u> , <u>Japan</u> , <u>Norway</u> , <u>Bahrain</u> , <u>Austria</u>
2020	<u>Scotland</u> , <u>Oman</u> , <u>Kuwait</u> , <u>Qatar</u> , <u>Romania</u> , <u>Slovenia</u> , <u>France</u> , <u>Finland</u> , <u>Estonia</u> , <u>Spain</u>
2021	<u>Ireland</u> , <u>Hungary</u> , <u>Belgium</u> , <u>Saudi Arabia</u> , <u>Hong Kong</u> , <u>China</u> , <u>Singapore</u>
2022	<u>Portugal</u> , <u>Latvia</u> , <u>Thailand</u>

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Sudo: Next, as a commercial update, I will explain about the three global strategic products. See page 12.

The first is Crysvita. As you can see, global sales have continued to grow steadily, even excluding the impact of foreign exchange rates, we believe that our sales are growing steadily.

We are not optimistic about the rate of progress toward the revised forecast, which we announced in the previous fiscal quarter, but we are seeing a steady flow of patients, and we will continue to work hard to achieve our goal.

In the EMEA, as we announced in August, we have received approval from the European Commission to expand the indications to include TIO. The product has been already on sale in Germany since September, although it is just beginning.

During the third quarter, the product was launched in Thailand for XLH in pediatric and adult patients.

In addition, as Mr. Kawaguchi mentioned earlier, we have assigned a dedicated person in charge of strategy development for Crysvita at each of our 11 branch offices in Japan. This is a very important unit that is responsible for building regional strategies about information provision and supporting the execution of such strategies, based on global strategies.

This unit, along with medical reps, intend to exchange information with healthcare professionals. We would like to establish a system to strengthen our efforts to find new patients and further accelerate our activities in Japan.

Regarding the transfer of North America commercialization, our commercial personnel have started working on site from Q4. In Q3, we conducted training for them, including compliance.

In order to complete the transfer smoothly, we are also revising the transfer scheme. I would like to talk a little about the US transfer on the next page. Next page, please.

Crysvita - Agreement for Transition Scheme Change -

Economic Terms

US & Canada

- Kyowa Kirin books sales
- 50/50 profit share for 5 years from the U.S. launch
- After 5 years, Kyowa Kirin pays tiered sales royalties in mid-high 20% range to Ultragenyx
- Supply price: 35% of net sales through 2022, 30% thereafter

- **No change in the above economic terms. From April 27, 2023, Kyowa Kirin will conduct promotional activities in the US & Canada, and pay sales royalties to Ultragenyx (and book them as COGs) as planned.**

[Key Changes]

- **For one year from April 27, 2023 to April 26, 2024, Kyowa Kirin will receive field support from Ultragenyx for its promotional activities, and both companies will work together to complete the transition smoothly.**
- **The support costs incurred by Ultragenyx will be shared by both companies properly.**

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First of all, as I have explained in the past, after April 2023, which will be the transition date, it is important for Kyowa Kirin to take the initiative and responsibility for promotional activities in the North America region. This is as per the original contract, and there are no changes.

Accordingly, preparations toward the transfer date, including the securing of sales personnel and the development of IT infrastructure, have been proceeding steadily on the same schedule as before.

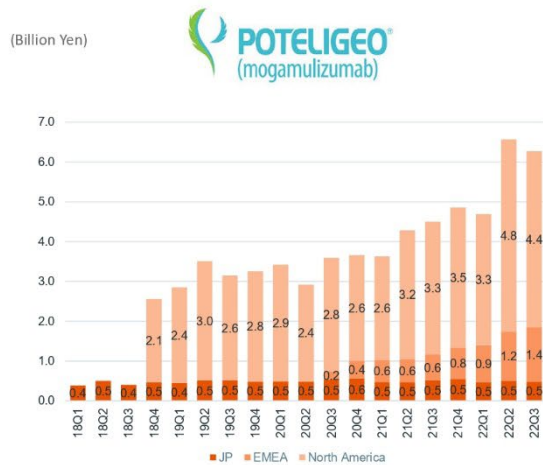
In terms of economic conditions, there is no change from what we have already reported to you in terms of the shift from a profit-sharing structure to a sales-based royalty payment scheme, starting next spring.

The transition date is April 2023. A partial change is that for one year from that date, we will work with employees employed by Ultragenyx on the front lines of the sales field.

We will be taking the lead, but with support from Ultragenyx, we hope to achieve a smooth transfer.

In addition, we have agreed that we will bear our share of the costs, mainly marketing costs, incurred by Ultragenyx as a result of this change.

Although this will result in a temporary increase in costs, for Ultragenyx and Kyowa Kirin, a smooth transition is the best way to ensure the delivery of this drug to patients and to achieve growth. I believe that we could have a solid plan in place.



* Excludes EAP patients and patients who have not started reimbursement process

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2022 Key Actions & Q3 Topics

2022 Key Actions

- EMEA: Continue to talk with payers to ensure reimbursement and patient access to product.
- US/EMEA: Work with HCPs to gather and share evidence such as clinical data in association of blood tumor burden to help understand better use of Poteligeo.

Q3 Topics

- US: Steady market penetration due to continued evidence-based promotion.
- EMEA: Newly launched in UAE. Sales increased YoY due to increase in launched countries.
- APAC: Received approval in Korea.

Launched Countries/Regions as of Sep 30, 2022

Bolded types: New launches in Q3 2022

2012	Japan
2018	USA
2020	Germany, Austria, Luxembourg
2021	Italy, Scotland, Netherlands, Belgium, Slovenia, Denmark, Spain, Finland
2022	Sweden, Saudi Arabia, Slovakia, England, Wales, Northern Ireland, France, Czech, UAE

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Let me now turn to Poteligeo.

First, as you can see from these figures, sales were down a bit this quarter compared to the previous quarter. This was due to a partial price increase in July, which caused a slight overload in demand prior to the price increase.

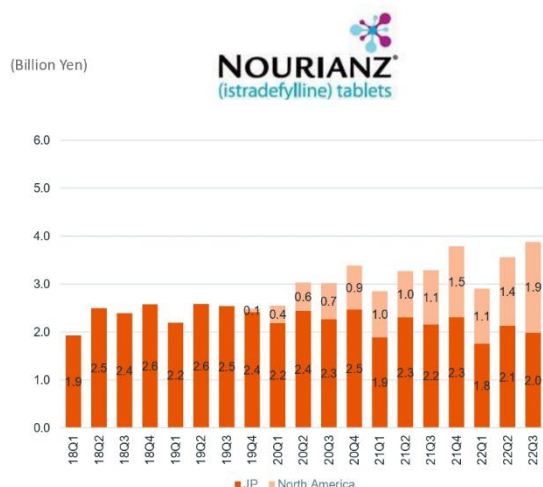
In addition, the number of operating days was slightly higher in Q2, resulting in slightly lower sales than in Q2.

On the other hand, promotional activities using evidence such as data on tumor cells in the blood have been spreading well. We have been able to confirm that the current market itself is solid in Q3.

In Europe, we have achieved a new launch in the UAE. We will steadily grow in the European market by expanding the number of countries where we launch the product and conducting promotional activities similar to those in the US.

As with Crysvita, we made a slight revision to our forecast in the previous fiscal quarter, and we will continue to do our best to meet our target.

Nourianz



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2022 Key Actions & Q3 Topics

2022 Key Actions

- North America: Focus on approaching potential prescribers and get their deeper understanding of the features of Nourianz such as safety, convenience, and novel mode of action.

Q3 Topics

- North America: In challenging environment of the branded PD drug market, sales increased YoY. Continuing promotional activities to HCPs/patients, appealing Nourianz's features by utilizing digital tools and leaflets.

Launched Countries/Regions as of Sep 30, 2022

2013 Japan
2019 USA

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Finally, Nourianz.

First of all, although the market environment for branded drugs in the PD field in the US continues to be difficult, as Mr. Kawaguchi explained earlier, the sales have been steadily growing year by year.

In our promotional activities, we will continue to promote the drug's features, such as ease of use and mechanism of action, while focusing more on leaflets and digital promotion. That is all from me.

Upcoming Events: Next-generation Strategic Products



✓ : Completed events from Aug 5, 2022, to Nov 4, 2022.

Code Generic Name	Event	Time Expected	Month Completed
KHK4083/AMG 451 rocatinlimab	Atopic dermatitis P3 restart	End of 2022 - Beginning of 2023	
ME-401 zandelisib	iB-NHL (mono, 3L+) P2 topline data (JP) CLL (combo, 2L+) P2 FPI	H2 2022 H2 2022	
RTA 402 bardoxione methyl	Diabetic kidney disease P3 LPO Diabetic kidney disease P3 topline data	H2 2022 H1 2023	
KHK7791 tenapanor	Hyperphosphatemia under maintenance dialysis submission (JP) ✓	H2 2022	Oct. 2022

FPI: first patient in; LPO: last patient out; CLL: chronic lymphocytic leukemia; iB-NHL: indolent B-cell non-Hodgkin lymphoma

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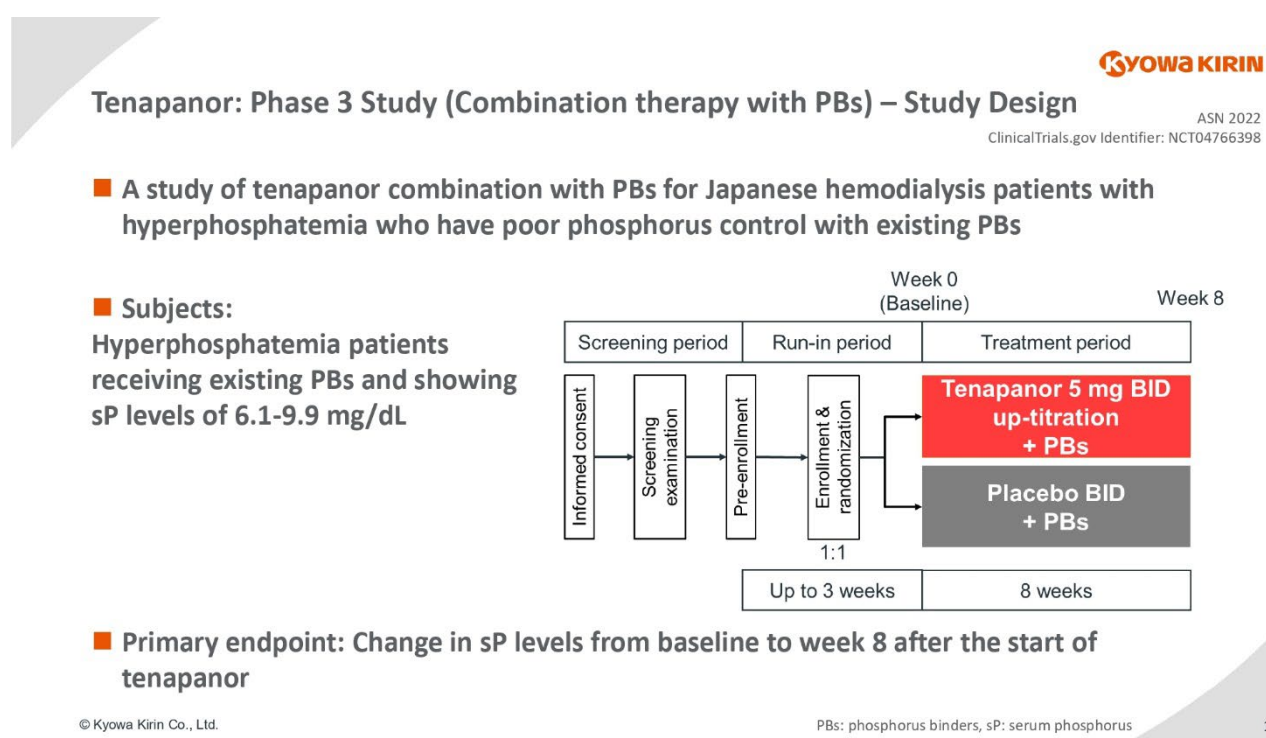
Torii: Next, I would like to give an update on R&D.

See the next page. This slide shows the newsflow that we can expect in the near future regarding next-generation strategic products.

First of all, KHK4083 (generic name: rocatinlimab): for the Phase 3 trial ROCKET, we reported in the last financial report that the enrollment of patients had been suspended. The trial is currently scheduled to be resumed from the end of the year to the beginning of next year 2023.

As for RTA402, the Phase 3 AYAME trial for diabetic kidney disease will reach its last patient out this year. Top-line data will be reported in H1 of next year.

In addition, we recently issued a press release announcing the filing of a domestic application for KHK7791, or tenapanor. Today, we would like to introduce some of the results of the domestic Phase 3 study that were presented at the American Society of Nephrology meeting, the results of which are also used in the package of a domestic application. See the next page.



Here, we present the results of a study of KHK7791 in combination with a phosphorus binder in hyperphosphatemic patients undergoing hemodialysis who have difficulty controlling serum phosphorus levels with existing phosphorus binders.

Patients with poorly controlled serum phosphorus levels, which exceed the upper limit of serum phosphorus concentration recommended by the guidelines despite the use of phosphorus binders, were randomly assigned 1:1 to a group in which KHK7791 or placebo was added to the existing phosphorus adsorbent, while the administration of the existing phosphorus adsorbent was left unchanged.

The primary endpoint is the change from baseline in serum phosphorus concentration after eight weeks of treatment. See the next page.

Tenapanor: Phase 3 Study (combination therapy with PBs) – Results

ASN 2022

ClinicalTrials.gov Identifier: NCT04766398

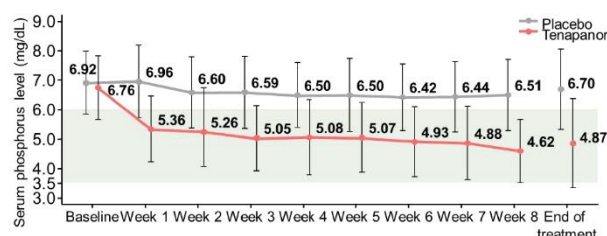
Primary endpoint

	Placebo (n=83)	Tenapanor (n=81)
Change in serum phosphorus level from baseline to week 8, mg/dL		
Mean (95% CI)	-0.24 (-0.52, 0.04)	-2.00 (-2.28, -1.72)
Difference (95% CI)	-1.76 (-2.16, -1.37)	
p-value	<0.0001	

Adverse effects

	Placebo (n=85)	Tenapanor (n=84)
TEAEs		
Total	53 (62.4)	72 (85.7)
Diarrhea	12 (14.1)	53 (63.1)
Severity		
Mild	9 (75.0)	40 (75.5)
Moderate	3 (25.0)	13 (24.5)
Severe	0 (0.0)	0 (0.0)
Discontinuation due to TEAEs		
Total	0 (0.0)	2 (2.4)
Diarrhea	0 (0.0)	0 (0.0)

Mean serum phosphorus levels over time



- Addition of Tenapanor to patients who have poor phosphorus control with existing PBs resulted in a statistically significant reduction in sP levels compared to placebo.
- Most diarrheas as predicted adverse effects were mild.

In another study*, tenapanor demonstrated the statistically significant reduction in sP levels as a single therapy as well.

* Subjects: Japanese hemodialysis patients with serum phosphorus levels of 3.5-6.0 mg/dL in a screening period and 6.1-9.9 mg/dL after washout of PBs.

The results are as follows. As shown here, for the primary endpoint, add-on administration of 7791 resulted in a statistically significant reduction in serum phosphorus concentration compared to placebo.

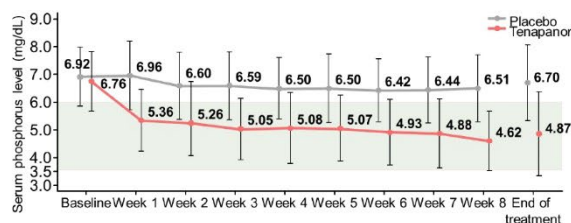
The graph on the right shows the average serum phosphorus concentration. That will also help you understand the effect of this product on lowering phosphorus concentration.

Regarding adverse events, the expected diarrhea was observed in 60% of the patients, but most cases were mild.

In a separate study, the single agent, unlike the combination, also reduced phosphorus levels by a statistically significant degree compared to placebo. See the next page.

What Kyowa Kirin expects from KHK7791

KHK7791 (tenapanor), a phosphorus absorption inhibitor with a new MOA different from conventional PBs, which inhibits phosphorus absorption from gastrointestinal tracts by inhibiting NHE3 (Na⁺/H⁺ exchange transporter 3)



A decrease in sP concentration was observed in patients who have poor phosphorus control with existing PBs



* This picture is for illustration purposes for an average number of tablets taken for two weeks at week 25-26.

Expecting to reduce pill burden for hyperphosphatemic patients

Kyowa Kirin aims to deliver Life-changing value to hyperphosphatemia treatment

KHK7791 inhibits phosphorus absorption from the gastrointestinal tract by blocking NHE3, a transporter that exchanges sodium and protons.

As indicated earlier, we have confirmed the efficacy for patients who have difficulty managing their phosphorus levels with existing phosphorus binders. Furthermore, it has been shown to be effective not only in combination, but also as a single agent.

Additionally, compared to existing phosphorus binders, 7791 is smaller in tablet size and is intended for a dosage of one tablet twice daily. We believe that this characteristic will contribute to reducing the burden of hyperphosphatemia treatment with phosphorus binders, which are generally known to have a high medication burden, or as we call it, pill burden.

We will continue to work diligently toward approval with the aim of providing life-changing value in the treatment of hyperphosphatemia. This concludes the R&D update.

Year-to-date Key News Flow ③

AS of November 4, 2022

Category	Date	Headline
LCM	Oct 17	Application for partial change of approved indication of Lumicef for Palmoplantar Pustulosis (Japan)
R&D	Oct 20	Data from Phase 3 clinical study of Tenapanor Hydrochloride (KHK7791) for hemodialysis patients on dialysis with hyperphosphatemia in Japan (American Society of Nephrology Meeting)
R&D	Oct 28	NDA submission of Tenapanor Hydrochloride (KHK7791) for improvement of hyperphosphatemia in chronic kidney disease patients on dialysis (Japan)
R&D	Nov 4	Final results of TIDAL Phase 2 clinical study FL cohort of Zandelisib, etc. (American Society of Hematology 2022 Annual Meeting)
Updates after the previous earnings announcement		

© Kyowa Kirin Co., Ltd. ESG: environmental, social, and governance; LCM: lifecycle management; R&D: research and development; SCM: supply chain management

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Yamashita: Lastly, I would like to introduce some news released since Q2. Please see page 24.

First, I would like to introduce our CVC activities released on October 5. As one of the measures to provide pharmaceutical products that satisfy unmet medical needs, we had been developing an internal structure for corporate venture capital as well as venture capital investment.

In September, we made our first investment in a US startup company with innovative technology in drug discovery approaches as part of our CVC activities.

Next, I would like to introduce the public lectures held in Japan on the occasion of World XLH Day, which is scheduled on October 23.

This event was held in collaboration with the STEP community operated by ASrid, a non-profit organization. At this event, both adult and pediatric endocrinologists provided disease information and Q&A sessions for patients and their families to educate them about X-linked hypophosphatemic rickets and osteomalacia.

Lastly, although not listed in this chart, AM-Pharma announced the discontinuation of the ilofotase alfa Phase 3 study that they are conducting. As explained earlier, we have recorded an impairment loss. This concludes my presentation.

Question & Answer

Yamaguchi [M]: I am Yamaguchi from Citigroup Global Markets. Thank you. The first question is about Ultragenyx's support for Crysvisa after the transfer of commercialization next year in the US. My understanding is that this is something that has not been discussed much before, but now it has come up, and I think there are pluses and minuses.

Of course, this would make things smoother, which is a plus, but it could increase costs to a certain degree. I believe Crysvisa costs about 50 million in the US. Could you please briefly explain the background behind the pros and cons that led to this discussion and how much you think this will increase costs?

Kawaguchi [A]: Thank you for your question, Mr. Yamaguchi. Let me first answer about the cost point.

We are now estimating that the amount will be approximately JPY1 billion for the one-year period from April 27 next year to April 2024.

Therefore, if we look at just FY2023, the burden will increase by about JPY700 million to JPY800 million. That's the sort of scale we're looking at. This is the amount of cost share that we bear.

Sudo [A]: Since about this time last year, we have been preparing and talking with Ultragenyx about this transfer. There are two main points.

The first thing is to make sure that patients are not inconvenienced by the transfer. The other thing is to make sure that the transfer would not have a negative impact on the business. For example, a decrease in the number of patients identified due to a decrease in activities to search for patients. These two points are very important for both Ultragenyx and our company.

It is also important to consider is the field activities and the patient support hub, where activities are carried out. I have been discussing about how important it is to make sure that these two activities do not have a negative impact on patients and our business as I mentioned earlier.

In fact, reps' activities are divided into several segments in the field. We have been discussing how to make transitions in this area, and whether there are any points of cooperation in terms of expanding activities in the future.

Simply put, in terms of sales, we need to expand the area while preserving our current extent during the transition. In addition, we have agreed that we would be able to make a smoother transition for current patients, for example, in the US, where there are more than 2,000 patients, by entering deeper into the market for one year through collaboration. This is the way we have decided to proceed.

Mr. Kawaguchi mentioned the JPY1 billion figure. We judged that this cost would be sufficient to pay for the transition of experience from Ultragenyx, so we decided to implement the project.

Similarly, patient hub that handles patient data also received an additional transition time of about one year to collaborate with each other to avoid gaps.

I hope that makes sense, even though I went into a bit of detail. That is all.

Yamaguchi [M]: Thank you. I sometimes wonder if it could be done for a year, and then identify and take out any capable employees. These are my impressions.

As I asked a long question, I'll go to the back of the queue. Thank you very much.

Hashiguchi [Q]: Hashiguchi, Daiwa Securities here, thank you. I'd like to ask about tech-licensing income. The rate of progress toward the full-year forecast up to Q3, both in Japan and overseas, in monetary terms, has been a little low. This is especially true in overseas markets. What do you identify as the causes of this? In addition, could you comment on the likelihood of achieving your plans for the full year?

Kawaguchi [A]: Thank you for your question, Mr. Hashiguchi. I will take your question.

As for tech-licensing income, the main reason for the large decrease in Q3 is the up-front cost of KHK4083, USD400 million. This is prorated over the period up to the expected FDA approval date, we call it a cumulative catch-up adjustment, which means that the amount of revenue recorded since last July has been adjusted to the new schedule due to the change in the development schedule of 4083. This adjustment includes those in prior years.

As of Q2, we were just aware of the fact that the Phase 3 trial was suspended, but a new study schedule had not been decided in Q2. This is why the correction has been made in Q3.

As a result, the period of deferral has been extended a little, which means that annual sales will be reduced by about JPY1.6 billion per year from the originally projected level.

In addition, there was about JPY800 million in adjustments for prior years, and we saw a decrease in that portion in Q3.

Approval is expected by the end of 2026. As a result, we believe that the annual forecast will also be slightly down for that part. Does that answer your question?

Hashiguchi [Q]: Excuse me, just to confirm, but is it my understanding correct that your latest full-year forecast is likely to be about JPY1 billion less than what you are presenting now?

Kawaguchi [A]: Yes, against this revised plan, it is a little less than JPY1 billion, I think, and we have also made some adjustments in the timing of the revision, so it is about JPY1 billion, as you say.

Hashiguchi [Q]: The figure was revised a little at Q2, but it did not reflect the changes completely, so it was revised once more in Q3, and compared to the revised plan made in Q2, the figure is likely to be a down revision of less than JPY1 billion.

Kawaguchi [A]: Yes, that is precisely correct.

Hashiguchi [Q]: Thank you very much. In your explanation of R&D and SG&A expenses, I think you mentioned some unused expenses. Could you explain the reasons for this, and the effect of this on the full-year results?

Kawaguchi [A]: Even against the revised plan, they are moving in the direction of being unused. There are several factors. One is the transfer of Crysvita, as Mr. Sudo explained earlier. In the course of discussions with Ultragenyx, the schedule has changed a bit from what we had in mind in last year's budgeting.

After discussions with Ultragenyx, we specifically decided to start transfer activities in the field in October, so we delayed the timing of recruitment there, since we no longer need to start hiring at the beginning of the year.

In this area, there are some unused personnel expenses for recruitment, and we estimate that these expenses amount to more than JPY1 billion.

I mentioned earlier that there will be an increase of JPY1 billion in the burden for one year from next April onward, but our current projection is that the unused amount for this year will be about the same size as planned.

In terms of R&D expenses, we knew about the 4083 suspension at the time of the revised forecast as I mentioned earlier, but the amount of expenses to be incurred during the current year was not totally factored in. We are currently estimating that the unused amount will be about JPY2 billion, and so our current forecast is that the unused amount will be about several billion yen less than the revised plan.

Hashiguchi [M]: Thank you very much. That is all.

Wakao [Q]: I am Wakao from JPMorgan Securities. You have just explained the various positive and negative factors, could you tell us about any predicted changes to your full-year forecast for core operating profit of JPY77 billion?

You said earlier that you will do your best and achieve the target, but as you explained now, the JPY1 billion in negative royalty income will be offset by the JPY1 billion in SG&A expenses. In addition, it was mentioned that R&D expenses will not be fully used. Furthermore, your company stands to benefit from a weaker yen. Given the current level of yen depreciation, I believe this will generate a positive effect.

With these in mind, it seems more likely that you will achieve the JPY77 billion core OP. Would this be a fair assessment?

Kawaguchi [A]: Indeed. We want to exceed that JPY77 billion figure, even if only slightly.

Wakao [Q]: Understood. My second question is about Crysvita sales in North America. Since I feel the trend was a little bit more subdued than in Q2, can I assume that the Q3 results were in line with the plan, especially excluding foreign exchange?

If results are strong in Q4 as well, can we assume that North America sales of Crysvita will swing upward against the revised plan in line with exchange rate changes?

Sudo [A]: Thank you, Mr. Wakao. First of all, it isn't the case that there was a slight downward trend in Q3, and as mentioned yesterday at Ultragenyx's call, good progress is being made in starting forms of patients. The level was at its highest in this quarter, and that is the trend we are seeing in patient registration. For this reason, I believe that this market has the potential for significant growth. I think we are still at the beginning of the way.

In that sense, the adult market in particular is one major point, but rather than a slight downward trend, I would rather see steady current growth and how we can increase patients, while still expanding the market and increase access for patients.

In terms of meeting the year-end target, there may be a degree of variability in figures, but from a broad perspective, I think we are well within range to achieve the target.

We will work to continue achieving the growth we presented today in page 12, both toward FY2023 and the 2021-2025 mid-term plan. There is still potential for the market to grow. That is all.

Wakao [Q]: Understood. Am I correct in saying that you are talking about results on a local currency basis, that is, excluding foreign exchange rates?

Sudo [A]: Yes, that's right. Seen in terms of patient numbers or local currency, we also observe the same trend.

Wakao [M]: Understood. Thank you. That is all.

Muraoka [Q]: Hello, this is Muraoka, Morgan Stanley MUFG Securities. Thank you.

I've grasped the situation for the current fiscal year, so I'd like to ask about next fiscal year. Since you mentioned earlier that the increase in additional payment is less than JPY1 billion, on the other hand, it seems that the growth of Crysvita on a dollar basis is indeed slowing down a little. Is it correct to say that double-digit profit growth is in sight for the next fiscal year?

Considering costs in North America, both for the current fiscal year and next year, there are several areas that are not clear to me, but I think that your company is capable of achieving double-digit profit growth normally. What's the best way to think about this?

Kawaguchi [A]: Thank you for your question. As for the next fiscal year, we are in the process of preparing a budget internally, so we will have to ask you to wait for the announcement of the financial results in February for more details.

We cannot say that Crysvita alone will be responsible for the overall increase in profit next year, so we are making our plans after taking various factors into account. Of course, we will aim to increase profits. We would also like to see a large scale of profit increase, but unfortunately, I would like to refrain from giving a definite double-digit profit growth at this point.

Muraoka [Q]: Okay. Looking at the next fiscal year, I think Crysvita in North America is the biggest swing factor. Other than that, there are not many other major trend changes that will occur, right?

Kawaguchi [A]: Yes, in terms of major changes, Crysvita is definitely the most important.

However, research and development expenses can be quite large, depending on the progress of various projects. We believe it is important to make a solid plan, including this type of aspect, and then work to realize it.

Muraoka [Q]: Okay. Thank you. The second question is about the KHK4951 eye drops. Regarding the Phase 1 results, if you look at ClinicalTrials.gov, the study completion is scheduled in December. It wasn't mentioned today, so I was wondering if you are planning to share any information about the trial in a Q4 call.

Torii [A]: This is Torii from R&D, thank you for your question. Right now, we are in the process of examining the results of Phase 1.

Although it is still difficult to give specific timing, we would like to explain the status of this item at an R&D Meeting or other event. That is all.

Muraoka [Q]: Is the R&D meeting in December?

Torii [A]: Yes, it will be held on December 5.

Muraoka [Q]: So we might get some information about it then.

Torii [A]: Yes, there are still some uncertainties as to how much information we can share, but we will keep you updated on the progress.

Muraoka [M]: Okay. Thank you. That is all.

Ueda [Q]: My name is Ueda from Goldman Sachs. First of all, I would like to ask you about the change of the scheme for the transfer of Crysvita commercialization in North America. Could you tell us anything about the discussions that took place in relation to the change at this timing?

I understand that you had been planning to make the transfer in April 2023, but I would like to know what kind of business environment and what kind of discussions between your company and Ultragenyx led to this change in scheme just six months before the transfer. Thank you.

Sudo [A]: I will take this question. In February, we signed a letter of agreement on what kind of work we would proceed with, and we have been moving forward with it.

In the course of these activities, there were some projects that required more careful attention than expected. We were wondering if we could start them in the summer, however, we needed to take a little time to complete the Amendment 12 signed at the end of September.

In light of this, on this timing six month before the transfer date, we concluded that rather than transferring everything in this six-month period, we would need some time after that to work together to achieve a smooth transfer of the operation. The conclusion of the discussion was that both parties agreed to achieve a smooth transfer in the next six months and after an additional year.

It is true that there were more complicating factors than we had anticipated, but we have taken steps to ensure that this will not affect the actual transfer.

Ueda [Q]: I understand. Thank you. Second, I would like to know about the trend in the US for Poteligeo.

In your explanation earlier, you mentioned a little bit about the timing of shipments and the number of business days, but if we look at volume trends on a current basis, for example, from Q2 to Q3, I get the sense that there has been a slight slowdown. Could you please explain a little more about the progress on a current basis?

Sudo [A]: Thank you for your question. We are now tracking the number of vials per week, but in terms of the number of vials per week or the number of patients, there has not been a particularly large change in shipments between Q2 and Q3.

As I mentioned earlier, there was a slight difference depending on the number of days of shipments, but on a weekly basis, there was no difference. I mentioned earlier that we are conducting market activities for blood involvement. We are seeing evidence that these activities are bearing fruit.

While there is little margin for error at present, we would like to deepen our understanding of this market as we watch developments in Q4. That is all.

Ueda [Q]: Thank you very much. I'm sorry, just as a follow-up, you said that there was not much increase from Q2 to Q3, which makes me think that the market has been on an expansion trend so far. Do you think that the market penetration has run its course to some extent or is there still a little more room for expansion in North America?

Sudo [A]: We are still in the early stage of market penetration. There is quite big space in the market and I think we will see further growth from here. As you mentioned, there is almost no difference between Q2 and Q3, so it is true that we are not seeing a tremendous numerical jump between quarters.

Ueda [M]: Understood. Thank you very much. That is all.

Sakai [Q]: This is Sakai, Credit Suisse Securities. I would like to ask you two quick questions.

The first is, can you tell us how much is the impact of unrealized profit elimination in Q3, compared to that of the last fiscal year?

Kawaguchi [A]: Thank you for your question, Mr. Sakai. I will answer. As you know, we changed the accounting treatment in Q1, so the forex impact from the elimination of unrealized income on inventories has not been affected this year at all, whereas in Q3 of last year, the impact was about JPY2 billion. So that's the YoY impact on the gross margin.

Sakai [Q]: Okay. Thank you. I'd also like to ask about this Crysvita scheme in the US. The product supply price is 35% of sales until FY2022, and 30% thereafter, and this will not be changed, but basically, the commercialization will be transferred to your company. In other words, since there is a threshold, the royalty payment, that is from 20%, or in the high 20s to the Crysvita revenue. To put it in an extreme way, this difference in gross profit will be retained by your company, is that correct?

Kawaguchi [A]: Yes, the difference in gross profit, or in other words, the difference between the current cost of sales in the profit-share scheme, which we deem to be 35%, and the actual cost of sales, which is not so high, is still 100% for us.

So, now 32.5% of revenue is paid to Ultragenyx deeming 35% as COGs. And also 30% after next January, so we will pay 35%, a half share of the remaining 70%.

In contrast, when the royalty rate is changed to the mid to high 20% range, the difference is the direct improvement in profit. So, regardless of how it looks, the real improvement will be seen there.

Sakai [Q]: So, as long as there is no increase in selling expenses or other costs, the improved portion will contribute to your company's profits from next year onward, even though there will still be some payments to Ultragenyx in the first year, is that correct?

Kawaguchi [A]: Yes. As sales expand, this delta will widen, meaning that the monetary benefits will widen.

On the other hand, the so-called sales activity expenses do not increase proportionally with sales, so I hope you understand that we can expect an improvement in the profit margin over the medium to long term.

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

Miura [Q]: Hello, this is Miura, Jefferies. I would like to ask two questions.

First of all, regarding the development of 4083, you said that it will be started by the beginning of next year, but I was wondering if there is anything that has taken longer than expected in the period up to Q2? What is its current status? When Phase 3 program starts, is there a possibility for starting further indications, other than ROCKET, as well?

Torii [A]: Mr. Miura, thank you for your question. As I explained at the time of the last financial announcement, the temporary suspension of Phase 3 due to the change in protocol were not happened by any particular problem with the safety or efficacy data, but rather to the study of more convenient administration methods and administration intervals.

We have reached an agreement with the FDA on this matter, and we are now preparing to resume the program by the end of this year or early next year according to this revised schedule.

We have positioned atopic dermatitis as the most important indication and are focusing on this area. At the same time, we are also studying other indications as LCM, in cooperation with Amgen. That is all.

Miura [Q]: Thank you very much. Secondly, I would like to confirm something regarding the balance sheet. Assets held for sale have appeared this time, amounting to approximately JPY4.2 billion. Can you confirm what this is, when it will be sold, and whether it will affect future P&L? Thank you.

Kawaguchi [A]: Thank you for your question. I will answer. Kyowa Hakko Bio's shares were transferred to Kirin Holdings three or four years ago, and we have held only 5% of those shares since then.

Based on the share transfer agreement, we have decided to exercise our option rights and sell the remaining 5% to Kirin Holdings as of January 1, 2023. Therefore, JPY4.2 billion will be transferred to assets held for sale and will be replaced by cash in January. Thank you.

Miura [Q]: So there is no particular impact on the P&L?

Kawaguchi [A]: That's right.

Miura [M]: Okay. Thank you. That is all.

Yamaguchi [M]: Yamaguchi from Citi again. Can I ask another question? You mentioned earlier about the number of patients in the US, I think the number of patients was 2,000, and the ratio of adult to pediatric was four to six or six to four. And the penetration rate for each was, as was mentioned in the Ultragenyx Q&A session yesterday, about 40% for children and 15% for adults, and there was talk of raising both rates. Do you think that this penetration rate is roughly correct, Mr. Sudo?

I think what you said today was that you aim almost everyone in the pediatric area use it, and aim for half in the adult area.

Sudo [A]: Yes, thank you for your question, Mr. Yamaguchi. There is no significant difference from what Ultragenyx has talked. However, in considering the number of adult patients, Ultragenyx is looking at a patient base of 9,000, while we are looking at 1 in 20,000 people, which gives a figure of 12,000 patients.

In this sense, I feel that the penetration rate of the drug has difference a little by a few percentage points, but we seem to be reaching to about 10%, and that the drug can be used by adult patients as well. For pediatric, we are same with Ultragenyx.

There was the statement that we aim to about half of the adult market, and I think that if we could reach to half of the market in the mid- to long-term, it would be a huge market. First off, we will aim for 20% or 30%.

We are currently looking at how much of this value we can deliver to adult patients. It would be great if we could really reach 50% of patients, however, as a company we would like to aim for at least 30%.

Yamaguchi [Q]: For children, it is almost the same, I think?

Sudo [A]: Yes, for children it is almost the same, I have the impression that we seem to reach to just over half.

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

Moderator [M]: This concludes the conference call regarding the financial results for the Q3 of the fiscal year ending December 31, 2022. Thank you very much for your participation today. Thank you.