



## **Kyowa Kirin Co., Ltd.**

Financial Results Briefing for the Fiscal Year 2021

February 8, 2022

## Event Summary

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<b>[Event Name]</b>	Financial Results Briefing for the Fiscal Year 2021	
<b>[Date]</b>	February 8, 2022	
<b>Number of Speakers]</b>	4	
	Masashi Miyamoto	President and Chief Executive Officer
	Motohiko Kawaguchi	Executive Officer, Director, Finance Department
	Yoshifumi Torii	Executive Officer, Vice President, Head, R&D Division
	Tomohiro Sudo	Executive Officer, Director, Global Product Strategy Department

# Presentation

**Moderator:** We will now hold a conference call regarding the financial results for the fiscal year ended December 31, 2021 of Kyowa Kirin Co., Ltd. which were announced at 15:30 yesterday.

Today's speakers and question-and-answer session participants are four people; Dr. Masashi Miyamoto, President and Chief Executive Officer; Mr. Motohiko Kawaguchi, Executive Officer, Director, Finance Department; Dr. Yoshifumi Torii, Executive Officer, Vice President, Head, R&D Division; and Mr. Tomohiro Sudo, Executive Officer, Director, Global Product Strategy Department.

Today's conference call is scheduled up to 90 minutes. First, Mr. Miyamoto will explain the overall financial results, and then we will take your questions. Please download the documents from our IR website. Well then, Mr. Miyamoto, please.



## 2021 Review

<b>Provide pharmaceuticals for unmet medical needs</b> <ul style="list-style-type: none"><li>■ <b>Maximize the value of G3B</b><ul style="list-style-type: none"><li>✓ Evolved OKK matrix structure to reinforce global product axis</li><li>✓ Crystvita: Grew as planned. Started the preparation for the business transition in North America from Ultragenyx</li><li>✓ Poteligeo: Recovering the growth in the US. Delayed in market launch in EMEA</li><li>✓ Nourianz: Delayed market penetration in the US due to COVID-19 impact. Not approved by EMA</li></ul></li><li>■ <b>Continue to create groundbreaking new drugs</b><ul style="list-style-type: none"><li>✓ Launched new R&amp;D organization; Candidates developed through Open Innovation activities entered the non-clinical stage</li><li>✓ Next-generation strategic products development progressed; KHK4083: met the P2b PE<sup>*1</sup> and entered a strategic alliance, ME-401: met the P2 PE</li></ul></li></ul>	<b>Address patient-centric healthcare needs</b> <ul style="list-style-type: none"><li>■ <b>Patient advocacy</b><ul style="list-style-type: none"><li>✓ Launched regional and cross-functional collaboration on patient advocacy activities</li><li>✓ Implemented the Early Access Program and the Named Patient Program to improve access to medicines</li></ul></li><li>■ <b>Provide value that goes beyond pharmaceuticals</b><ul style="list-style-type: none"><li>✓ Newly established the dedicated team to meet society's medical needs beyond pharmaceuticals</li></ul></li></ul>
<b>Reinforce human resources and structures that support the creation of Life-changing value</b> <ul style="list-style-type: none"><li>■ <b>Cultivate human resources, Strengthen organizations, Build digital platforms, and Others</b><ul style="list-style-type: none"><li>✓ Expanded the Corporate Culture Reform Initiatives globally</li><li>✓ Transitioning to the new normal working style through COVID-19</li><li>✓ Adopted the global DE&amp;I Statement</li><li>✓ Introduced the Global Talent Management System</li><li>✓ Re-organized ICT system to support the operational excellence</li><li>✓ Developed human resources and data infrastructure for driving DX</li><li>✓ Adopted the revised Corporate Governance Code</li></ul></li></ul>	<b>Retain the trust of society</b> <ul style="list-style-type: none"><li>■ <b>Ensure stable supplies of high-quality pharmaceuticals</b><ul style="list-style-type: none"><li>✓ Improved the accuracy of demand forecast and systematically organized the global production and supply system</li><li>✓ Raised quality awareness among all employees and fostered trust in stakeholders</li></ul></li><li>■ <b>Help to protect the global environment</b><ul style="list-style-type: none"><li>✓ Disclosed the support for the TCFD declaration and environmental information</li><li>✓ Expanded the introduction of renewable energy<sup>*2</sup>; reduced annual CO<sub>2</sub> emissions by approximately 39%</li><li>✓ Expanded Scope 3 disclosure data</li></ul></li></ul>

© Kyowa Kirin Co., Ltd.      \*1: Primary Endpoint      \*2: Introduced TEPCO Energy Partner, Inc.'s Aqua Premium at Fuji Plant since January 2022      5

**Miyamoto:** Good morning, everyone. Thank you for taking time out of your busy schedule to participate in this event. I'm Miyamoto from Kyowa Kirin.

Now, I would like to explain the financial results using the materials.

I think you have the document at hand, so please see page five. First, I would like to provide a qualitative review of our progress in 2021, which was the first year of our medium-term management plan until 2025.

As you can see, we are proceeding with our business in accordance with the four management strategies in this mid-term plan.

First, let's talk about the provision of pharmaceuticals for unmet medical needs. I believe that the three global strategic products have achieved steady growth as pillars supporting our growth. We have started management under a new structure that adds a product axis to the One Kyowa Kirin structure, a global operation started in 2019, to maximize product value with a focus on patients more than ever before.

With regard to the continuous creation of groundbreaking new drugs, in addition to the steady progress in the development of next-generation strategic products, several early-stage themes have entered the non-clinical development stage through the utilization and integration of in-house technologies and open innovation. We have also implemented organizational changes in the R&D department to enable more flexible and agile responses. The progress of the pipeline will be explained later.

Next, I would like to talk about addressing patient-centric healthcare needs. In order to bring a smile to the faces of patients and those who care for them, Kyowa Kirin continues to listen to the voices of patients, take on the challenge of continuously creating innovations needed by patients, and working to bring the Life-changing value created to even more people.

As part of our efforts to connect these activities and promote patient-centric business activities, we have begun to collaborate globally on patient advocacy activities. In addition, we will work to improve access to medicines by implementing the Early Access Program and the Named Patient Program, etc.

Concerning retaining the trust of society. We recognize stable supplies of high-quality pharmaceuticals as an extremely important challenge for pharmaceutical companies, and Kyowa Kirin is working diligently to improve the accuracy of supply and demand forecasts and to develop a global production and supply system.

As for our contribution to global environmental conservation, we have expressed our support for the TCFD Declaration. In addition, we are actively expanding the use of renewable energy sources to reduce CO2 emissions.

With regard to strengthening human resources and infrastructure to realize Life-changing value, we have been working to foster a corporate culture suitable for a global specialty pharmaceutical company, and last year we expanded this activity globally. We have also issued a DE&I statement to further instill DE&I, which is necessary for a team that can make diversity a force to be reckoned with. By further promoting DE&I within the Company, we will create a foundation for creating Life-changing value. In addition, we are strengthening our human resource development to promote digital transformation so that we can respond flexibly to changes in the environment.

## Summary of FY2021 Results

**KYOWA KIRIN**

( Billion Yen / Rounded )

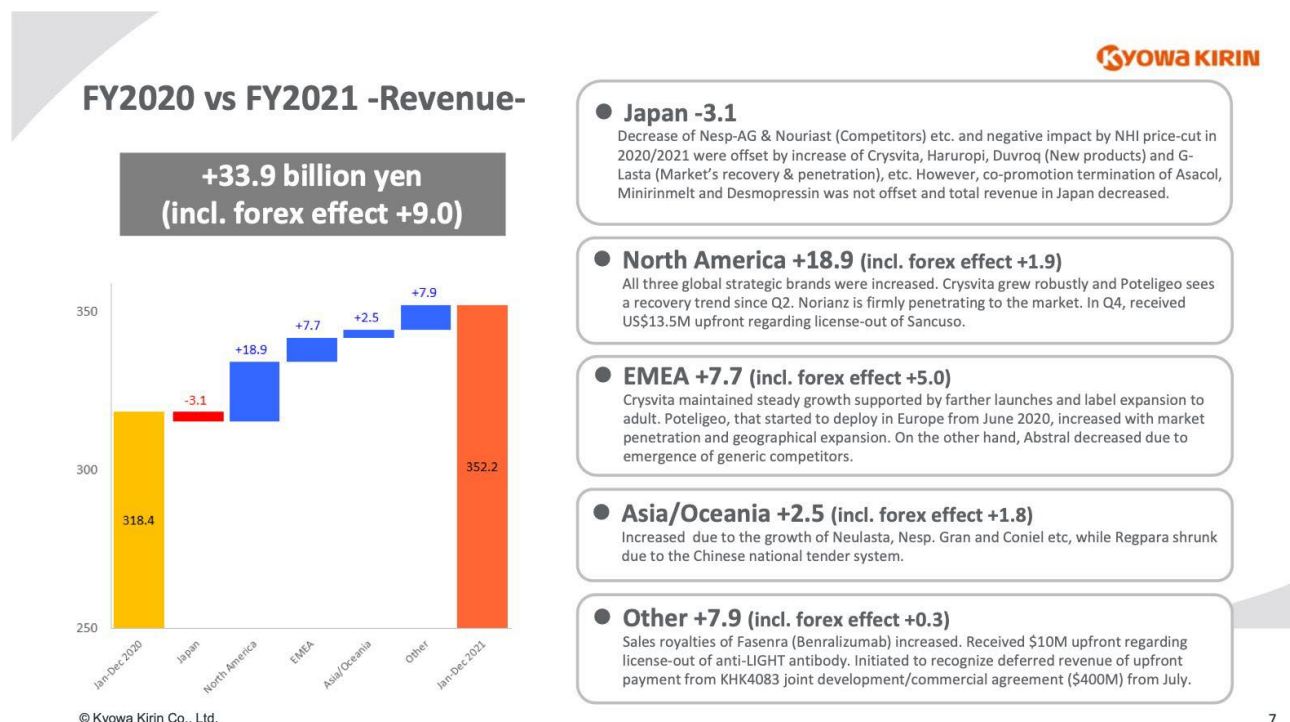
	2020 Results	2021 Results	Changes	2021 Plans	Achieved
Revenue [Overseas Ratio]	318.4 [48%]	352.2 [54%]	+33.9 (+11%)	351.0 [54%]	100%
Gross Profit [Gross Profit Margin]	237.9 [75%]	264.4 [75%]	+26.5 (+11%)	270.0 [77%]	98%
SG&A [SG&A Ratio]	126.6 [40%]	145.6 [41%]	+19.0 (+15%)	141.0 [40%]	103%
R&D [R&D Ratio]	52.3 [16%]	57.7 [16%]	+5.4 (+10%)	65.0 [19%]	89%
Gain/Loss on Equity Method	1.0	4.6	+3.6 (+374%)	1.0	457%
Core Operating Profit [Core OP Margin]	60.0 [19%]	65.7 [19%]	+5.7 (+10%)	65.0 [19%]	101%
Profit	47.0	52.3	+5.3 (+11%)	50.0	105%
Return on Equity	6.8%	7.3%		7.0%	
Dividend Payout Ratio*1	50.3%	43.2%		48.5%	

\*1 Figure for FY2020 is based on EPS and figure for FY2021 is based on Core-EPS (EPS calculated using "Core profit," profit without other income/losses and related taxes).

Now, let me introduce the financial results. Please see page six.

As you can see on the right side of the table for comparison with the plan, we have achieved our targets for the first year of the medium-term management plan, with revenue of JPY352.2 billion, a 100% achievement rate; core operating profit of JPY65.7 billion, a 101% achievement rate; and profit of JPY52.3 billion, a 105% achievement rate.

Both revenue and profits YoY increased by 10% to 11%. ROE has also improved to 7.3%.



I will explain the details on page seven. This is a YoY analysis of revenue broken down by the four region of the One Kyowa Kirin structure.

In Japan, revenue of Nesp AG decreased due to the penetration of biosimilars, and the so-called mid-year NHI price revision had a negative impact, but these were offset by increased revenues of new products such as Crysvita and G-Lasta, etc. As a result, the impact of the termination of joint promotion of Asacol and other products in 2020 remained, resulting in a decrease of JPY3.1 billion in revenue.

In North America, revenue of each of the three global products increased. In addition, Sancuso was out-licensed in the fourth quarter, and an upfront payment of USD13.5 million was recorded as revenue. The total increase in revenue for the year was JPY18.9 billion.

In EMEA, revenue of Abstral decreased due to the impact of generics, but sales of Crysvita and Poteligeo each grew, resulting in an increase of JPY7.7 billion.

In Asia, sales of Regpara, which had been growing steadily by being listed in the NRDL and NEDL in China, turned down due to the impact of the Chinese national tender system since October. On the other hand, other products, such as Neulasta and Nesp, covered for the increase in revenue, resulting in an increase of JPY2.5 billion.

As for Other, there were no major events in the fourth quarter, but royalty income from Fasenra and deferred revenue of the upfront payment of KHK4083 resulted in an increase of JPY7.9 billion.



## Revenue of Major Items (Japan)

(Billion Yen / Rounded)

Item	2020 Results	2021 Results	Changes	Reasons	2021 Plans	Achieved
Nesp + Nesp-AG*1	29.5	26.3	-3.3 (-11%)		23.2	113%
Nesp	4.4	4.0	-0.4 (-9%)	Biosimilars' penetration & NHI price-cut	3.8	105%
Nesp-AG	25.2	22.3	-2.9 (-11%)		19.4	115%
Duvroq	0.6	2.6	+2.0 (+344%)	Launched in Aug 2020	4.0	64%
Regpara	3.8	2.9	-1.0 (-25%)	Shift to Orkedia	2.0	143%
Orkedia	9.1	9.9	+0.7 (+8%)	Shift from Regpara	10.4	95%
G-Lasta	26.7	29.4	+2.7 (+10%)	Market's recovery & penetration	29.8	98%
Poteligeo	2.1	2.0	-0.1 (-3%)		2.0	102%
Rituximab BS	11.8	11.2	-0.6 (-5%)	NHI price-cut	11.5	97%
Romiplate	7.6	7.3	-0.3 (-4%)	Supply constraints (Jun 2020-Mar 2021)	8.7	83%
Allelock	8.6	8.0	-0.5 (-6%)	Generics' penetration & NHI price-cut	6.8	118%
Patanol	10.6	10.7	+0.1 (+1%)		10.9	98%
Nouria	9.4	8.7	-0.7 (-8%)	Competitors' penetration	9.1	95%
Haruropi	0.9	3.1	+2.2 (+243%)	Launched in Dec 2019	4.6	68%
Crysvita	3.8	7.2	+3.4 (+90%)	Launched in Dec 2019	5.5	130%
Tech-licensing	2.0	1.6	-0.3 (-18%)		2.5	67%

\*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.

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Now, please see page eight. These are the major items in Japan.

There are several negative products, such as Nesp and Nesp AG with negative JPY3.3 billion and Nouria with negative JPY0.7 billion. On the other hand, Duvroq, G-Lasta, Haruropi, and Crysvita have shown significant growth in numbers, which means that they have covered the negative aspects including the NHI price revision.

Compared to the plan, revenues of the new products Duvroq and Haruropi, for which we could not conduct promotional activities as expected due to the impact of COVID-19, were 64% and 68%, respectively, and Romiplate, for which it took time to recover after the shipment restriction was lifted, was 83%. They significantly underachieved. Most recently, we have seen steady growth in both Duvroq and Haruropi, and Romiplate is also progressing at a level higher than before the shipment restriction, so we are expecting a good year for 2022.

## Revenue of Major Items (ex-Japan)

(Billion Yen / Rounded)

Item	2020 Results	2021 Results	Changes	Reasons	2021 Plans	Achieved
Crysvita	54.4	78.3	+23.9 (+44%)	[North America] Market penetration & Additional indication (TIO) [EMEA] Geographical expansion & Additional indication (Adult) [Asia/Oceania] Launched in China	77.2	101%
North America	42.4	57.7	+15.3 (+36%)			
EMEA	12.0	20.6	+8.6 (+72%)			
Asia / Oceania	—	0.0	+0.0 (—)			
Poteligeo	11.5	15.3	+3.7 (+33%)	[North America] Market recovery & penetration [EMEA] Launched in Germany in Jun 2020 & Geographical expansion	17.3	88%
North America	10.8	12.7	+1.8 (+17%)			
EMEA	0.7	2.6	+1.9 (+279%)			
Nourianz	2.6	4.5	+1.9 (+74%)	Market penetration	6.7	68%
Abstral	10.2	8.5	-1.6 (-16%)	Generic's penetration & Supply constraints	8.1	106%
Regpara	8.3	7.4	-0.9 (-11%)	Listed on Chinese tender list* <sup>1</sup> in Oct 2021	9.3	79%
Tech-licensing	17.5	24.5	+6.9 (+40%)	Growth of Fasenra & Upfront revenue of anti-LIGHT antibody & Deferred revenue of KHK4083 upfront	23.7	103%
Benralizumab Royalty* <sup>2</sup>	11.0	16.8	+5.8 (+53%)			

\*<sup>1</sup> Volume-Based Procurement (VBP) program that has been launched 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.

\*<sup>2</sup> Sales royalties of Fasenra, marketed by AstraZeneca (Including our own estimation)

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

Now, please see page nine.

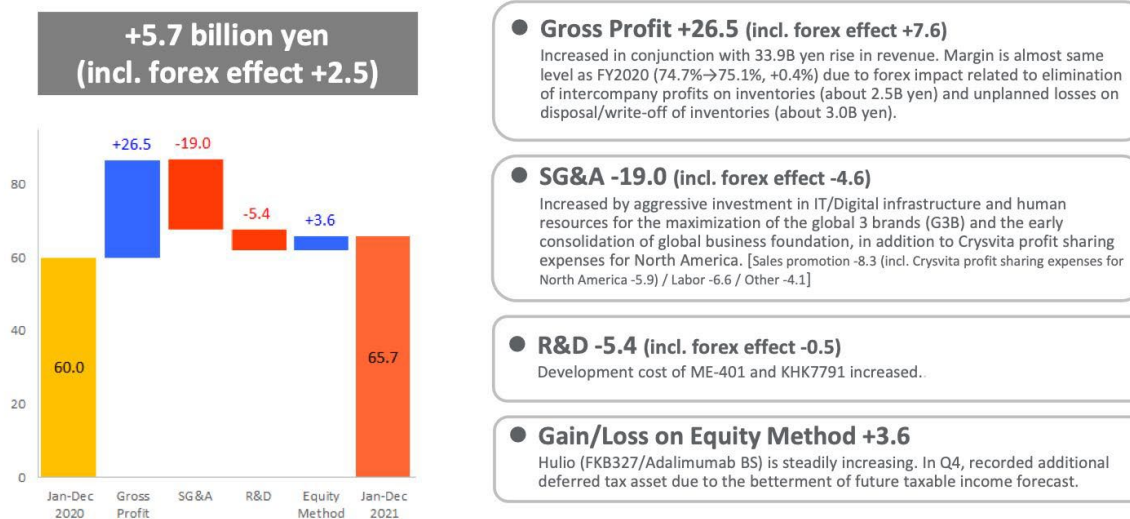
Crysvita continued to grow strongly, achieving its full-year plan with 44% YoY revenue growth. Poteligeo also continued to grow steadily, with a 33% YoY increase. The main reason for the shortfall of 88% to the plan was the delay in the launch schedule in EMEA.

About Nourianz, the revenue was YoY positive 74%. We believe that Nourianz has penetrated well in the market, but it was 68% to the plan. In light of the situation, we have put together a plan to increase revenue this year, which I will introduce later.

As I mentioned earlier, revenue of Regpara in Asia decreased due to the impact of the tender system in China and fell short of the plan. As many of you may know, this system was launched in 2018 as a measure to reduce medical costs in China. The winning bidders are guaranteed a certain quantity, but the selling price drops significantly. In the case of our Regpara, the sales volume has decreased significantly since October due to the fact that it was not selected as a result of the bidding process.



## FY2020 vs FY2021 -Core OP-



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Please look at page 10. This shows the core operating profit.

Gross profit increased by approximately JPY26.5 billion. As mentioned in the callout, the gross profit margin improved by only 0.4% due to negative factors on the cost like forex impact related to elimination of intercompany profits on inventories of approximately JPY2.5 billion and disposal/write-off of inventories of about JPY3 billion.

As for SG&A expenses, we spent aggressively in order to maximize the value of our global strategic products and to establish a global business foundation as quickly as possible. The breakdown of the JPY19 billion increase is as shown in the column, and sales promotion expenses increased by JPY8.3 billion. Of this amount, JPY5.9 billion is from the increase in profit sharing expenses in North America due to the increase in Crysvida revenue, and the remaining increase includes the rebound from the decrease in activity due to the pandemic in 2020.

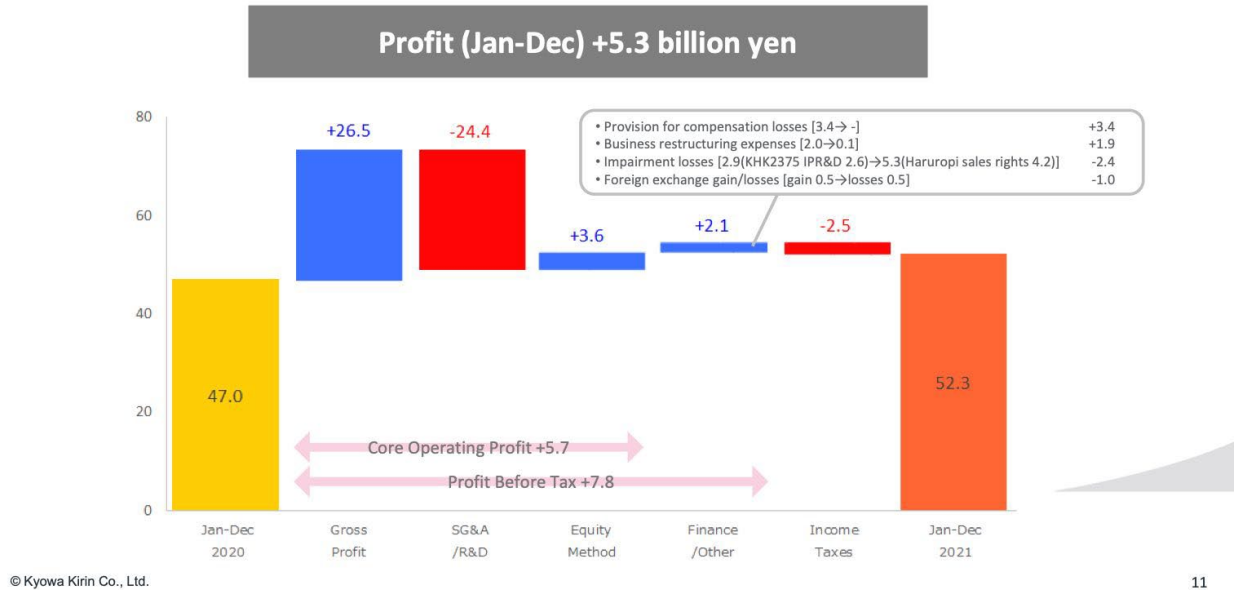
Personnel expenses increased by JPY6.6 billion. Looking at the comparison between the end of FY2020 and FY2021, the number of employees increased by 329. The increase in the number of personnel is mainly due to the strengthening of quality assurance, pharmacovigilance, and supply chain as the foundation of our pharmaceutical company, as well as sales and medical personnel required as more countries handle our global strategic products and human resources and IT.

Other than that, the investment of JPY4.1 billion is mainly in IT infrastructure such as the domestic sales support system, global quality management system, and working from home support including security enhancement. This also includes the cost of preparing for the European launch of Istradefylline, which unfortunately could not receive approval.

R&D expenses totaled JPY5.4 billion, mainly due to increased development costs for ME-401 and KHK7791, our next-generation strategic products, while gain on equity method was a significant factor with JPY3.6 billion. This was mainly owing to the steady growth of Hulio and the significant improvement in FKB's profit and loss as a result of additional deferred tax assets recorded in the fourth quarter for the improved outlook for future taxable income.



## FY2020 vs FY 2021 -Profit-



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Now, please turn to page 11, which will be the last page for FY2021.

After Core-Operating Profit, Finance/Other showed positive JPY2.1 billion. As shown in the column, this is because the losses that existed in FY2020 have decreased or disappeared. The main loss in 2021 was an impairment loss of JPY4.2 billion on the reduced sales of Haruropi, which was recorded in the third quarter.

As a result, profit before tax increased by JPY7.8 billion, with a corresponding increase in tax expenses of JPY2.5 billion, resulting in an increase of profit by JPY5.3 billion.

## 2022 Goals

### Provide pharmaceuticals for unmet medical needs

#### ■ Maximize the value of G3B

For the further market penetration;

- ✓ Steadily implement the Crysvita transition plan in North America and increase launched countries globally
- ✓ Develop approaches that utilize evidence and features of Poteligeo/Nourianz
- ✓ Keep evolving the OKK system through collaboration among regions, functions, and franchises

#### ■ Continue to create groundbreaking new drugs

- ✓ Promote next-generation strategic products development and formulate marketing strategies
- ✓ Expand early-stage development pipeline using Technology axis x Disease biology axis x Open Innovation axis
- ✓ Explore external innovation through the CVC

### Reinforce human resources and structures that support the creation of Life-changing value

#### ■ Cultivate human resources, Strengthen organizations, Build digital platforms, and Others

- ✓ Continue the Corporate Culture Reform Initiatives globally
- ✓ Spread DE&I throughout the company
- ✓ Operate the Global Talent Management System
- ✓ Develop the strategic IT/digital environment for use
- ✓ Unify global ERP system among overseas subsidiaries
- ✓ Introduce the global budget system to improve the budgeting process
- ✓ Optimize the procurement cost

### Address patient-centric healthcare needs

#### ■ Patient advocacy

- ✓ Promote patient advocacy activities
- ✓ Penetrate "Patient Centricity" mindset in the company
- ✓ Develop a drug access policy

#### ■ Provide value that goes beyond pharmaceuticals

- ✓ Take concrete steps to "Provide value that goes beyond pharmaceuticals"

### Retain the trust of society

#### ■ Ensure stable supplies of high-quality pharmaceuticals

- ✓ Enhance the production and storage capacity with global supply perspective
- ✓ Take efforts to prevent counterfeit drugs
- ✓ Complete the installation of eQMA and keep improving its operation
- ✓ Use quality risk management for preventive quality assurance
- ✓ Establish a "quality culture"

#### ■ Help to protect the global environment

- ✓ Reduce CO<sub>2</sub> emissions through the expanding the renewable energy and progress in the solar power introduction plan

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Now let's talk about this year's forecast. Please see page 13.

In 2022, the second year of our five-year mid-term plan, we plan to tackle the various issues shown here, based on last year's achievements and activities. We will further evolve as a global specialty pharmaceutical company by continuing to take on new challenges, in addition to our ongoing efforts to strengthen our foundation starting in 2021.

## Summary of FY2022 Plans

( Billion Yen / Rounded )

	2020 Results	2021 Results	2022 Plans	Changes
Revenue <i>[Overseas Ratio]</i>	318.4 <i>[48%]</i>	352.2 <i>[54%]</i>	380.0 <i>[59%]</i>	+27.8 (+8%)
Gross Profit <i>[Gross Profit Margin]</i>	237.9 <i>[75%]</i>	264.4 <i>[75%]</i>	298.0 <i>[78%]</i>	+33.6 (+13%)
SG&A <i>[S&amp;G Ratio]</i>	126.6 <i>[40%]</i>	145.6 <i>[41%]</i>	164.0 <i>[43%]</i>	+18.4 (+13%)
R&D <i>[R&amp;D Ratio]</i>	52.3 <i>[16%]</i>	57.7 <i>[16%]</i>	70.0 <i>[18%]</i>	+12.3 (+21%)
Gain/Loss on Equity Method	1.0	4.6	3.0	-1.6 (-34%)
Core Operating Profit <i>[Core OP Margin]</i>	60.0 <i>[19%]</i>	65.7 <i>[19%]</i>	67.0 <i>[18%]</i>	+1.3 (+2%)
Profit	47.0	52.3	53.0	+0.7 (+1%)
Return on Equity	6.8%	7.3%	7.1%	
Dividend Payout Ratio*	50.3%	43.2%	47.9%	

\* Figure for FY2020 is based on EPS and figures for FY2021/FY2022 are based on Core-EPS (EPS calculated using "Core profit," profit without other income/losses and related taxes).

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Please see page 14.

As we continue with these activities, here is the summary of our earnings forecast for FY2022. Revenue will increase by JPY27.8 billion, up 8%, core operating income by JPY1.3 billion, up 2%, and profit by JPY0.7 billion, up 1%. As a result, we plan to achieve ROE of 7.1% and a dividend payout ratio of 47.9%.

## FY2022 Plans of Major Items (Japan)

( Billion Yen / Rounded )

Item	2020 Results	2021 Results	2022 Plans	Changes	Reasons
Nesp + Nesp-AG <sup>*1</sup>	29.5	26.3	19.5	-6.8 (-26%)	
Nesp	4.4	4.0	3.1	-0.9 (-23%)	Penetration of biosimilars/HIF-PHIs & NHI price-cut
Nesp-AG	25.2	22.3	16.4	-5.8 (-26%)	
Duvroq	0.6	2.6	5.5	+3.0 (+116%)	Market penetration (Launched in Aug 2020)
Regpara	3.8	2.9	2.4	-0.4 (-15%)	Shift to Orkedia
Orkedia	9.1	9.9	10.0	+0.2 (+2%)	Shift from Regpara
G-Lasta	26.7	29.4	31.5	+2.1 (+7%)	Market's recovery & penetration
Poteligeo	2.1	2.0	1.9	-0.1 (-3%)	
Rituximab BS	11.8	11.2	9.7	-1.5 (-13%)	NHI price-cut
Romiplat	7.6	7.3	10.0	+2.7 (+38%)	Recovery from supply constraints & Market penetration
Allelock	8.6	8.0	6.6	-1.4 (-18%)	NHI price-cut & Generics' penetration
Patanol	10.6	10.7	3.9	-6.8 (-63%)	NHI price-cut & Generics' penetration
Nouriast	9.4	8.7	8.4	-0.3 (-3%)	Competitors' penetration
Haruropi	0.9	3.1	5.5	+2.4 (+78%)	Market penetration (Launched in Dec 2019)
Crysvita	3.8	7.2	10.0	+2.8 (+40%)	Market penetration (Launched in Dec 2019)
Tech-licensing	2.0	1.6	1.0	-0.7 (-41%)	

<sup>\*1</sup> 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.

Let's start with the top line. Please look at page 15. These are the major items in Japan.

First of all, revenues are expected to increase by a total of more than JPY8 billion owing to further market penetration of Duvroq, Haruropi, and Crysvita, and by JPY2.1 billion owing to the growth trend of G-Lasta, and by JPY2.7 billion, owing to the elimination of the impact of shipment restrictions and market expansion of Romiplat.

On the other hand, here are the items that decrease revenue. Revenue of Nesp and Nesp AG are expected to decrease by JPY6.8 billion, taking into account the impact of the switch to biosimilars and HIF-PH inhibitors, as well as the NHI price revision. That of Rituximab BS is expected to decrease by JPY1.5 billion due to the impact of the NHI price-cut. That of Patanol is expected to significantly decrease by JPY6.8 billion due to the launch of generics in the end of the last year and the NHI price-cut.

As a result, revenue in Japan is expected to decrease by JPY7.9 billion.

## FY2022 Plans of Major Items (ex-Japan)

( Billion Yen / Rounded )

Item	2020 Results	2021 Results	2022 Plans	Changes	Reasons
Crysvita	54.4	78.3	105.2	+26.9 (+34%)	Market penetration & Geographical expansion
North America	42.4	57.7			
EMEA	12.0	20.6			
Asia / Oceania	—	0.0			
Poteligeo	11.5	15.3	22.5	+7.3 (+48%)	Market penetration & Geographical expansion
North America	10.8	12.7	15.0	+2.3 (+18%)	
EMEA	0.7	2.6	7.6	+5.0 (+192%)	
Nourianz	2.6	4.5	6.6	+2.1 (+46%)	Market penetration
Abstral	10.2	8.5	6.7	-1.8 (-21%)	Generic's penetration
Regpara	8.3	7.4	3.7	-3.7 (-49%)	Listed on Chinese tender list*1 in Oct 2021
Tech-licensing	17.5	24.5	34.3	+9.8 (+40%)	Growth of Fasenra & Deferred revenue of KHK4083 upfront (6→12months worth)
Benralizumab Royalty*2	11.0	16.8			

\*1 Volume-Based Procurement (VBP) program that has been launched 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, marketed by AstraZeneca (Including our own estimation)

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

Please look at page 16. This is for overseas.

Crysvita is targeting JPY105.2 billion with 34% growth. Since we are forecasting JPY10 billion for Crysvita in Japan, the global total will be JPY115.2 billion, which will be the birth of Kyowa Kirin's first in-house blockbuster, and we are determined to achieve this goal.

Poteligeo is targeting a 48% increase to JPY22.5 billion and Nourianz is targeting a 46% increase to JPY6.6 billion. Revenue of Abstral and Regpara are expected to decrease significantly due to the impact of generics and the full year impact of the tender system, respectively.

Tech-licensing is expected to increase by JPY10 billion owing to the continued increase in sales royalties from Fasenra and a six-month increase in deferred upfront revenue from KHK4083.

As a result of the above, we are aiming for a total increase of JPY26.7 billion in revenue from overseas regions, and JPY8.9 billion in revenue from other areas, including tech-licensing.

## FY2021 vs FY2022 -Core OP-

Core OP +1.3 billion yen



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### ● Gross Profit +33.6

Due mainly to 27.8B yen rise in revenue (Japan+7.9, North America+22.1, EMEA+6.4, Asia/Oceania+1.8, Other+8.9) and absence of FY2021's negative factor on COGS. Margin is expected to improve by 3.4% (75.1%→78.4%).

### ● SG&A -18.4

Due to transient investment for preparation toward self-commercialization of Crysvida in North America starting from spring FY2023, in addition to growing Crysvida's profit sharing expenses. Will continue our aggressive investment in IT/Digital infrastructure and human resources for the maximization of the global 3 brands (G3B) and early consolidation of the global business base.

[Main factor of increase]

- Crysvida profit sharing expenses for North America
- Expenses for building a self-commercialization structure for Crysvida in North America (HR, Activities, IT, etc.) [approx. 5.0B yen]
- Human resources (mainly for global functions) [approx. 4.5B yen]
- IT/Digital (Global ERP, Global budget system, Global quality management system, Sales supporting system in Japan, Global IT help desk, Cyber security enhancement, etc.) [approx. 2.0B yen]
- Launch readiness for next generation strategic products [approx. 1.5B yen]

### ● R&D -12.3

Due to the late phase development costs of next generation strategic products centered on KHK4083.

### ● Gain/Loss on Equity Method -1.6

Due to the rebound from last year's positive deferred tax impact, while Hulio (FKB327 /Adalimumab BS) grows.

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Please see page 17.

In addition to a total increase in revenue of JPY27.8 billion, the elimination of approximately JPY5.5 billion of deteriorating factors in cost of sales that occurred in FY2021 will result in an increase in gross profit of JPY33.6 billion. We also plan to improve the gross profit margin by 3.4% to 78.4%.

SG&A expenses are planned to increase by JPY18.4 billion. The main factors for the increase are listed in the column. First of all, profit sharing expenses increases due to the growth of Crysvida sales in North America. The amount is not disclosed here.

The second is about JPY5 billion in preparation costs for the in-house sales of Crysvida in North America, which will start in the spring in 2023. In the spring of this year, one year before the transfer, we plan to establish a system within our company in parallel with Ultragenyx's operations, synchronize with Ultragenyx's activities, and absorb their know-how. Half of Ultragenyx's costs will still be borne by us, so that means we will have to make a new investment up front. This is a situation where there will be overlap, so to speak. This will be resolved in spring in the next year, so we hope you understand that this is a temporary situation that will last from this spring to next spring.

In addition, we will invest JPY4.5 billion in human resources, approximately JPY2 billion in IT digital investment, and JPY1.5 billion in preparation costs for the launch of ME-401 and other products.

R&D expenses are expected to increase by JPY12.3 billion for the late-stage development expenses for next-generation strategic products such as KHK4083.

In addition, on equity method, decrease will be JPY1.6 billion because the tax impact that existed in 2021 will be eliminated.

As a result, gross profit will increase by more than JPY30 billion, but the quantitative plan of core operating profit for FY2022 is slight YoY increase of JPY1.3 billion.

As you can see from our business performance and pipeline, overseas sales are increasing year by year, and we are planning to obtain approval and launch next-generation strategic products from around 2023 at the earliest. We recognize that now is the time for Kyowa Kirin to build a solid business foundation as a global company, and we will continue to make solid investments in 2022. By solidifying this foundation, we are determined to achieve medium- to long-term growth on a global scale. I would be grateful for your support in this regard.



## Shareholders Return

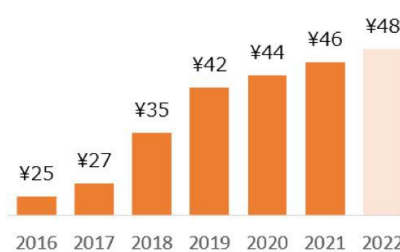
- ✓ FY2021 dividend is **46** yen, and FY2022 to be **48** yen (plan)
- ✓ Plans **6-year consecutive rises** since FY2017

Year	Dividend (yen)		Payout Ratio <sup>*1</sup>	Return on Equity
	Interim	Year-end		
2016	12.50	12.50	25.00	44.9%
2017	12.50	14.50	27.00	34.4%
2018	15.00	20.00	35.00	35.2%
2019 <sup>*2</sup>	20.00	22.00	42.00	33.7%
2020	22.00	22.00	44.00	50.3%
2021 <sup>*3</sup>	23.00	23.00	46.00	43.2%
2022 (Plan)	24.00	24.00	48.00	47.9%

<sup>\*1</sup> FY2021/2022 figures are payout ratios against the Core EPS that is calculated based on the Core Earnings (= Profit - Other income/losses - Related income taxes)

<sup>\*2</sup> Repurchase of 10.7M own shares (¥22.6B) executed on February 6, 2019. Total return ratio for FY2019 is 67.3%.

<sup>\*3</sup> Year-end dividend of 23 yen/share will be submitted to the 99th Ordinary General Meeting of Shareholders to be held on March 25, 2022.

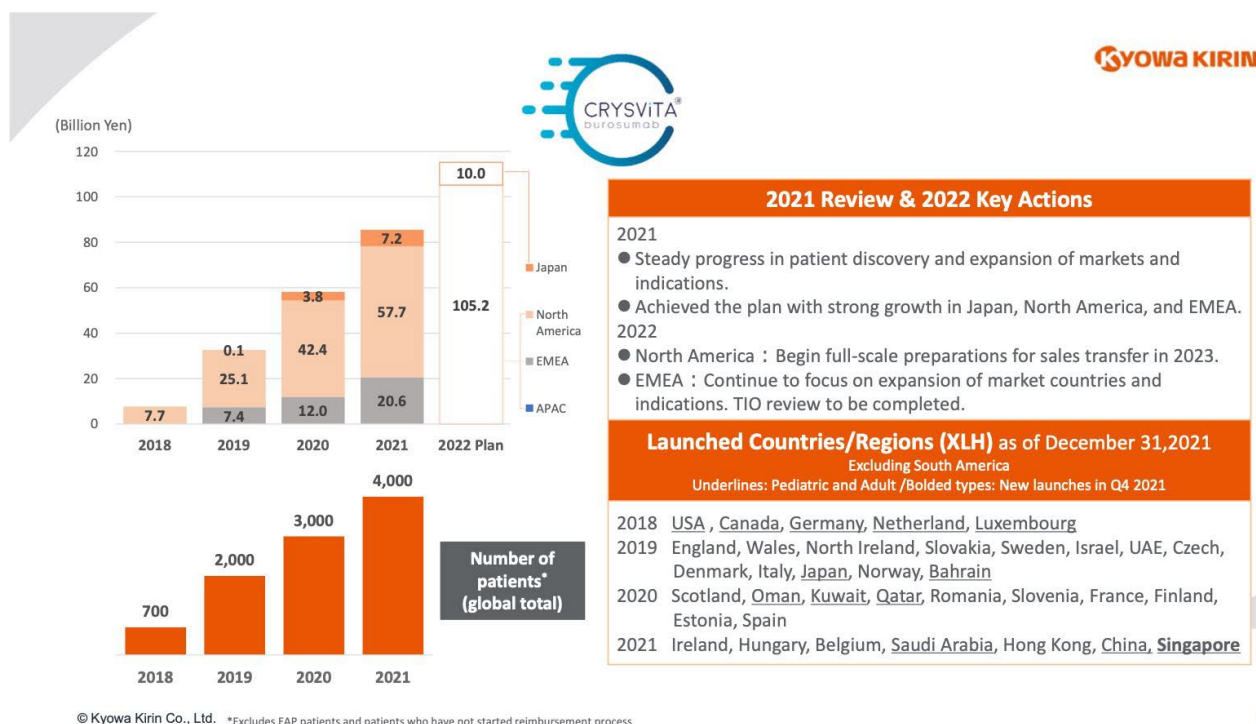


Now, please turn to page 19. This shows shareholders return.

We plan to pay a dividend of JPY46 per share for FY2021 and JPY48 per share for FY2022.

As shown in the graph, we plan to increase dividends for the sixth consecutive year since 2017. The Company's dividend policy during the current medium-term management plan is to aim for a dividend payout ratio of 40%, and to aim for a stable and sustainable increase in dividend levels in line with medium- to long-term profit growth.



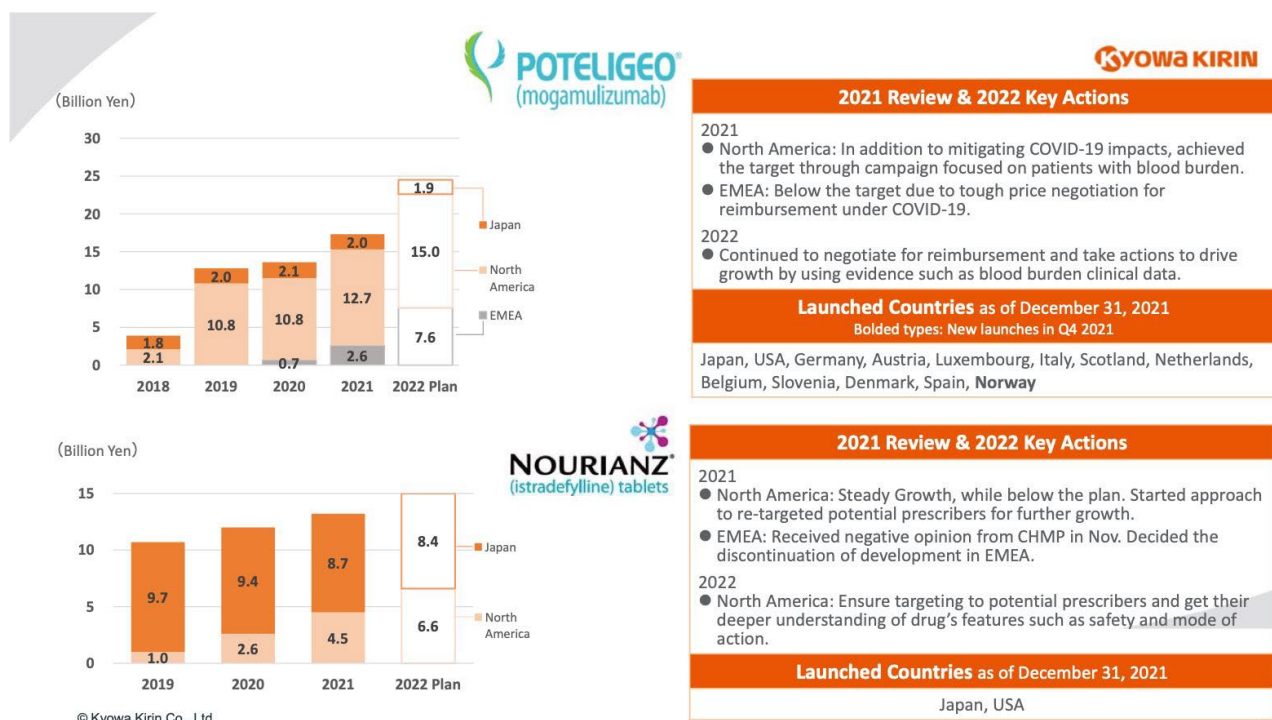


Please turn to page 21. Moving on to the commercial update. First of all, this is Crysvida.

The chart on the top left shows the four-year results from 2018, the year of launch, and the forecast for 2022. It has shown strong growth so far, and we will work for further penetration in the market, launch the product in new countries and regions, and expand its indications so that this growth trend will continue.

We have been working to bring Crysvida, a Life-changing drug, to as many patients as possible, and in 2021 we continued to identify more patients and expand the number of countries and indications for which Crysvida can be marketed. As a result, there are an estimated 4,000 patients being treated with Crysvida globally.

In 2022, we will finally begin full-scale preparations for the transfer of sales in the US, which is coming next spring. In addition, in EMEA and Asia Pacific regions, we will maximize our efforts to further identify patients, launch countries, and expand indications, and in Europe, TIO review is expected to be completed.



Please turn to page 22. This is about Poteligeo.

In the four years since 2018, the year of global launch, sales have been steady, and in 2021, we have seen a recovery from the impact of COVID-19 in North America, and activities focused on patients with hematological tumors, etc. Several factors have come together to achieve our plan.

Negotiations for reimbursement in EMEA are progressing, but not at the speed originally planned, and there are still countries in the process of negotiations. In 2022, we will continue to negotiate for insurance reimbursement in order to increase the number of countries where the product is sold, and we will also work to increase the speed of market penetration.

Nourianz. In the US, we are growing steadily. In order to ensure market penetration and growth, last year we started a new approach based on prescriber targeting. In 2022, we will steadily carry out these activities to establish a solid positioning as a safe, easy-to-use drug with a distinctive mechanism of action, and work to penetrate the market.

On the other hand, in Europe, the decision was made to discontinue the development of Istradefylline after it was not approved. That's it for the commercial update.

## Upcoming Events: Next-generation Strategic Products

Underlined: Completed events from Jan 1 to Nov 1, 2021  
 ✓: Completed events from Nov 2, 2021, to Feb 7, 2022

Code Generic name	H1 2021	H2 2021	H1 2022	H2 2022
KHK4083/ AMG 451	Atopic dermatitis <u>P2b topline data</u>	Atopic dermatitis <u>P2b topline data</u>	Atopic dermatitis P3 FPI	
KW-6356			Parkinson's disease P3 FPI Parkinson's disease P2b detailed data	
ME-401 Zandelisib	FL (3L+, mono) <u>P2 LPI</u> MZL (3L+, mono) <u>P2 FPI</u>	FL (3L+, mono) P2 topline data ✓ FL/MZL (2L+, combo) <u>P3 FPI</u>	FL (3L+, mono) P2 detailed data* CLL (2L+ combo) P2 FPI iNHL (3L+, mono) P2 topline data (JP)	
RTA 402 Bardoxolone methyl	ADPKD <u>P3 FPI (JP)</u>	Alport syndrome <u>MA (JP)</u>	DKD P3 LPO	
KHK7791 Tenapanor	Hyperphosphatemia under maintenance dialysis <u>P3 FPI (JP)</u>	Hyperphosphatemia under maintenance dialysis P3 topline data ✓	Hyperphosphatemia under maintenance dialysis Submission (JP)	

\*: a more complete report of the P2 TIDAL data reported on Nov. 30, 2021, to be provided; FPI: first patient in; LPI: last patient in; LPO: last patient out; FL: follicular lymphoma; MZL: marginal zone lymphoma; iNHL: indolent B-cell non-Hodgkin lymphoma; CLL: chronic lymphocytic leukemia; ADPKD: autosomal dominant polycystic kidney disease; DKD: diabetic kidney disease; MA: marketing application

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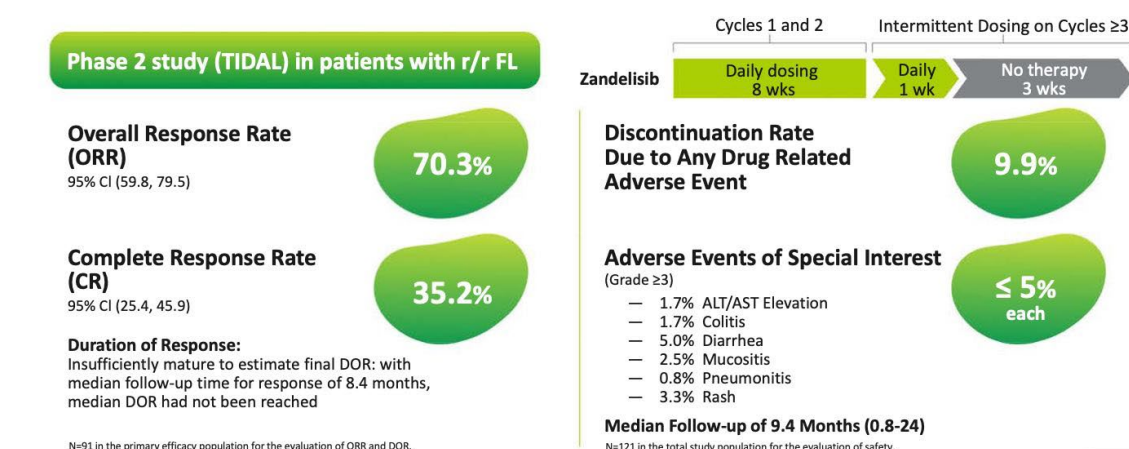
Now, please see page 24. The left side of the table shows the events we have accomplished in the last year regarding next-generation strategic products. There are two events accomplished since the last earnings announcement.

The first is ME-401, zandelisib. Top-line data from the Phase II TIDAL study for follicular lymphoma was announced on November 30. This one will be briefly outlined later.

Secondly, we announced that the Phase III study of KHK7791, tenapanor, with hyperphosphatemia patients on dialysis met its primary endpoint on December 13. Detailed data will be presented at a future conference or in a paper.

The right side of the table shows the events that are expected to be achieved during 2022. Following last year, we will continue to make steady progress in the development of each of them this year, and we hope you will look forward to the next news.

## Update 1: Zandelisib Global Ph2 TIDAL Study Topline Data



Note: ORR assessed by IRC after a minimum follow-up of 6 months and represents the primary endpoint of the TIDAL study. Safety and duration of response data are as of the data cutoff date; the data cutoff date is approximately 6 months after the last patient in the primary efficacy population received their first dose of zandelisib. With exception of the ORR and CR data reported in the primary follicular lymphoma efficacy population of 91 patients, the data reported today provides an initial look at the data as of the data cutoff date and is interim and subject to change as more patient data become available. Because the data reported today is from an ongoing study, the final data may differ materially from the data reported in this presentation.

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Please see page 25. This is an overview of the top-line data from the Phase II TIDAL study of zandelisib in patients with relapsed/refractory follicular lymphoma. The data were analyzed at the data cut-off point, which was set at approximately six months after the first administration for the last patient.

The design of the study is shown in the figure on the upper right. After eight weeks of daily dosing, an intermittent dosing on cycle of four weeks, consisting of one week of daily dosing, and three weeks of no therapy period was conducted. As a result, the overall response rate was 70.3% and the complete response rate was 35.2%. In addition, the discontinuation rate due to drug-related adverse events was 9.9%. Among the notable adverse events commonly seen with PI3 kinase inhibitors, the incidence of grade 3 or higher adverse events is less than 5%, as shown in the table below.

The current data show high efficacy with a favorable safety profile, which is consistent with the data obtained so far from the Phase Ib study. We will continue the trial to pursue the duration of response and safety, while discussing with our partner MEI Pharma and FDA. We will also continue to seek to maximize the value of this drug by conducting trials for indications other than follicular lymphoma and marginal zone lymphoma.

## Update 2: Bardoxolone Methyl (RTA 402)

### • Regulatory review for Alport syndrome will continue after Q1 2022 in Japan

- ✓ FDA Cardiovascular and Renal Drugs Advisory Committee voted no on bardoxolone methyl's efficacy and risk-benefit for Alport syndrome in the US.
- ✓ Kyowa Kirin is addressing the PMDA's review in Japan, considering Reata's policy.

### • LPO of the phase 3 study for DKD is expected to be in H2 2022 in Japan

- ✓ PMDA pointed out the importance of long-term data in discussions with Kyowa Kirin.
- ✓ Kyowa Kirin decided on a 6-month study extension to obtain 3-year or longer data for more patients.

Please see page 26. This will be an update on the status of RTA 402.

We filed an application for Alport syndrome in Japan in July last year, and at this point, the review process is expected to continue beyond the first quarter. The FDA's advisory committee held on December 8, last year, expressed a negative opinion on the efficacy and risk-benefit of the drug for Alport syndrome based on the data to date. Kyowa Kirin will continue to respond to the PMDA's review, taking into account the thoughts of Reata, our partner for the application in the US.

As for diabetic kidney disease, we expect the last patient out in the second half of this year. In our discussions with PMDA, we have received a view that long-term data is important. We have also decided to extend the trial by six months in order to collect long-term data on more subjects.

Due to this, the schedule for this drug made when the mid-term plan was developed is delayed. However, we would like to collect long-term data from as many subjects as possible in order to accumulate reliable evidence.

## Update 3: Next-generation Strategic Products

As of Feb 7, 2022

	Country / region* <sup>1</sup>	Indication* <sup>2</sup>	Approval year* <sup>3</sup>	Total addressable market* <sup>4</sup>	No. of patients* <sup>5</sup>
KHK4083/ AMG 451	NA/EU/JP	Atopic dermatitis	2025/2026	★★★	16,000K
KW-6356	NA/EU/JP	Parkinson's disease	2026	★★★	3,500K
ME-401	NA/EU/JP	Follicular lymphoma Marginal zone lymphoma	2023	★★★	~800K
RTA 402	JP/Asia	Alport syndrome Diabetic kidney disease Autosomal dominant polycystic kidney disease (ADPKD)	TBD 2024 2025	★★★	2,500K~
KHK7791	JP	Hyperphosphatemia under maintenance dialysis	2023	★☆☆	250K

\*1 Countries or regions where Kyowa Kirin currently has marketing rights and will launch products (or will conduct marketing activities); products may not be launched in all countries or regions shown in the table

\*2 Expected indications as of the date of this document; indications may ultimately differ to expectations due to status of approvals from regulatory authorities

\*3 Expected year of first approval

\*4 Expected total addressable market, which is the sum of all products for the indications shown in \*2, in all countries or regions defined in \*1, not projected sales or the Company's targets; ★ = less than ¥50bn, ★★ = ¥50-100bn, ★★★ = Over ¥100bn

\*5 Total number of estimated patients in all countries or regions defined in \*1.

\*6 The size of the total addressable market and patient numbers are based on our estimates

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Now let's turn to the last slide, page 27. This section provides a brief overview of the latest profiles of next-generation strategic products.

This is an updated version of the list we presented when we announced our mid-term plan, based on our current progress. Although there are some development products for which the expected approval date is a little further away, we believe that overall progress is being made steadily.

I'm sorry I took so long, but that's all I have to say.

## Question & Answer

**Moderator [M]:** We would now like to move on to the question-and-answer session. Thank you.

Our first question comes from Mr. Wakao of JPMorgan Securities Japan Co., Ltd. Mr. Wakao, please go ahead.

**Wakao [Q]:** I'm Wakao from JPMorgan. Thank you. I would like to ask you two questions related to Crysvita.

First, please tell us about Crysvita's performance in the fourth quarter and the outlook for this fiscal year. As for North America, I think the second and third quarters of last year were somewhat flat, and there was a slightly large jump up in the fourth quarter, so again, please tell us about the results in the US and the outlook for this fiscal year. Also, in Europe, I think the Early Access Program had an impact. Please tell me how you look at it in 2022. Thank you. This is my first question.

**Moderator [M]:** Mr. Sudo will now answer.

**Sudo [A]:** Hi Mr. Wakao, thank you for your question.



I would like to answer to the first question. In the third quarter, I said that I was basically taking a positive view of the situation from the fourth quarter onward, and indeed, the fourth quarter has seen significant growth. I think a specific number is shown for each quarter, but the numbers actually grew significantly as well.

This is because, as I mentioned before, we raise prices in January, so wholesalers purchased a lot of inventory in December. I think this had a big impact. However, if you look at the sales curve from 2018, which is shown in the document that Miyamoto explained earlier, you can see that sales have been gaining momentum, and we expect this momentum to continue in the future. Looking at patient-based data and other data, we are feeling a definite response. This is the first point.

The second point is about the Early Access Program in Europe. This year, we will further obtain insurance reimbursement for adult indication and start selling them. So, we will be able to add the sales on the commercial sales which was sold through the Early Access Program until last year, and the impact of expanding to adults is significant, so we would like to anticipate the expansion in Europe this year. We are positive about all of these.

**Wakao [Q]:** Thank you very much. In Europe, I understand that there was a delay in insurance reimbursement, and while the number through the Early Access Program increased, sales at reimbursed prices did not grow so much. You expect that this will be improved, and insurance reimbursement will contribute to the sales, or it has already contributed. Is that correct?

**Sudo [A]:** Yes. I think it's fine to take it that way.

**Wakao [Q]:** Okay, thank you very much.

Secondly, you mentioned that the preparation for self-commercialization of Crysvita in the US will cost JPY5 billion temporarily this fiscal year, but how much will be the cost of that from 2023? I think this is a very important part to achieve 25% or higher OP margin target. Is it safe to assume that the OP margin as a whole will improve toward 25% from the next fiscal year? That's all.

## Crysvita - Collaboration with Ultragenyx -



Territories	Economic terms
U.S. & Canada	<ul style="list-style-type: none"> <li>Kyowa Kirin books sales</li> <li>50/50 profit share for 5 years from the U.S. launch</li> <li>After 5 years, Kyowa Kirin pays tiered sales royalties in mid-high 20% range to Ultragenyx</li> <li>Supply price: 35% of net sales through 2022, 30% thereafter</li> </ul>
Europe	<ul style="list-style-type: none"> <li>Kyowa Kirin books sales</li> <li>Kyowa Kirin pays sales royalties in up to 10% range to Ultragenyx</li> <li>*Ultragenyx have sold a royalty right on/after 2020 to Royalty Pharma</li> </ul>
Latin America	<ul style="list-style-type: none"> <li>Ultragenyx books sales</li> <li>Kyowa Kirin receives low single-digit sales royalties from Ultragenyx</li> <li>Supply price: 35% of net sales through 2022, 30% thereafter</li> </ul>
Turkey	<ul style="list-style-type: none"> <li>Ultragenyx books sales</li> <li>Kyowa Kirin receives sales royalties in up to 20% range from Ultragenyx</li> </ul>
Asia & Others	<ul style="list-style-type: none"> <li>Kyowa Kirin books sales</li> </ul>

\* Kyowa Kirin supplies commercial products in all territories.



**Kawaguchi [A]:** I am Kawaguchi from the finance department and will answer this question. Mr. Wakao, thank you for your question.

The first point is how expenses will be incurred from the next fiscal year. You can read more about our collaboration with Ultragenyx on page 30 of this slide.

How will it be from April, five years after the launch? First of all, we are now paying half of the gross profit in the form of profit sharing. Specifically, we calculate the cost of goods as 35% of sales, so we pay half of the 65%, or 32.5%, as half of gross margin. In next fiscal year, that will be in the mid to late 20% range, so there will be a certain amount of profit improvement here.

On the other hand, since it is a profit share, if we were to bear all of the sales promotion costs that we now bear on a 50/50 basis, this is a negative factor. So, the total improvement would not be that great. In total, this will not lead to a significant improvement.

We have not seen a significant increase in our sales activities compared to the current sales activities of Ultragenyx, so by firmly controlling these activities and sales will increase, the profit margin will improve. I would like you to see it in this way.

I would like to add one more point: when the scheme will change, the profit-sharing expenses that are now included in SG&A expenses will be included in the cost of sales, so the apparent high SG&A ratio appears to have been reduced.

As for the improvement of the profit margin, as I mentioned, we will not see a dramatic improvement in this scheme change next year, but we are aiming to improve the profit margin by self-commercialization, which is of course the goal for CrysVita in North America.

Concerning the mid-term plan goal of 25%, unfortunately, the profit margin fell slightly this year, and even without the impact of the JPY5 billion, the improvement was only a little. However, from next year, we will start to improve this situation. We plan the profit-margin improvement from FY2023 toward 25%. That is all.

**Wakao [Q]:** I understand very well. Thank you very much. Can I understand that the portion related to SG&A in the US will be kept at about the same amount as Ultragenyx?

**Kawaguchi [A]:** We would like to reduce the number if possible, compared to that. We are still working on the details now, so I can't say anything definite, but we don't envision a JPY5 billion increase or anything like that.

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

**Moderator [M]:** Thank you very much.

The next question is from Mr. Yamaguchi, Citigroup Global Markets Japan Inc. Mr. Yamaguchi, please.

**Yamaguchi [Q]:** This is Yamaguchi from Citi, thank you very much.

The first question is a little bit overlapping with the previous question, but among the JPY18 billion significant increase in SG&A expenses, I understand the profit-sharing portion and the cost of establishing the self-commercialization system, but there are various other items such as JPY4.5 billion for human resource investments and JPY2 billion for IT investments.

I understand that you are investing this much in the current fiscal year for a step-up cost in the process of building a global structure, but will they continue to be incurred in the next fiscal year and beyond? Or are

there quite a few expenses that, after a certain amount is paid out, will then run their course? I would like to start by asking you what the costs are for the next fiscal year and the current fiscal year in terms of non-Crysvita.

**Miyamoto [A]:** Thank you very much, Mr. Yamaguchi. This is Miyamoto.

As you mentioned concerning the cost, the reason why the growth rate is so high is because we want to build a solid foundation first, so we are investing heavily in that area.

We have already reached a point where we have decided not to grow at this rate in the next fiscal year and beyond, and I don't think we will see a decrease in SG&A expenses compared to this fiscal year. However, it is not the case that we will increase the rate of growth more than the top line growth, for example, but we will keep the growth rate lower than that of the current fiscal year.

We'll give you some more details from Kawaguchi.

**Kawaguchi [A]:** As Miyamoto mentioned, if we do not control this area, we will not be able to improve the profit margin. We recognize that the important points are to make the necessary investments while firmly controlling the rate of increase and to firmly lower the costs that can be lowered. Thank you very much.

In short, the strengthening of our business foundation includes the fact that we are now able to see and control costs on a global scale, so in this sense, I think you can consider that we are becoming much more capable.

**Yamaguchi [Q]:** I understand. When I heard what you said, I thought that you are managing costs on a global basis, so there are so-called normal costs and these are controlled by the IT system. Is it correct to say that such controls are in place globally?

**Kawaguchi [A]:** In order to further strengthen these areas, we are working to improve the global budget system, as mentioned in the IT Digital Investment section, as well as the accounting system, which is not unified globally and was not visible in a timely manner. So, we are still in the process of making improvements.

**Yamaguchi [Q]:** Okay, thank you very much.

Secondly, I would like to ask you about the update on RTA 402. First of all, as for Alport syndrome, the estimated completion period for the review has passed, but you are still working on. As for the outlook for the future, it is still based on the same data in the US, so the voting result at AdCom in the US is having an impact, and I hate to say this, but I wonder if you are in a situation where you will not be able to get approval in the short term.

**Torii [A]:** Thank you for your question.

As a sponsor, it is difficult for me to give a clear answer since it is the opinion of the authorities, but I can honestly say that FDA's opinion certainly may have an impact. However, concerning this, there are some gaps in the view between the FDA and sponsors. So, we would like to obtain additional data and work with our partner Reata, while Kyowa Kirin will continue to monitor FDA's trends and consult with PMDA in Japan.

**Yamaguchi [Q]:** I understand. As for DKD in Phase III below, of course, the doses are different and there are various differences, but one of the topics discussed at the AdCom for AS this time was that the chart was created to show that the renal function may not have improved in the long term, and various reviews were conducted. I am somewhat concerned about the importance of the long-term data for DKD, as it seems to be in the same context. Is this a completely different story? And, of course, the data read-out will be next year,

not this year with collected long-term data, but I think it is delayed to next year. If the next year read-out sounds positive, it will move on to filing an application. Am I correct?

**Torii [A]:** Thank you for your question.

As you said, the pathogenesis of Alport syndrome and DKD are quite different, so I don't think the AS screening status will have a direct impact. On the other hand, PMDA is of the opinion that long-term data is important, so we will have to be behind schedule by about six months.

However, as Miyamoto mentioned earlier, if we can get event-based data that is close to the true endpoint in a larger number of patients, and if the results are as expected, we will be able to proceed with negotiations with the authorities with more reliable evidence. So, we take it positively and made this decision.

**Yamaguchi [M]:** Thank you. That is all from me.

**Miyamoto [A]:** In addition, as Torii just explained, as for the DKD study, as you know, it is a double-blind trial, and we are doing a very large study in Japan. If we can get solid long-term data, depending on the results of course, but if we can get solid event-based data, I think it will be very easy for us to expand into commercialization. This six-month postponement itself is a negative factor in terms of schedule, but if the data is good, we consider it as a positive factor. That's all.

**Yamaguchi [M]:** Thank you very much. That is all from me.

**Moderator [M]:** The next question is from Mr. Kohtani, Nomura Securities Co., Ltd. Mr. Kohtani, please go ahead.

**Kohtani [Q]:** This is Kohtani from Nomura Securities. Thank you.

I'm incredibly curious about bardoxolone, and I'm sure it's not the same because it is for Alport syndrome and kidney disease, but I still think it's a hard hurdle to overcome when I hear what the FDA is saying.

Summarizing FDA's opinion at the advisory committee meeting, firstly, the efficacy of bardoxolone in improving eGFR was only a pharmacodynamic effect and not a disease modifying drug. Secondly, in terms of safety, albuminuria was observed, which raises concerns about hyperfiltration, weight loss, and increased blood pressure was also observed.

First, I would like to ask about efficacy. This is Alport syndrome, so it is not the same as chronic kidney disease, but what I would like to ask is that the FDA documents seem to say that even if eGFR is improved, it does not mean much. Putting hyperfiltration aside for a moment, is there anything wrong with improving eGFR in this area of Alport syndrome or chronic kidney disease? This certainly seems to return to its original state when the medication is stopped, but I think it is good that the eGFR is improving normally. I would like to hear your view.

**Torii [A]:** Thank you for your question.

As you mentioned, in the case of kidney disease, DKD is based on the period of time required for an event to occur that is close to the true endpoint, but in the case of Alport syndrome, it is a rare disease, and we cannot design it that way, so we have to use eGFR as the surrogate marker. We have been discussing this with the KOLs, and I think they are basically aware that it is an effective surrogate marker, so I think you are right there.

The FDA is saying that the washout is not sufficient for the long term, and that it may require a longer period of time, but as I said earlier, we will negotiate with them with additional data.

Also, in the second year, after the 4-week washout, the effect seems somewhat weakened in terms of the eGFR change rate compared to placebo, but the efficacy of the drug is also recognized during the period of continued treatment. We will continue to negotiate with the authorities to see if we can bring new benefits from this drug.

**Kohtani [Q]:** This is saying, in short, that eGFR is improving due to short-term pharmacodynamic effects, but in the end, the fact that eGFR is improving is good in itself, isn't it?

**Torii [A]:** Yes, it is my understanding.

**Kohtani [Q]:** I understand.

Next, let's talk about safety. If we look at the TSUBAKI study for diabetic chronic kidney disease that your company conducted, there was no increase in blood pressure, there was weight loss, but it was not accompanied by creatine kinase, which indicates muscle loss, and there was no increase in creatinine in the urine. The albumin in the urine is increasing, but this is being interpreted in the exact opposite way, as the albumin is increasing due to the increased filtration rate caused by the increased surface area of the glomerulus and not the damage to the kidney caused by hyperfiltration.

I think the FDA suspected hyperfiltration and lack of a scientific mechanism for this drug, and is looking at the data with doubt. In this safety, as far as TSUBAKI is concerned, there is no problem, and hyperfiltration has been denied to some extent. Is this correct?

**Torii [A]:** Thank you for your question.

As I have said before, based on the non-clinical data, I think there is no risk of hyperfiltration. As mentioned earlier, the most important is clinical data. We are conducting the AYAME study on a scale of more than 1,000 patients, so we will make a final decision based on the results.

**Kohtani [Q]:** But if the data like TSUBAKI can be reproduced, there may not be much problem in obtaining approval in Japan. I think the FDA is looking at the safety of the drug while picking the past BEACON study rather than the CARDINAL study for Alport syndrome. They are only concerned about the safety concerns there, and your company, of course, had very different data from BEACON for Japanese TSUBAKI, so in that sense, if you can reproduce the TSUBAKI data, can we assume that it is not such a problem?

**Torii [A]:** Yes, I recognize that, and I would just like to say here that we don't fully agree what the FDA is claiming.

**Kohtani [Q]:** I apologize that I am asking so many. You are extending the study duration a little bit, and the estimated study completion has been shifted from the first half of 2022, does this mean that you took a longer washout period?

**Torii [A]:** We have not changed the washout period. At the data cutoff stage, we decided on a six-month extension in order to accumulate three years of data on all the subjects who participated in the clinical trial before submitting the application.

**Kohtani [Q]:** The FDA says that the washout takes about 60 days, but your company and PMDA do not agree to that. Am I correct?

**Torii [A]:** In Japan, we have already agreed with PMDA on the design of Phase III, which I believe was 14 weeks, but it is a design that will be evaluated after a longer washout period rather than four weeks, for which the FDA is saying too short.

**Kohtani [M]:** I understand. Thank you very much.

**Torii [M]:** Thank you very much for the questions.

**Moderator [M]:** The next question is from Mr. Hashiguchi, Daiwa Securities Co. Ltd. Mr. Hashiguchi, please go ahead.

**Hashiguchi [Q]:** I'm Hashiguchi. Thank you.

The first is about the design of the KHK4083 Phase III trial. The details may not be finalized yet, but if you have almost decided on the general framework, could you please share it? In particular, I would like to know what kind of ingenious ideas you have for the study design in order to make it more clearly differentiated from the preceding products.

**Torii [A]:** Thank you for your question.

We are working with Amgen on this project, and we will release a press release on the Phase III design when we start the trial. We are sorry to say, but please wait for the press release.

**Hashiguchi [Q]:** I understand.

My second question is about FKB. Your domestic technology revenue target for the previous period was not met, and the outlook for future taxable income sees improvement on gain/loss on equity method. Could any of these factors be the reason that these are the items that have been dropped from the development pipeline in FKB? Or, if you have another reason, could you please share it with us?

**Kawaguchi [A]:** Thank you for your question.

I am answering your first point that domestic technology revenue fell slightly short of the plan. In the plan, we were going to have some transitory milestones, but there are no longer any such milestones. I would like to refrain from introducing or explaining the contents here.

On the other hand, regarding the additional positive tax effect due to improvement of FKB's future outlook on equity method, the main reason here is that sales of Hulio have been steadily increasing, and the probability of future prospects has increased. Also, FKB had been issuing more and more bonds to cover its insolvency, but from the end of this year, it has entered the collecting phase of the bonds.

We decided to estimate future cash flow once more, and when we estimated it based on FKB's plan for 2022 and beyond, we found that we would be able to collect all the bonds. In addition, it is expected that the most of tax loss carryforwards that are accumulating to date will not expire and can be used almost completely in the future.

**Hashiguchi [Q]:** Thank you very much. What you just told me is related to the change in the development plan of new products? Or is it just due to the reflection of the sales situation?

**Miyamoto [A]:** Thank you. This is Miyamoto.

I assume you are asking about FKB's business. If you are asking if there is anything new, such as the development of new products, then there is not. I hope I answered your question.

**Hashiguchi [Q]:** So, you have no further plans for new products at the moment?

**Miyamoto [A]:** It means that we don't have anything concrete to explain at the moment.

**Hashiguchi [M]:** I understand. That's all. Thank you very much.

**Moderator [M]:** The next question is from Mr. Muraoka, Morgan Stanley MUFG Securities Co., Ltd. Mr. Muraoka, please go ahead.

**Muraoka [Q]:** Hello. This is Muraoka from Morgan Stanley. Thank you.

I would like to have your explanation about ME-401, including the industry environment. I know very well that TIDAL in Phase II was great.

On the other hand, your competitors, such as Gilead, Incyte, TG Therapeutics, have been issuing very negative news in the past couple of months. The reason is that the review for PI3K inhibitors by the authority has been getting stricter regarding a matter of safety and efficacy? I think the slide shows the 2023 launch schedule for ME-401, am I correct in assuming that ME-401 is okay? If there are a few concerns in your company, it would be helpful if you could share them with us. This is my first question.

**Torii [A]:** Thank you for your question.

First of all, we are internally reviewing it. FDA's policy is that a confirmatory Phase III study must be completed after the accelerated approval. These are the conditions. Recently, various competitors have withdrawn their accelerated approvals or NDAs because they have not yet started these confirmatory studies, or they have started them but have not been able to complete them at the right time. I think there is a complicated mix of factors such as various side effects, etc., and I am guessing that this may have had an impact.

On the other hand, zandelisib, as you mentioned, has shown very effective results in TIDAL, and the confirmatory study has already been conducted as a Phase III trial, with the first patient dosing last year. This is the situation. Maybe next month, we will be negotiating with the FDA about the timing of the submission for accelerated approval based on the current situation, and we are making preparations for that. That's all.

**Muraoka [Q]:** Thank you very much. In other words, you are basically saying that there is good data out there, so there is no need for me to extend my concerns about other companies to you.

**Torii [A]:** Yes, we have obtained very promising data, and we believe that this is worth bringing to the market.

**Muraoka [Q]:** I understand. Thank you very much.

Also in the pipeline, there is KHK4951, tivozanib eye drop for AMD. I thought the Phase I results would be out by now, so I looked at ClinicalTrials.gov, and the trial was scheduled to end in February, but it has been moved to September for some reason, and it looks like it has increased the size of the trial by about 30 patients. It would be helpful if you could explain what the situation is now, and what was behind the change in the study design, or rather the timing of the end of the study, etc. Was there a story that boosted your confidence, or was there a factor that made you a bit more cautious?

**Torii [A]:** Thank you for your question.

This does not mean that we are changing the design of the trial in particular, but we are asking not only healthy adults but also wet AMD patients to enter the Phase I trial, and to be honest, we found the trial requires some more time for enrolment. So, it does not mean that there will be any major changes in the design.

**Muraoka [Q]:** I thought that the increase in scale meant that you expanded the patient part, but is that not the case?

**Torii [A]:** We are expanding based on various possibilities including the dosage and administration, and the number of cases is increasing.

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

**Moderator [M]:** The next question is from Mr. Miura, Jefferies Japan Limited. Mr. Miura, please go ahead.

**Miura [Q]:** This is Miura from Jefferies Securities. I would like to ask two questions.

First of all, with regard to the SG&A expenses, which have been questioned before, you have commented that you will control the increase in the next fiscal year compared to the current fiscal year, but you do not expect it to decrease. Is it correct to assume that the current level of SG&A expenses will continue for the remaining four years of the medium-term management plan through FY2025? This is my first question.

**Kawaguchi [A]:** Thank you for your question, Mr. Miura.

In terms of the amount, it will increase gradually. In terms of the cost-to-sales ratio, our mid-term plan is to reduce this ratio. Did I answer to your question?

**Miura [Q]:** The reason for the gradual increase in value is that the SG&A expenses related to Crysvita, etc., that are selling well, and the next generation products, and the IT infrastructure, etc. that seem to be transient, are not increasing. Is that correct?

**Kawaguchi [A]:** Now is the time to invest in the infrastructure very firmly, and the increase in this area is expanding, but we are still lacking in it as a global company. Therefore, it is not the case that the portion of the increase in IT investment here will be dramatically reduced. Promotion expenses, which occurred in line with sales, will not increase in proportion to sales, so please understand that the ratio of sales promotion expenses will decrease if the top line increases to a certain degree.

**Miura [Q]:** I understand. Thank you very much.

Secondly, for Crysvita, I think it is difficult to foresee how the COVID-19 pandemic will develop in the future, but what assumption about the pandemic growth is the base of your significant growth plan through this fiscal year?

**Sudo [A]:** I would like to answer to you.

Basically, we are assuming a trend of improvement, but as you know, we have seen it growing very strongly over the past year or two, so basically we can continue this growth. Or if the situation of COVID-19 improves and we are able to be more active, including in sales activities, then we can hope for more. We may be able to achieve more than that, depending on the situation. Basically, as I said, the situation of COVID-19 is improving, but we are not going back to the way it was before, and the situation is based on the assumption that we are entering a new era.

**Miura [Q]:** I understand. The price of Crysvita was increased by about 6% in January of this term. Of course, inflation in the US is accelerating rapidly, so I assume that you are increasing your prices in line with that, but I have an impression that inflation in the US is likely to continue, so is there a possibility that you will raise prices further this fiscal year? Also, I think that the material cost increases accordingly. Is it possible to improve the actual profit margin of Crysvita and other products by raising prices?

**Sudo [A]:** I would like to answer this question.



First of all, price increases are based on the overall situation, so it is difficult to say whether or not to raise prices at this point. The reason why we made this price increase by 6% this time is because we thought that 6% would be appropriate as inflation rate when looking at the overall current situation, so we will see what happens in the future. As for the profit margin, of course, there is the matter of raw materials and the SG&A expenses I mentioned earlier, but we are not expecting a large improvement in the profit margin by raising prices for that purpose. That is all from me.

**Miura [M]:** I understand. Thank you very much. That's all.

**Moderator [M]:** The next question is from Mr. Ueda of Goldman Sachs Japan Co., Ltd. Mr. Ueda, please go ahead.

**Ueda [Q]:** This is Ueda from Goldman Sachs.

I would like to start by asking about the premise of biosimilar products in Japan. With regard to Nesp AG, you mentioned earlier that the impact of biosimilars and oral drugs has been factored in. I would like to know any impact of oral drugs at the moment and how you look to them in the future. Regarding Rituximab BS, you only mentioned the NHI price revision, but I would like you to explain how you are looking at the volume.

At the same time, I believe that incentive evaluation for the use of biosimilars have been discussed in the individual revision items of the *Chuikyo*, so I would like you to comment on the impact of these on the biosimilar business. Please answer to this question.

**Miyamoto [A]:** Mr. Ueda, thank you. This is Miyamoto.

First of all, regarding Nesp AG, I think your question is about the impact of HIF-PH inhibitors, and I believe this does to a certain extent. Both Nesp AG and biosimilars are used to a certain extent in patients with anemia in the pre-dialysis phase, and in these areas, the market is more favorable for oral drugs, so I think there is a possibility to be replaced. On the other hand, the dialysis market will change to a certain extent with oral drugs, of course, but it remains to be seen whether HIF-PH inhibitors will be able to gain a large share of the market here, so we will have to wait and see.

As for the Rituximab BS, we were selling it almost exclusively until the middle of last year, but there is now competing BS, so there is a possibility that there will be an impact on volume. However, basically, as you mentioned, there is a movement to promote the use of BS, so we believe that there is still room for growth in volume. I believe that the NHI price revision is the major factor.

**Ueda [Q]:** Thank you very much. If that is the case, is it correct to say that the risk of the HIF-PH inhibitor has been factored in because it may come out this year, rather than that it will have any impact on the current situation?

**Miyamoto [A]:** As you know, we also sell Duvroq, and we are putting a lot of effort into this. In particular, it is very convenient for patients in the pre-dialysis phase, and we believe it is a good drug, so we would like to see it used by many patients.

I believe that there will be a certain amount of progress in switching to oral drugs rather than biologics that require injections. We think that it has an impact a little at the moment. We have not yet been able to analyze the market in detail, but of course we believe that our patients will switch. We believe that this will have an impact in the future.

**Ueda [Q]:** Thank you very much.

Secondly, I would like to ask an additional question about the self-commercialization of Crysvita in the US. Ultragenyx has been able to increase the sales amid the pandemic by doing very well with e-marketing, and it seems to have accumulated knowledge in marketing. I would like to know if it is possible to use this kind of system at your company as it is, and if there is any possibility of transferring people, such as salespeople or sales strategy people, and to what extent, what you have built at Ultragenyx, can be transferred to your company. I know this is a qualitative question, but could you please explain?

**Sudo [A]:** Thank you for your question, Mr. Ueda. This is Sudo and I will reply to you.

Specific preparations are underway with Ultragenyx for the transfer in April of 2023.

You mentioned about e-marketing, but since the launch in 2018, we've basically been doing meeting for sales four times a year, and we've been doing other marketing meetings jointly. We have globally used the knowledge in the US market. We have accumulated a lot of know-how and experience in this area, and we would like to use it to make a smooth transition in April 2023.

I can't talk about the details at this time, but we are making preparations so that we can transfer the so-called sales methods and experience that I mentioned earlier, including the system. We will have another chance to give you more details when the time comes.

**Miyamoto [A]:** Mr. Ueda, this is Miyamoto.

As an additional comment, as you know, Crysvita is a very important product for us and also very important for Ultragenyx. As Kawaguchi explained earlier, the profit structure will change in the future, and they will move toward earning royalties, but it will be a very large revenue stream for Ultragenyx.

Therefore, a smooth transition here is very important for both companies, probably one of the most important transitions, and we are working very closely to create the self-commercialization system on our side. I have been getting a lot of questions like this, and I hope you can get an idea of how closely we work together.

**Ueda [M]:** Thank you very much. I understand. That concludes my questions.

**Moderator [M]:** The next question is from Mr. Sakai of Credit Suisse Securities Limited. Mr. Sakai, please go ahead.

**Sakai [Q]:** I'm Sakai from Credit Suisse.

I'd like to take over the previous question, but I think there might be a lot of Crysvita in stock in North America. Therefore, I understand very well that the transition is very important, including in this area.

It seems that the details will be discussed later, but I think it will be in the second half of this year that we will be able to see the actual implementation of these moves, such as the transfer of inventory, human resources, and know-how, so that the impact on Crysvita sales should be kept to a minimum. In addition to the forecast for 2022, there is no disclosure of Crysvita's overseas sales by country or region, so I would like to ask you about that. This is my first question.

I believe the approval for Crysvita's launch in China was given in August of last year, but I was wondering what the situation was like after that, including the possibility to be listed in the NRDL. On the other hand, if it happens, the price will drop considerably, so please update us on the situation. This is my second question.

**Sudo [A]:** Thank you very much, Mr. Sakai. This is Sudo and I will reply to you.

First of all, you mentioned about inventory. Actually, the holder of the market authorization, has been Kyowa Kirin since we launched the product in the US in 2018. Therefore, the sales activities facing customers and medical activities have been led by Ultragenyx, but CMC, supply chain, PV, and QA have already been carried out mainly by Kyowa Kirin. In that sense, I think we can make transitions without having a lag.

There are definitely some areas where we need to improve our inventory, but this is not a matter between Ultragenyx and us, but rather a problem that needs to be improved within Kyowa Kirin, and we are working on it.

About your second question. As you mentioned, we received approval from China in August last year, and we will internally discuss to take a concrete approach to negotiate the NRDL price. At this point, we are selling the drug on an individual basis, and I think there are four or five cases, which is a very small number of patients, but some patients are using the drug. As Mr. Sakai knows, the situation of the NRDL is changing in many ways, so I can't say anything definite, but we will try to deliver this drug to patients in China as soon as possible. **Sakai [Q]:** Thank you very much. In that case, I would like to confirm that, in terms of inventory, recently, the amount of unrealized profit has become quite large due to foreign exchange fluctuations at the end of the period. In that case, the inventory level which I think is owing to Crysvita will have to be adjusted to some extent, but if the absolute amount does not change that much, the amount of unrealized profit will not change significantly, although I think this will be affected by foreign exchange rates. Am I correct?

**Kawaguchi [A]:** I am Kawaguchi from the finance department and will answer this question.

As for your question on unrealized profit, as you mentioned, the biggest impact is the large amount of Crysvita inventory that we ship to North America at transfer pricing. If the exchange rate applied to them changes, it has an impact, like this time. However, if the exchange rate remains constant, there will be no impact on profit and loss, and on the other hand, if the yen appreciates, there will be a positive impact. In order to reduce the impact, we need to reduce and improve our inventory in North America. Please note that this transfer won't affect these points much.

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

**Moderator [M]:** Thank you very much.

As we are running out of time, I would like to conclude with a question from the next person. The next question is from Mr. Tanaka of Mizuho Securities Co., Ltd. Mr. Tanaka, please go ahead.

**Tanaka [Q]:** This is Tanaka from Mizuho Securities.

My first question is about VBP for Regpara in China. This happened in October last year, and of course you were not able to win the tender, but are there any more products that your company sells in China that could be affected by such system in the future? Also, in Japan, Orkedia is the successor to Regpara. Is it correct to assume that Kyowa Kirin does not have the rights to this product in China?

**Miyamoto [A]:** Thank you very much, Mr. Tanaka. This is Miyamoto.

We are not able to inform you of other potential products for national bidding because we have no list here. As you know, the regulations are changing at a rapid pace, and it is difficult to keep up with them. We have to follow it up.

You asked us how to address underperformance of Regpara. One is that Nesp has already been approved, and since Nesp is not yet included in the NRDL, we will first negotiate for Nesp to have it included in the NRDL, and we hope to keep our sales activities in the renal field somehow.

As for Orkedia, we don't have enough information now to say for sure that this is the case.

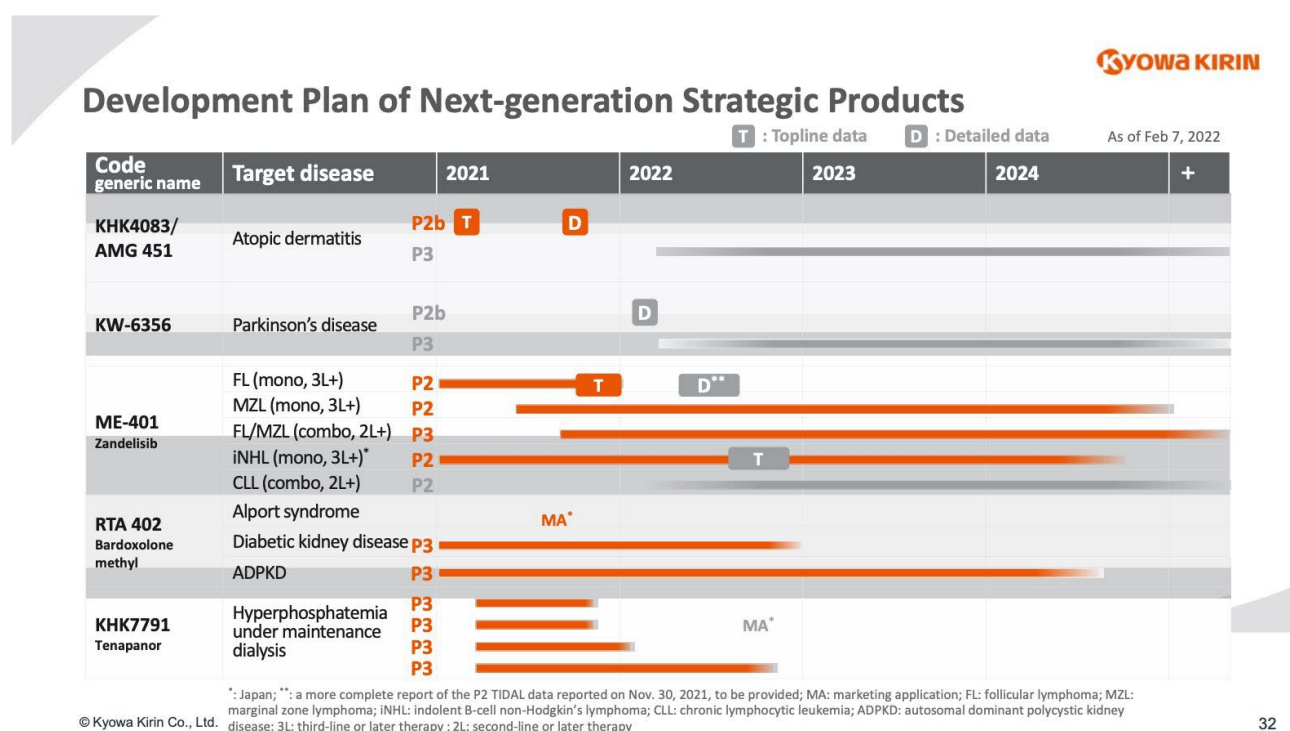
**Tanaka [Q]:** In your company's China business, other than Regpara, what is the main focus of this China business, in terms of disclosed products? Is it Gran?

**Miyamoto [A]:** Regpara has been leading the way so far, but recently, I think it is Gran. In that sense, I think the key to our business in China, as I mentioned earlier with Crysvita, is how quickly we can launch other products. On the other hand, as I mentioned earlier, the regulations change very quickly, so this is definitely a country that is very difficult for us to plan for.

We are also reviewing our local operations in China and our strategy team to see if we can upgrade them. We are internally reviewing it.

**Tanaka [Q]:** This time, the bidding of Regpara was in October, but I don't think you told us that before that, like in the third quarter, so I would like you to disclose that quickly and properly.

**Miyamoto [A]:** Understand your point. We will certainly try to do that as soon as we can disclose.



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**Tanaka [Q]:** Secondly, on page 32 of the slide, where it talks about the next generation strategic products, of course Phase III will start for KW-6356, but I think that the character "D" in the chart meaning detailed data, means that the paper will be published. Can we expect the paper will be published soon? In Phase III, will it be a single agent for the time being, or will it basically be a combination?

**Torii [A]:** Thank you for your question.

I apologize for the delay in publishing the paper, but it has taken some time to coordinate the opinions with KOLs, and we are preparing to submit the paper soon, which should be published in the first half of this year.

As for the design of Phase III, we have already started negotiations with the FDA, and we are preparing for various developments globally. We are considering it from various viewpoints, including mono therapy. As for

the details, we will disclose the design and other information after the FPI, so please wait until then. That's all.

**Tanaka [M]:** I understand. Thank you very much.

**Moderator [M]:** Thank you very much.

Thank you very much for joining us today, everyone. We would like to ask for your continued support.