Kyowa Kirin Co., Ltd.

Financial Results Briefing for the Fiscal Year 2024

February 7, 2025

Event Summary

[Event Name]	Financial Results Briefing for the Fiscal Year 2024	
[Date]	February 7, 2024	
[Number of Speakers]	5	
	Masashi Miyamoto	Representative Director, President and Chief Executive Officer
	Takeyoshi Yamashita	Director, Senior Managing Executive Officer and Chief Medical Officer
	Motohiko Kawaguchi	Managing Executive Officer and Chief Financial Officer
	Abdul Mullick	Managing Executive Officer and Chief International Business Officer
	Hiroki Nakamura	Global Corporate Communications Head

Presentation

Nakamura: Ladies and gentlemen, thank you very much for taking time out of your busy schedules to attend our financial results briefing today. My name is Nakamura from the Global Corporate Communication of Kyowa Kirin Co., Ltd., and I will serve as today's moderator. Thank you very much for your cooperation.

We will now begin the briefing of Kyowa Kirin's financial results for the fiscal year ended December 31, 2024, which was announced at 3:30 PM yesterday.

Prior to the start of the briefing, there are a few notes to be made. Please note that we will keep the names and company names of those who participated today at the venue and online as a participant list for a certain period of time. Please note that the content of this briefing will be distributed on demand and published on our website as a transcript. Please bear this in mind when you state.

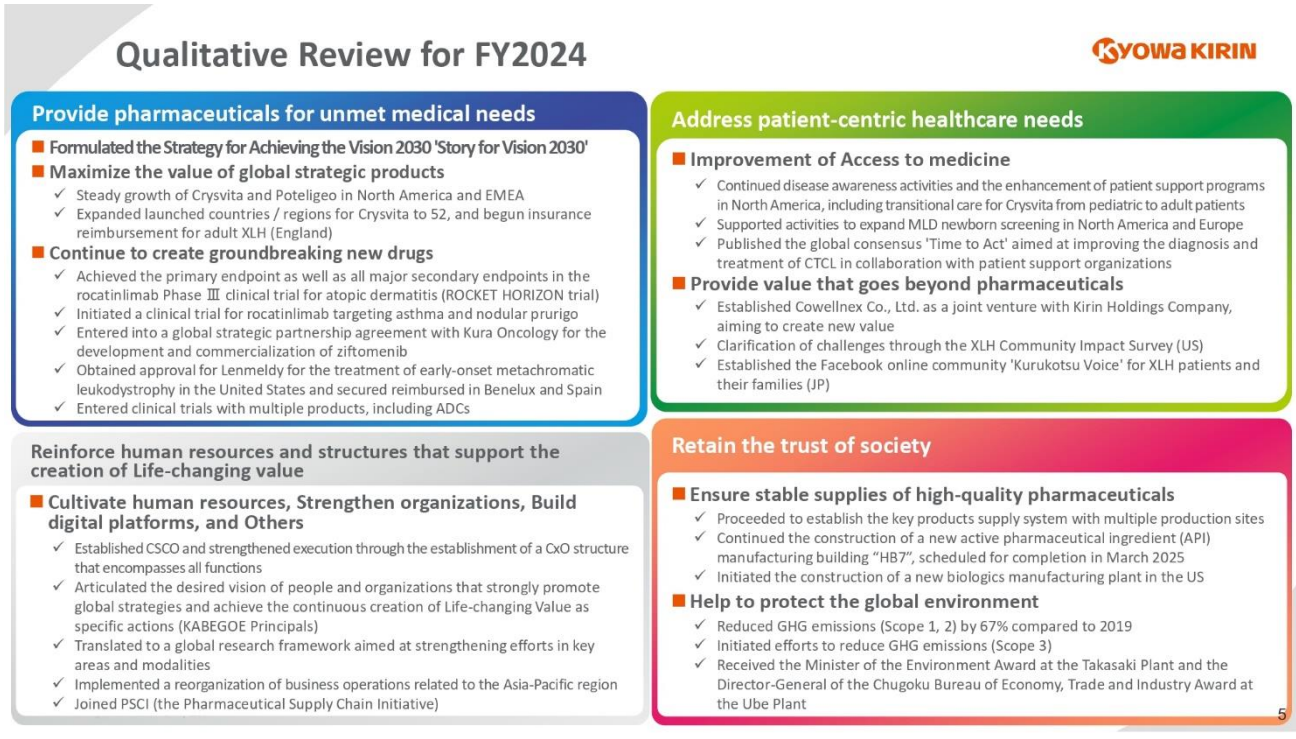
The information presented today contains forward-looking statements. Please note that there is uncertainty due to various risks.

A question-and-answer session will be followed by the presentation.

Today's speaker is Masashi Miyamoto, Representative Director, President, and Chief Executive Officer. In addition to Miyamoto, the Q&A session will be led by Takeyoshi Yamashita, Director, Senior Managing Executive Officer, and Chief Medical Officer; Motohiko Kawaguchi, Managing Executive Officer, and CFO; and Abdul Mullick, Managing Executive Officer, and Chief International Business Officer.

Today's briefing is scheduled for 100 minutes, including the presentation and question-and-answer session. This will be a long one time-wise, and the speaker officers will be seated during the briefing. Please understand this in advance.

Let's move on to the briefing.



Miyamoto: Good morning. Thank you very much for taking time out of your busy schedule to attend this meeting. Once again, my name is Miyamoto from Kyowa Kirin. I would like to explain using the slides.

To begin, I would like to review the last year's progress qualitatively. Regarding the provision of pharmaceuticals that address unmet medical needs, we took a significant step toward realizing our vision by formulating the Story for Vision 2030 last year and proceeding with initiatives based on a more clearly defined strategic roadmap.

Crysvita and Poteligeo have continued to grow steadily in 2024. On the R&D front, the ROCKET program for rocatinlimab is progressing well and has achieved the primary endpoint, as well as all major secondary endpoints, in the HORIZON trial.

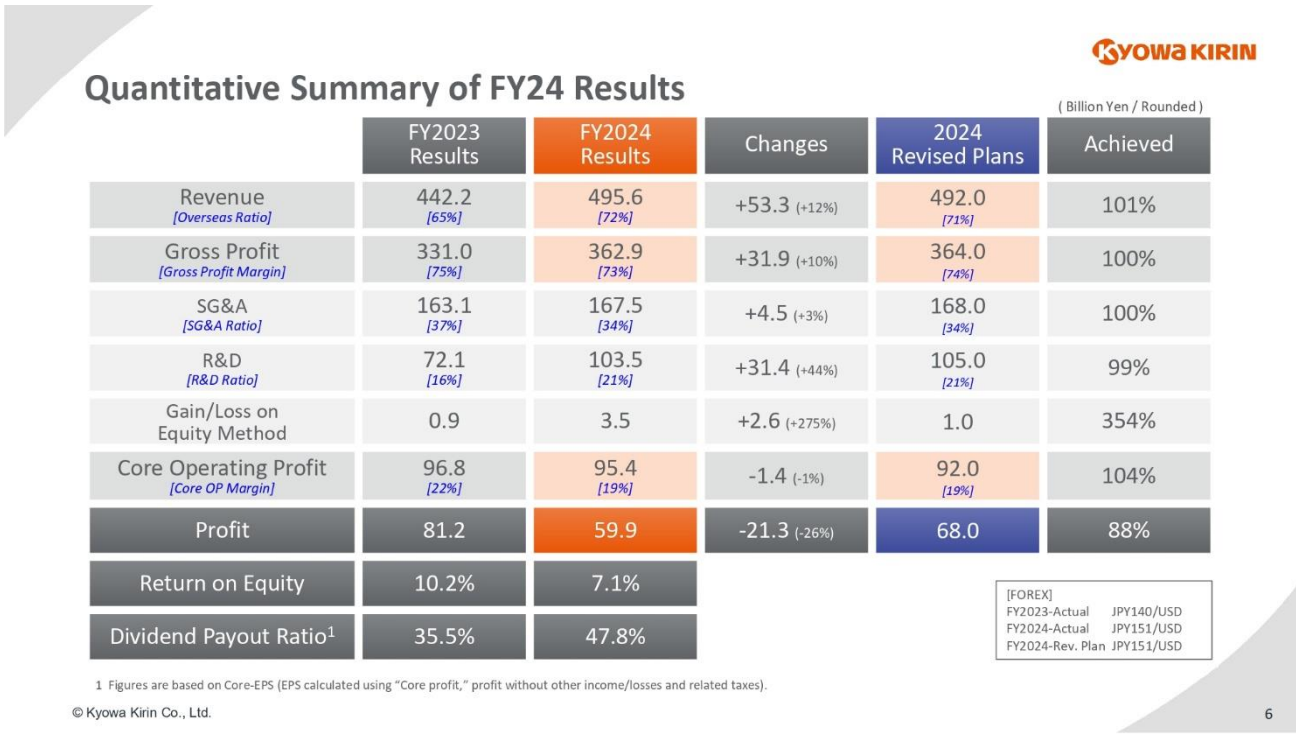
Trials for diseases other than atopic dermatitis have also been initiated. Our strategic partnership with Kura Oncology has enabled us to expand our late-stage global development pipeline in hematologic oncology and refractory hematologic diseases.

Furthermore, several early-stage candidates have entered clinical trials, significantly broadening our pipeline this year.

In terms of addressing patient-centric healthcare needs, we continue to enhance access to medicines through disease awareness initiatives, partnerships with patient organizations, while also continuing patient support programs tailored to specific regions.

In addition, Cowellnex, a joint venture with Kirin Holdings Company, was established to create new value.

While I will not go into detail on every initiative, we have executed the majority of our planned efforts to retain the trust society and reinforce human resources and structures that support the creation of Life-changing value.



Performance summary.

This is a comparison with the same period of the previous year. Revenue was JPY495.6 billion, an increase of JPY53.3 billion, or 12%; core operating profit was JPY95.4 billion, a decrease of JPY1.4 billion, or 1%; and profit was JPY59.9 billion, a decrease of JPY21.3 billion, or 26%.

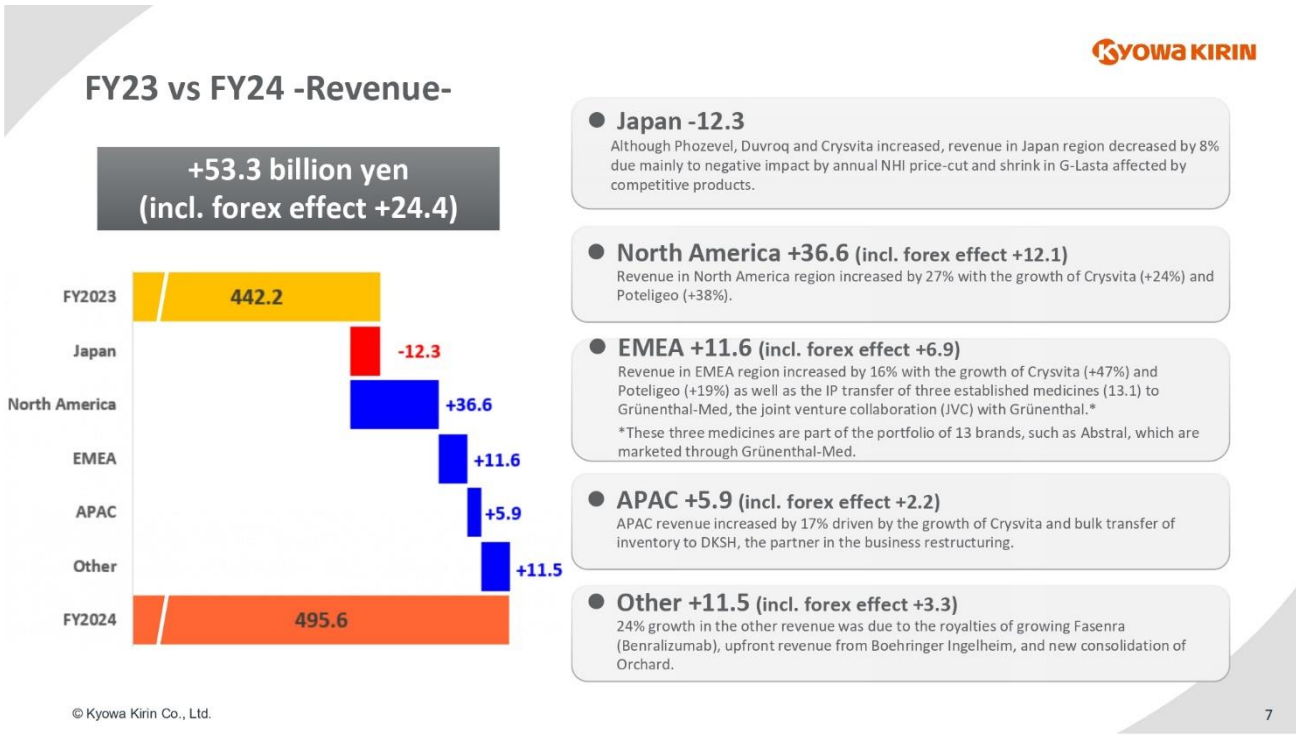
Revenues increased 12% due to growth in global products and technology revenues, as well as the impact of foreign exchange rates.

Core operating income decreased 1%, despite a JPY31.9 billion increase gross profit. This was due to the significant increase in R&D expenses of JPY31.4 billion, or 44%, following progress in the development of KHK4083 (rocatinlimab) and the new consolidation of Orchard.

Profit decreased by 26%. This was due to the reaction to the recognition of JPY 14.8 billion in gains from the sale of shares and valuation gains associated with the joint venture of the established pharmaceuticals business in Europe in 2023, as well as the impact of derivative valuation losses related to the transfer of the same business that occurred in 2024.

As for the achievement rate against the revised forecast for the full year, which was revised in Q2, progress is almost in line with the plan for sales revenue, SG&A expenses, and R&D expenses. The core operating margin was 104%, with a slight upturn in equity in earnings of affiliates.

Profit was 88% achieved due to the impact of the loss on the valuation of derivatives related to the transfer of the established medicines business in Europe, which I mentioned earlier.



This is a YoY analysis of sales revenue by region.

In Japan, sales were down 8%, unchanged from Q3. In North America, sales were up 27% due to strong growth in Crysvita and Poteligeo, as well as the impact of the yen's depreciation.

In EMEA, in addition to the sales growth of Crysvita and Poteligeo, the early transfer of the marketing rights for three of the thirteen established medicine brands sold in partnership with Grünenthal resulted in sales of JPY 13.1 billion, leading to a 16% increase in revenue.

In APAC, in addition to the growth of Crysvita and other products, sales increased by 17% due to the bulk transfer of established medicines inventory to our partner, partly due to business restructuring, as announced in August.

The 24% growth in other revenue was due to royalties from the growing Fasenra, upfront contract revenue from out-licensing to Boehringer Ingelheim, and sales revenue of hematopoietic stem cell gene therapy from the newly consolidated Orchard.

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FY23 vs FY24 -Revenue of Major Items in Japan-

(Billion Yen / Rounded)

Item	FY2023 Results	FY2024 Results	Changes	Reasons	2024 Rev. Plans	Achieved
Crysvita	10.5	11.7	+1.2(+12%)	Market penetration (Launched in Dec 2019)	12.9	91%
Poteligeo	1.9	1.8	-0.1 (-5%)		1.9	95%
Nesp + Nesp-AG[1]	17.1	14.2	-2.9 (-17%)		14.4	99%
Nesp	3.2	2.6	-0.5 (-16%)	NHI price-cut & Biosimilars' penetration	2.8	96%
Nesp-AG	14.0	11.6	-2.4 (-17%)		11.7	99%
Duvroq	9.9	12.7	+2.8 (+28%)	Market penetration (Launched in Aug 2020)	12.2	104%
Phozevel	-	4.7	+4.7 (- %)	Launched in Feb 2024	3.3	141%
Orkedia	10.6	10.4	-0.2 (-1%)		11.7	89%
G-Lasta	31.9	20.5	-11.4 (-36%)	NHI price-cut & Biosimilars' penetration	20.5	100%
Rituximab BS	9.0	7.8	-1.2 (-13%)	NHI price-cut	7.9	99%
Romiplate	12.0	13.9	+2.0 (+16%)	Market penetration	13.2	106%
Nouriast	7.6	6.9	-0.6 (-8%)	Competitors' penetration	7.1	98%
Haruropi	4.5	4.6	+0.1 (+3%)	Market penetration	5.2	89%

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.

* 2024 Revised Plan announced on August 1, 2024, there is no changes to the "Revenue of Major Items (Japan)"

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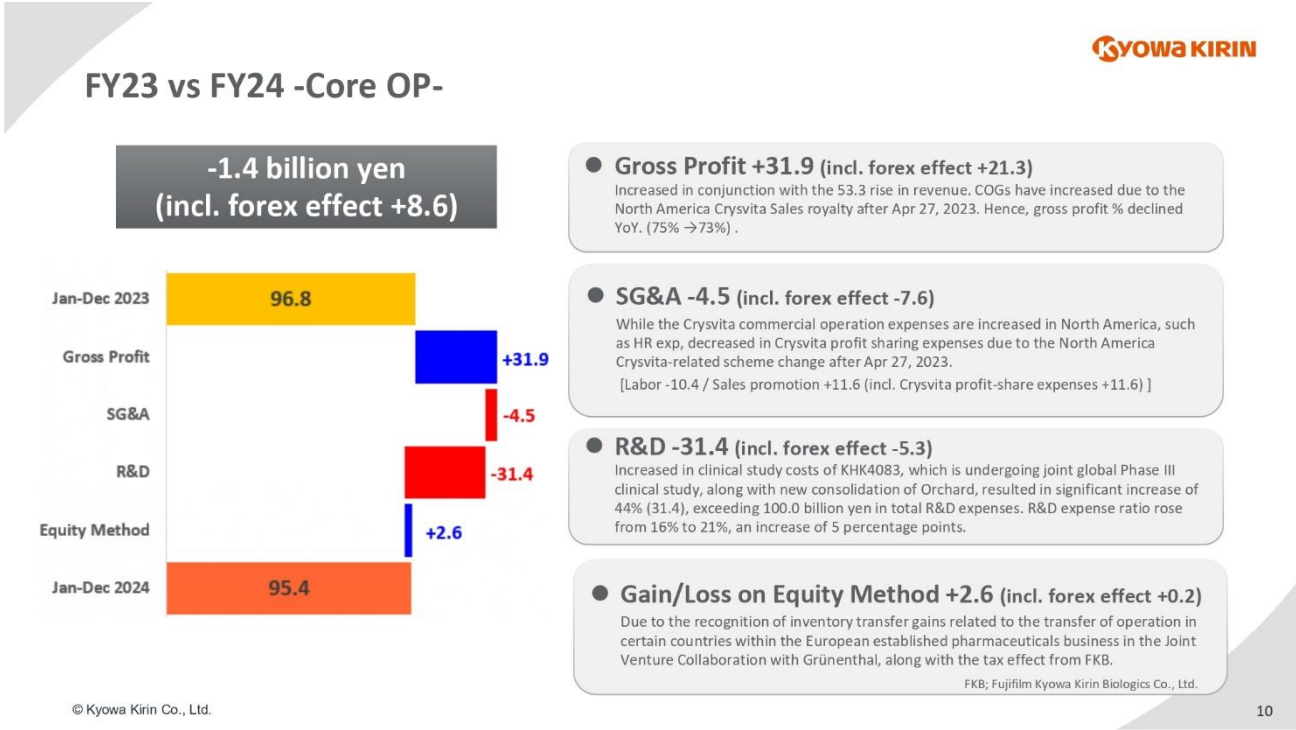
FY23 vs FY24 -Revenue of Major Items outside Japan-

(Billion Yen / Rounded)

Item	FY2023 Results	FY2024 Results	Changes	Reasons	2024 Rev. Plans	Achieved
Crysvita	142.0	184.8	+42.8 (+30%)		187.8	98%
North America	105.2	130.0	+24.8 (+24%)	Market penetration		
EMEA	35.1	51.5	+16.4 (+47%)			
APAC	1.6	3.3	+1.7 (104%)			
Poteligeo	28.4	38.1	+9.7 (+34%)		34.8	110%
North America	21.5	29.7	+8.3 (+38%)	Market penetration	25.1	119%
EMEA	6.9	8.2	+1.3 (+19%)		9.3	89%
APAC	0.0	0.1	+0.1 (-%)		0.5	32%
Libmeldy / Lenmeldy	-	3.3	+3.3 (-%)	New consolidation of Orchard (FDA approval in Mar 2024)	4.9	67%
Nourianz	8.2	8.8	+0.5 (+6%)		9.1	96%
Nesp[1]	9.1	9.7	+0.6 (+7%)		10.7	91%
Gran[1]	6.9	5.4	-1.5 (-22%)	Business transfer to WinHealth in Oct 2024	7.2	76%
Tech-licensing	40.7	47.8	+7.1 (+18%)	Upfront revenue from Boehringer Ingelheim and growth of Fasenra	47.8	100%
Benralizumab Royalty[2]	27.4	31.4	+4.0 (+15%)			

1 Shipments to partners (WinHealth and DKSH) after the restructuring of the APAC business (October 2024) are not included.
2 Sales royalties of Fasenra which has been marketed by AstraZeneca. Including our own estimation.

We will skip the explanation of revenue from the sales of major items since the trends have not changed much over the previous three quarters.

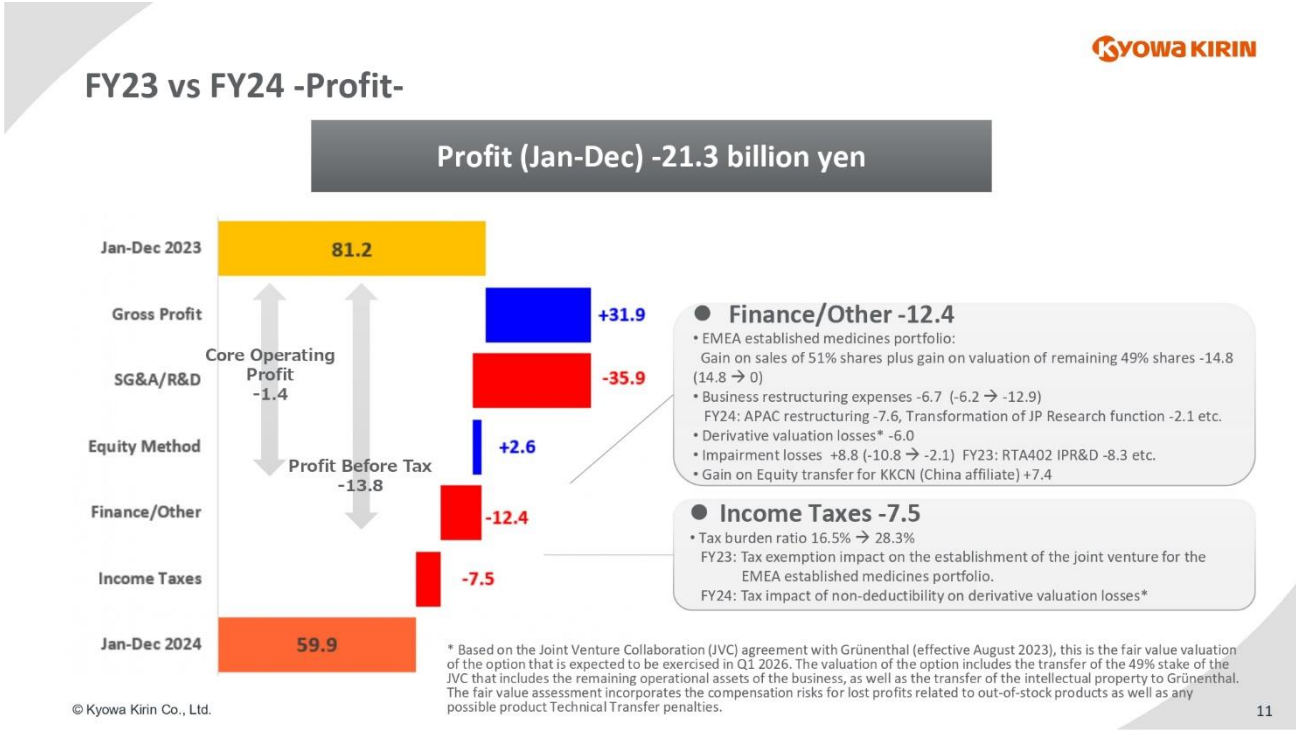


Gross profit increased by JPY31.9 billion, or 10%, in line with the increase in sales revenue. SG&A expenses increased by JPY4.5 billion, or 3%, due to the new consolidation of Orchard and the impact of foreign exchange rates, in addition to increases in personnel and other expenses.

R&D expenses increased significantly by JPY31.4 billion, or 44%, from the same period last year to more than JPY100 billion level, due to progress in the development of rocatinlimab and the new consolidation of Orchard. The R&D ratio also increased by 5 percentage points, from 16% the previous year to 21%.

Gain and loss on the equity method increased by JPY2.6 billion. In the established pharmaceuticals business in Europe, conducted in partnership with Grünenthal, profits have been generated in certain countries due to inventory transfers associated with sales transfers. Additionally, deferred tax assets were recognized at FKB, a biosimilars company, contributing to the increase in profit.

As a result of these factors, core operating profit decreased by JPY1.4 billion compared to the same period of the previous year.

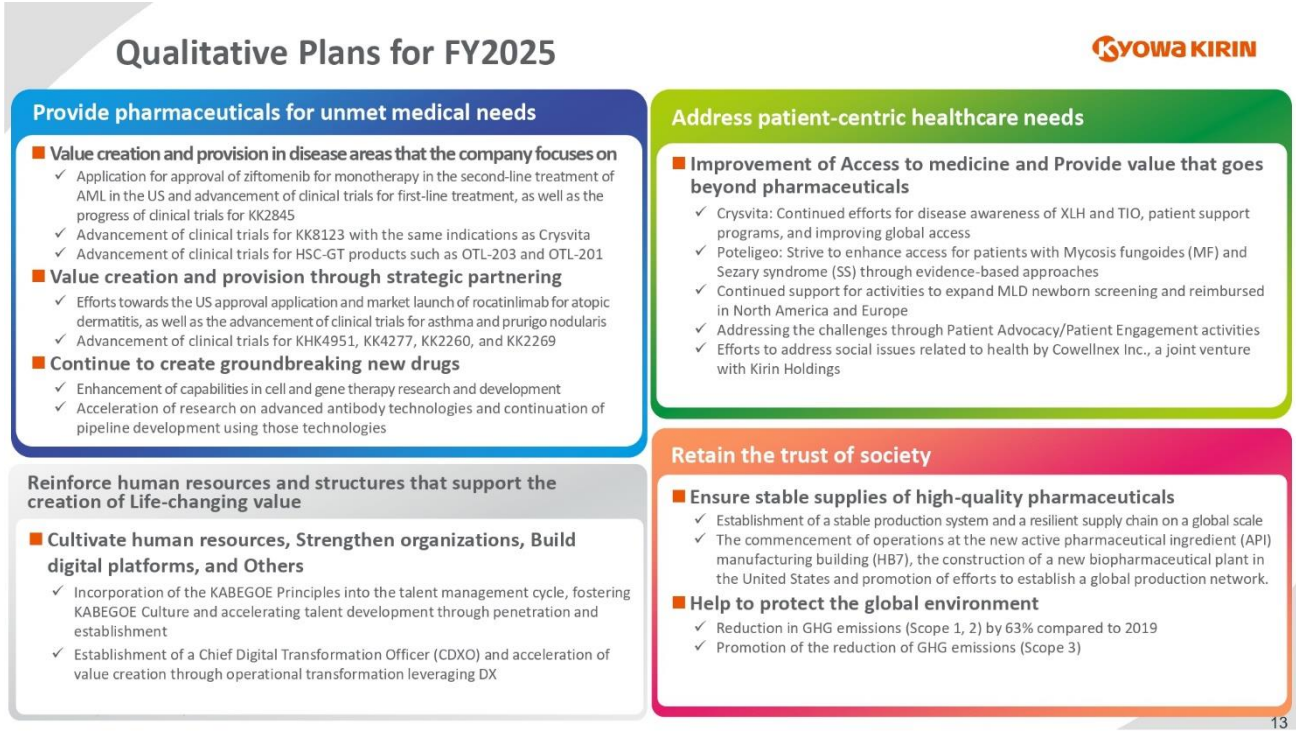


Financial and other decreased by JPY12.4 billion. While a gain of JPY7.4 billion was recorded from the transfer of a subsidiary in China, there was an absence of the sale of shares and the valuation gain of JPY14.8 billion related to the establishment of a joint venture in the established medicine business in Europe, which had been recorded in the previous year.

Additionally, a JPY6 billion loss was recognized on the valuation of derivatives related to the transfer of the business, along with a JPY6.7 billion increase in business restructuring expenses due to the reorganization of the Asia-Pacific region. These factors contributed to a significant YoY decline.

Tax expenses increased by JPY7.5 billion. As we have reiterated, the effective tax rate was 16.5% in 2023, benefiting from tax exemptions related to the established medicine business in Europe and joint ventures. On the flip side, in 2024, the tax burden rose to 28.3%, primarily due to the impact of derivative write-downs and other factors.

As a result, profit decreased by JPY21.3 billion, or 26%, compared with the same period last year.



Then, here are the FY2025 plans. On the qualitative side, we remain committed to aggressive R&D investment and will continue driving initiatives under the strategic framework of the Story for Vision 2030.

With collaboration with Kura Oncology, we will proceed with preparations for the US regulatory submission of ziftomenib. Then, we will proceed with clinical trials and launch preparations for the US regulatory submission of rocatinlimab for the atopic dermatitis indication.

We will also continue promoting innovation by strengthening our capabilities in cell and gene therapy and accelerating research in advanced antibody technologies to expand our pipeline of breakthrough medicines.

In addressing patient-centric healthcare needs, we are reinforcing efforts to improve access to medicines, particularly in the disease areas where we have global strategic products. These efforts will be supported through patient advocacy/patient engagement activities.

To retain the trust of society, we will improve our biopharmaceutical production capabilities, one of our core strengths. This will be achieved by promoting the global circulation of technology and talent through the Takasaki Plant, where the biopharmaceutical API manufacturing building will soon begin operations, and the North Carolina Plant, which recently began construction.

As for reinforcing human resources and the structure that supports the creation of life-changing value, we formulated the KABEGOE Principles at the end of last year. These Principles articulate "how people and organizations should act to strongly promote our global strategy and continuously create life-changing value."

In 2025, we will accelerate the penetration and establishment of the KABEGOE principles, further embedding them into talent development and corporate culture.

Additionally, we appointed a chief digital transformation officer (CDXO) in April 2024. Under the leadership of the CDXO, we will leverage DX-driven operational transformation to accelerate value creation.

Quantitative Summary of FY25 Plans

(Billion Yen / Rounded)

	FY2023 Results	FY2024 Results	FY2025 Plans	Changes
Revenue *[Overseas Ratio]*	442.2 *[65%]*	495.6 *[72%]*	478.0 *[70%]*	-17.6 (-4%)
Gross Profit *[Gross Profit Margin]*	331.0 *[75%]*	362.9 *[73%]*	352.0 *[74%]*	-10.9 (-3%)
SG&A *[SG&A Ratio]*	163.1 *[37%]*	167.5 *[34%]*	166.0 *[35%]*	-1.5 (-1%)
R&D *[R&D Ratio]*	72.1 *[16%]*	103.5 *[21%]*	107.0 *[22%]*	+3.5 (+3%)
Gain/Loss on Equity Method	0.9	3.5	1.0	-2.5 (-72%)
Core Operating Profit *[Core OP Margin]*	96.8 *[22%]*	95.4 *[19%]*	80.0 *[17%]*	-15.4 (-16%)
Profit	81.2	59.9	57.0	-2.9 (-5%)
Return on Equity	10.2%	7.1%	6.6%	
Dividend Payout Ratio[1]	35.5%	47.8%	50.3%	

[FOREX]
FY2023-Actual JPY140/USD
FY2024-Actual JPY151/USD
FY2025-Plan JPY145/USD

1 Figures are based on Core-EPS (EPS calculated using "Core profit," profit without other income/losses and related taxes).

Here is an overview of our performance projections.

Revenues are projected to decrease by JPY17.6 billion, or 4%, to JPY478 billion. R&D expenses will increase by JPY3.5 billion to JPY107 billion. Also, the R&D ratio will increase to 22%, with aggressive investment planned following 2024.

As a result, core operating profit is projected to decrease by JPY15.4 billion, or 16%, to JPY80 billion. Profit is expected to decrease by JPY2.9 billion, or 5%, to JPY57 billion. ROE is projected to be 6.6%.

FY25 -Revenue of Major Items-

(Billion Yen / Rounded)

Item		FY2023 Results	FY2024 Results	FY2025 Plans	Changes	Reasons
Crysvita		152.4	196.6	210.2	+13.7 (+7%)	
	JP	10.5	11.7	13.1	+1.3 (+11%)	
	NA	105.2	130.0			Market penetration
	EMEA	35.1	51.5	197.1	+12.3 (+7%)	
	APAC	1.6	3.3			
Poteligeo		30.3	39.9	45.4	+5.5 (+14%)	
	JP	1.9	1.8	1.9	+0.1 (+3%)	
	NA	21.5	29.7	34.1	+4.3 (+15%)	Market penetration
	EMEA	6.9	8.2	9.2	+1.0 (+12%)	
	APAC	0.0	0.1	0.3	+0.2 (+98%)	
Libmeldy / Lenmeldy		-	3.3	6.9	+3.6 (+109%)	Market penetration (FDA approval in Mar 2024)
Phozevel	JP	-	4.7	8.9	+4.2 (+91%)	Market penetration (Launched in Feb 2024)
Duvroq	JP	9.9	12.7	15.5	+2.8 (+22%)	Market penetration
Nesp + Nesp-AG[1]	JP	17.1	14.2	11.6	-2.7 (-19%)	NHI price-cut & Biosimilars' penetration
G-Lasta	JP	31.9	20.5	17.0	-3.5 (-17%)	NHI price-cut & Biosimilars' penetration
Romiplate	JP	12.0	13.9	14.6	+0.7 (+5%)	Market penetration
Tech-licensing		41.9	48.8	52.3	+3.5 (+7%)	Growth of Fasenra
	Benralizumab Royalty 2	27.4	31.4			

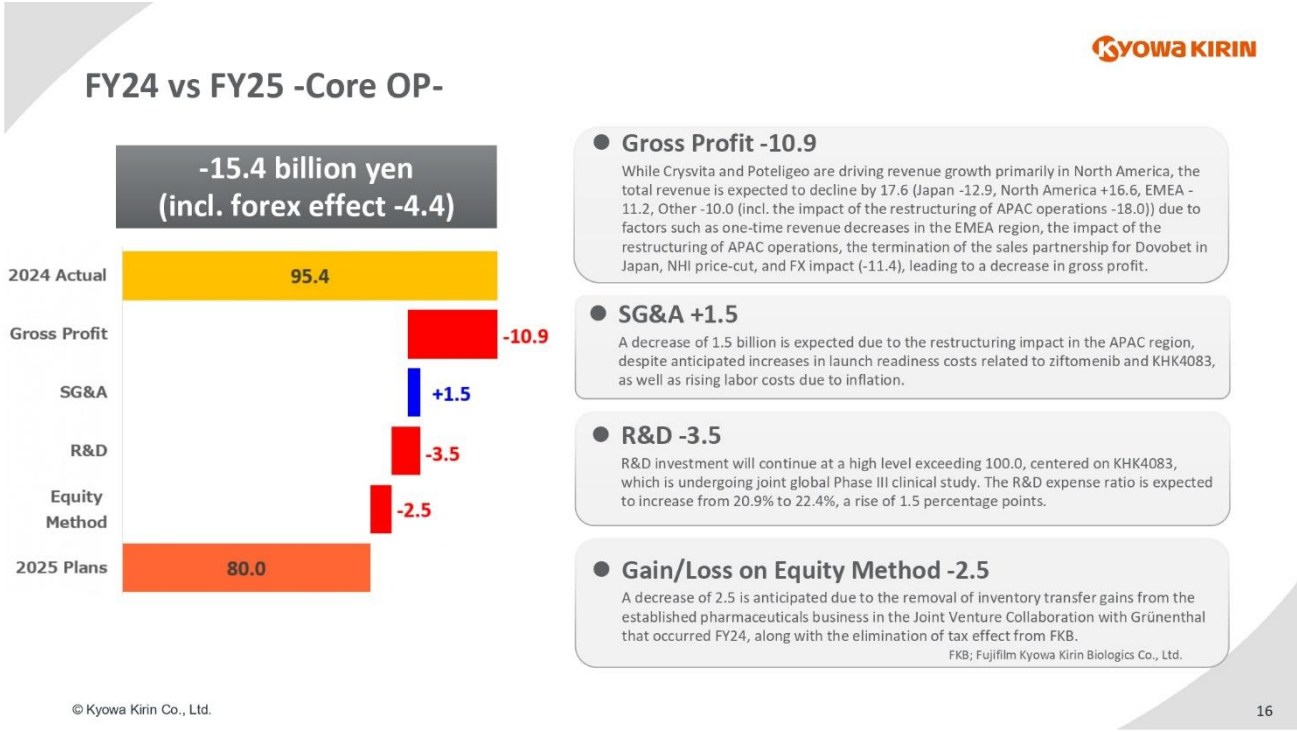
1 AG stands for Authorized Generic. Official product name is Darbepoetin Alfa [KKF]. Kyowa Kirin Frontier is a marketing authorization holder; Kyowa Kirin is a distributor.
2 Sales royalties of Fasenra which has been marketed by AstraZeneca. Including our own estimation.

Major product plans.

We have been presenting the information separately for Japan and overseas, but we have now combined it into one. Global strategic products will be explained in the commercial update section, so I will focus on other products.

Libmeldy/Lenmeldy aims for JPY6.9 billion in Europe and the US combined. Last year, we identified quite a few patients in the US, but unfortunately, many of them were a little too late for treatment with Lenmeldy. This year, we successfully treated our first patient in the US in January.

Phozevel has been well received for its ability to reduce the medication burden since its launch in February 2023, and we are hopeful for significant growth this year as well. Tech-licensing revenues are expected to continue benefiting from increased Fasenra sales royalties, though we anticipate that the exchange rate will shift slightly toward a stronger yen.

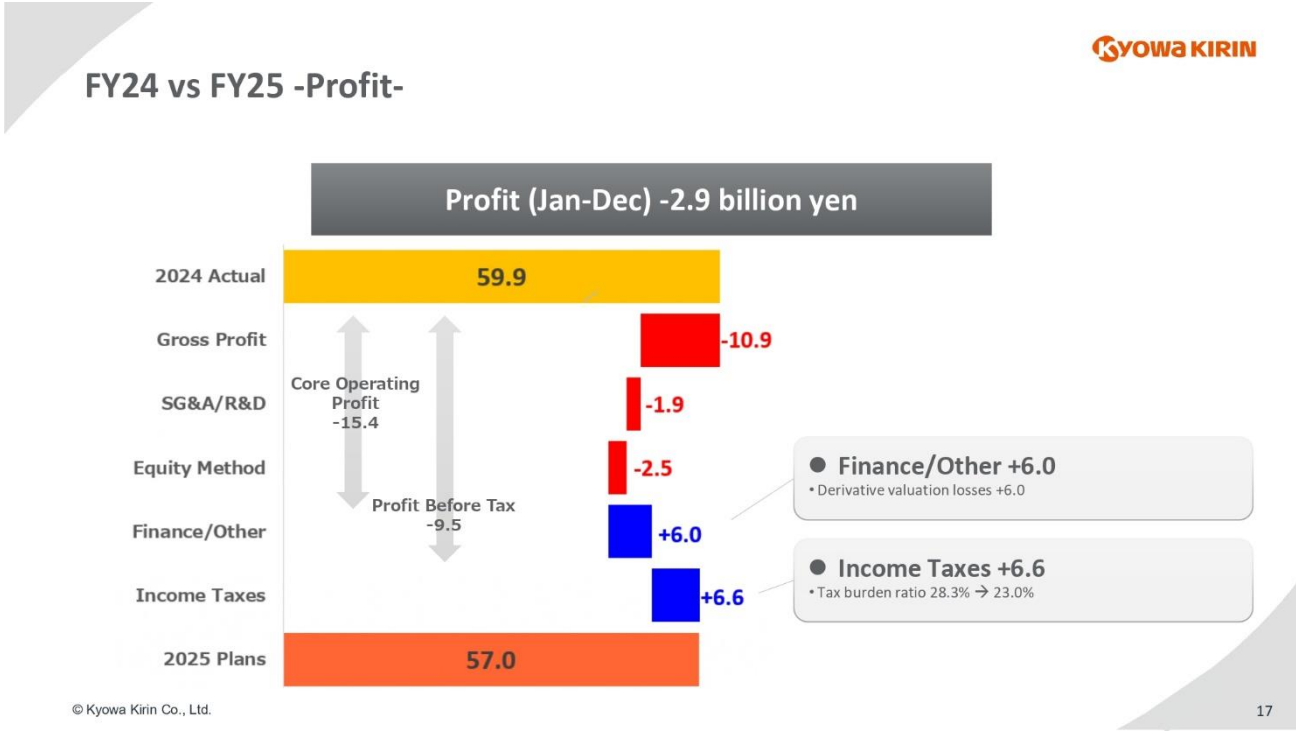


Next, I would like to break down the changes in core operating profit. Gross profit is expected to decrease by JPY10.9 billion due to the decrease in sales revenue.

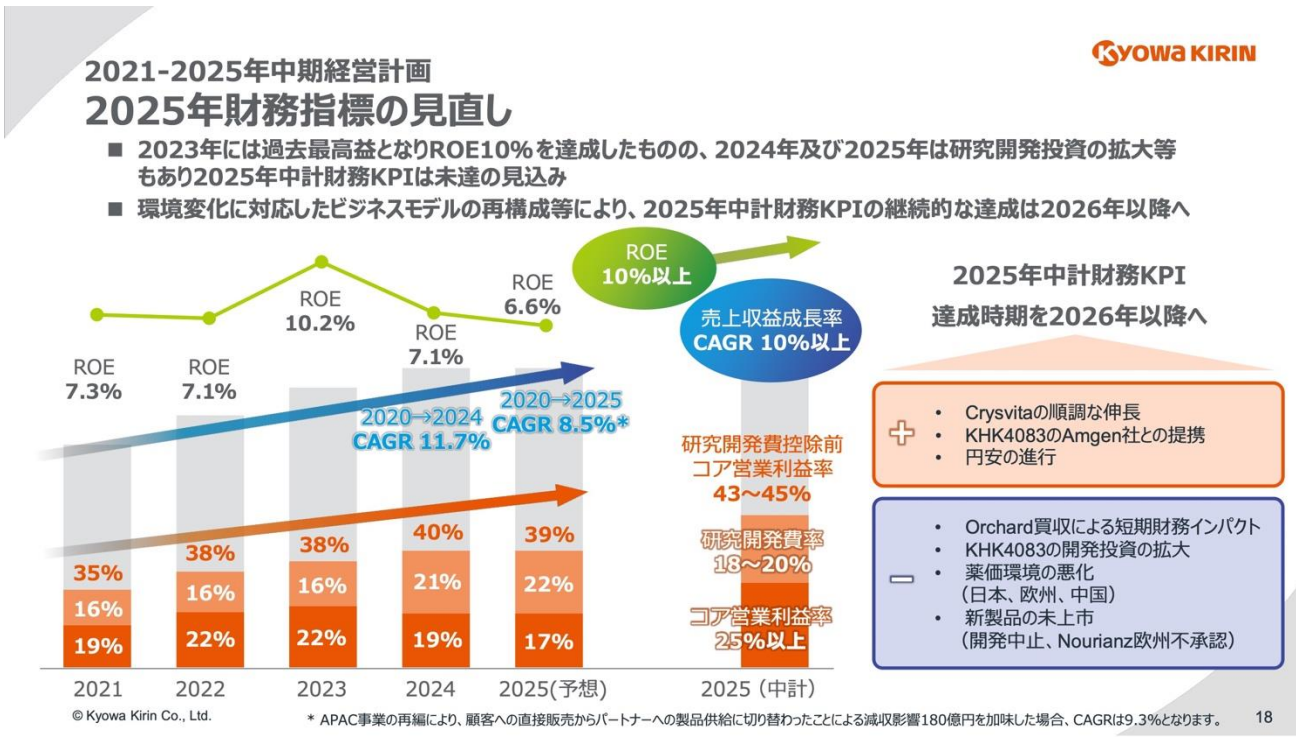
While we anticipate continued growth for Crysvita and Poteligeo, revenue will decline due to a decrease in one-time revenue from the EMEA region, the impact of the APAC business restructuring, the termination of the sales partnership for Dovobet in Japan, the NHI price-cut, and foreign exchange rate fluctuations.

SG&A expenses are expected to decrease by JPY1.5 billion. While costs related to launch preparations for ziftomenib and rocatinlimab will rise, along with increased labor costs due to inflation, these will be offset by savings from APAC restructuring and other factors. R&D expenses will continue to remain high, in excess of JPY100 billion, centered on rocatinlimab.

Gain/loss on the equity method is expected to decrease by JPY2.5 billion. As a result, we anticipate a decrease of JPY15.4 billion YoY in core operating profit.

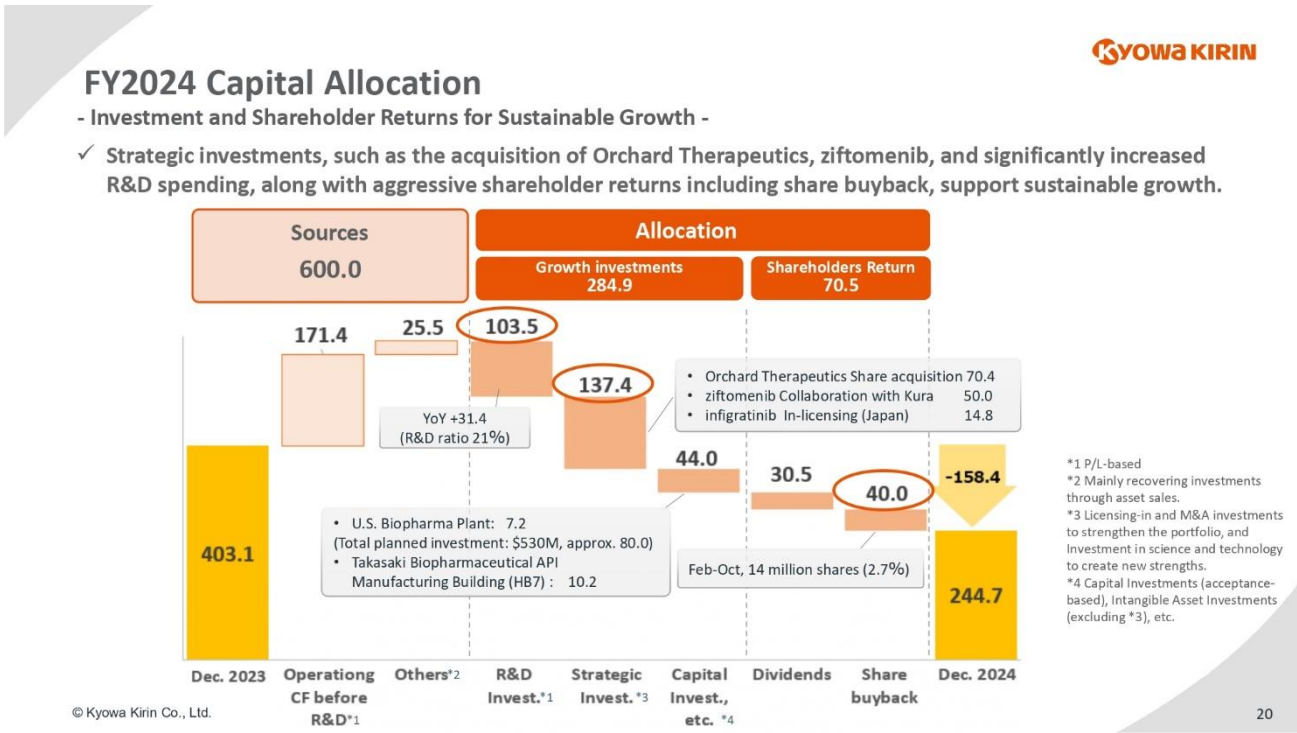


Items below core operating profit, both finance/ other, and income taxes are expected to decrease in FY2025. A JPY6 billion increase in profit is expected in finance and other. Additionally, a JPY6.6 billion increase in profit is anticipated in tax expenses, as the tax burden is projected to return to the normal level of 23% in 2025, compared to the elevated 28% in 2024.



As it was explained in February of last year, we unfortunately do not expect to achieve the financial KPIs of the 2025 mid-term management plan this year.

To achieve our Vision 2030 and sustain growth beyond it, we recognize the need to drive bold reforms at this stage. Additionally, we have determined that further R&D investments and growth investments are also necessary, and we have made this review accordingly.



Now, I move on to capital allocation and shareholder returns.

We are showing you our capital allocation for the last year. At the end of 2023, our cash balance stood at JPY403.1 billion. Combined with operating cash flow before deducting the R&D expenses and other items for the period, this resulted in a total available cash of approximately JPY600 billion.

In 2024, we invested JPY137.4 billion in strategic investments, including the acquisition of Orchard and the collaboration of ziftomenib. Additionally, we invested over JPY100 billion in R&D, bringing the total growth investments to JPY284.9 billion, reflecting our continued commitment to aggressive investments.

In terms of shareholder returns, we increased dividends for the eighth consecutive year and executed a record JPY40 billion shares buyback.

As a result, cash on hand decreased by JPY158.4 billion, bringing the year-end cash balance to JPY244.7 billion.

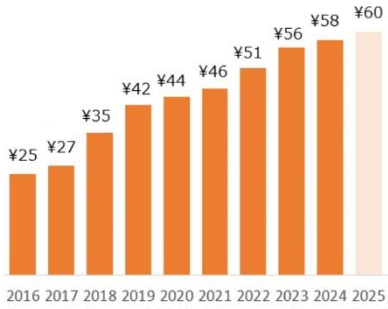
Our capital policy prioritizes growth investments to drive sustainable growth and maximize corporate value. In 2024, we continued to invest aggressively in growth while also returning profits to shareholders. Looking ahead, we will maintain our focus on R&D and strategic investments this year.

Shareholders Return

- ✓ FY24 dividend is **58** yen, and FY25 to be **60** yen (plan)
- ✓ Plans **9-year consecutive rises** since FY17
- ✓ FY21-25 weighted average payout ratio is **42.6%** (plan)

(Mid-term guidance for payout ratio "Targeting sustained dividend hikes with 40%")

Year	Dividend (yen)			Payout Ratio*1	Return on Equity
	Interim	Year-end			
2016	12.50	12.50	25.00	44.9%	5.3%
2017	12.50	14.50	27.00	34.4%	7.2%
2018	15.00	20.00	35.00	35.2%	8.6%
2019*2	20.00	22.00	42.00	33.7%	10.1%
2020	22.00	22.00	44.00	50.3%	6.8%
2021	23.00	23.00	46.00	43.2%	7.3%
2022	24.00	27.00	51.00	38.9%	7.1%
2023	27.00	29.00	56.00	35.5%	10.2%
2024*3*4	29.00	29.00	58.00	47.8%	7.1%
2025 Plan	30.00	29.00	60.00	50.3%	6.6%



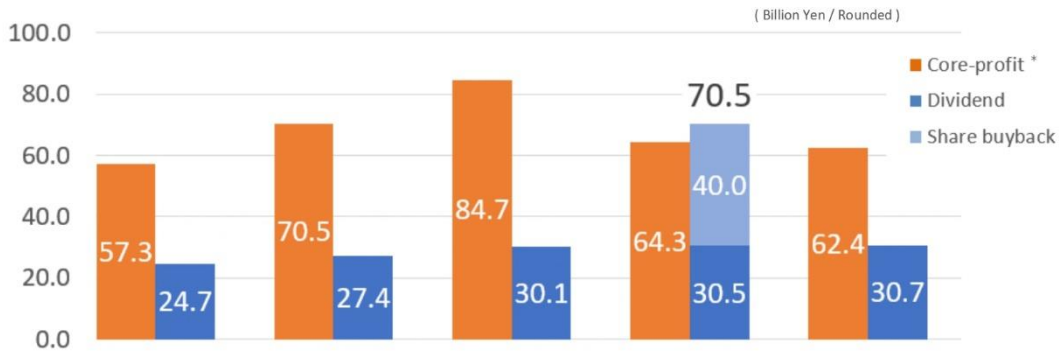
*1 Payout ratio for FY2021/beyond are payout ratios against the Core EPS that is calculated based on the Core Earnings (= Profit - Other income/losses - Related income taxes)
*2 Buyback of 10.7M own shares (¥22.6B) executed on February 6, 2019. Total return ratio for FY2019 is 67.3%.
*3 Buyback of 14.366M own shares (¥40.0B) executed from Feb to Oct 2024. Total return ratio for FY2024 is 109.6%.
*4 Year-end dividend of 29 yen/share will be submitted to the 102nd Ordinary General Meeting of Shareholders to be held on March 19, 2025.

For FY2024, we plan to pay a year-end dividend of JPY29, bringing the total annual dividend to JPY58 per share, an increase of JPY2 from the previous year.

For FY2025, we plan to further raise the dividend by JPY2 to JPY60 per share, marking the ninth consecutive year of dividend increases. Based on our plans for FY2025, the five-year weighted average dividend payout ratio is projected to be 42.6%.

Share buyback and cancellation of treasury shares

- ✓ To improve capital efficiency and shareholder returns, the company implemented its largest-ever share buyback and cancellation of 40.0 billion (14 million shares, 2.7%) from February to October 2024.
- ✓ Total return ratio for FY2024 is 109.6%

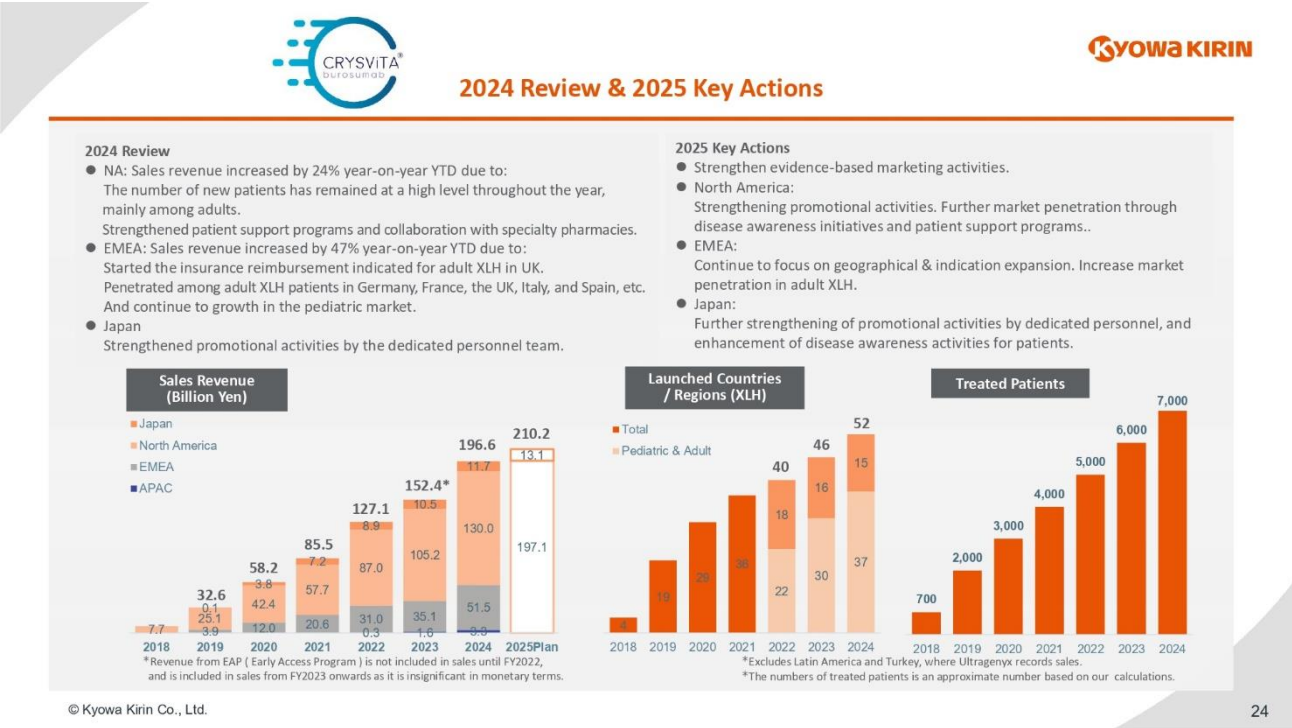


	2021	2022	2023	2024	2025(Plan)
Dividend (Yen/share)	46.0	51.0	56.0	58.0	60.0
Payout ratio	43.2%	38.9%	35.5%	47.8%	50.3%
Total return ratio	43.2%	38.9%	35.5%	109.6%	50.3%

* "Core profit," profit without other income/losses and related taxes). Payout ratio is payout ratios against the Core EPS that is calculated based on the Core Earnings

From February to October 2024, we conducted a share buyback and cancellation of treasury shares. This share buyback aimed for improving capital efficiency and shareholder return.

During this period, we repurchased a record JPY40 billion worth of shares from February to October, equivalent to 14 million shares or 2.7% of total shares, and subsequently canceled all repurchased shares. As a result, the total return ratio combined with dividends was 109.6%.



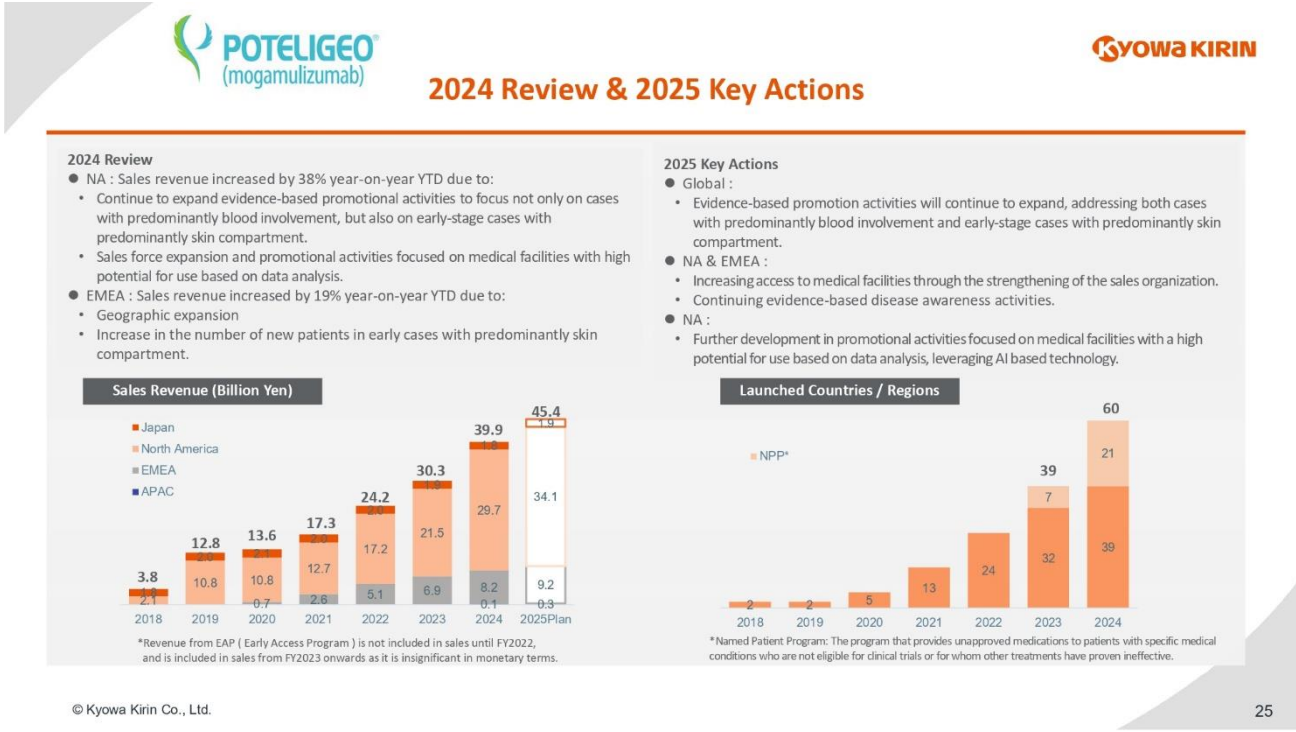
Next, the commercial update.

First, Crysvita. In FY2024, we delivered to approximately 7,000 patients and expand our market area to 52, exceeding the planned 50 by the end of FY2025. We achieved a significant increase in sales revenue, with growth generally tracking as planned, further supported by favorable foreign exchange effects.

Although our sales plan for 2025 looks a little weak in light of the foreign exchange impact, we aim to evolve our ongoing efforts in each region to achieve continued growth.

In North America, the number of new patients continues to grow steadily. We remain committed to strengthening disease awareness activities and enhancing patient support programs in 2025, particularly for patients transitioning from childhood to adulthood, and aim for continued growth.

In Europe, reimbursement for adult XLH in the UK is set to begin in 2024, and market penetration is already progressing in launched countries and regions. we will continue efforts to further expand market penetration for 2025.



Next is Poteligeo.

Poteligeo also continues to grow strongly. In North America, we continue to expand access to patients with tumor cells in the blood and those presenting with skin symptoms through evidence-based promotion.

Additionally, our targeted promotional activities focused on medical facilities with higher potential for administration based on data-driven analysis have contributed significantly to this growth.

In Europe, we continue to grow through regional expansion and engaging with patients via disease awareness activities.

In 2025, we aim to build on these efforts by enhancing the efficiency of promotional activities through AI-driven data analysis and other advanced methods. These initiatives will also support our preparations for the future launch of ziftomenib in North America.

News Flow of Development Pipeline Products

KYOWA KIRIN

As of Feb. 6th, 2025

Products	Diseases under development	Events	Status/Schedule
rocatinlimab KHK4083/AMG 451	Moderate to severe atopic dermatitis	ROCKET HORIZON (P3) Detailed data	1H 2025
		ROCKET SHUTTLE (P3) Topline data ROCKET IGNITE (P3) Topline data	Q2 2025
	Prurigo Nodularis	P3	In progress
	Moderate to severe asthma	P2	In progress
ziftomenib	AML (1L combo/2L+ combo)	KOMET-007 (P1a, P1b) P1a data presentation	Dec. 2024
	AML (2L+ mono)	KOMET-001 (P2) Topline data	Feb. 2025
	AML (1L combo)	KOMET-017 (P3) initiation	2H 2025
OTL-203	MPS-IA (Hurler Syndrome)	Registrational study (Equivalent to P3 study)	In progress
KK8398 infigratinib	Achondroplasia	P3	Preparation underway
KHK4951 tivozanib eyedrop	DME	P2	In progress
	nAMD	P2	In progress
OTL-201	MPS-IIIA (Sanfilippo syndrome typeA)	PoC study (Equivalent to P1-2 study)	In progress
KK4277	SLE, CLE	P1	In progress
KK2260	Advanced or metastatic solid tumors	P1	In progress
KK2269	Advanced or metastatic solid tumors	P1	In progress
KK2845	AML	P1	In progress
KK8123	XLH	P1 initiation	Nov. 2024

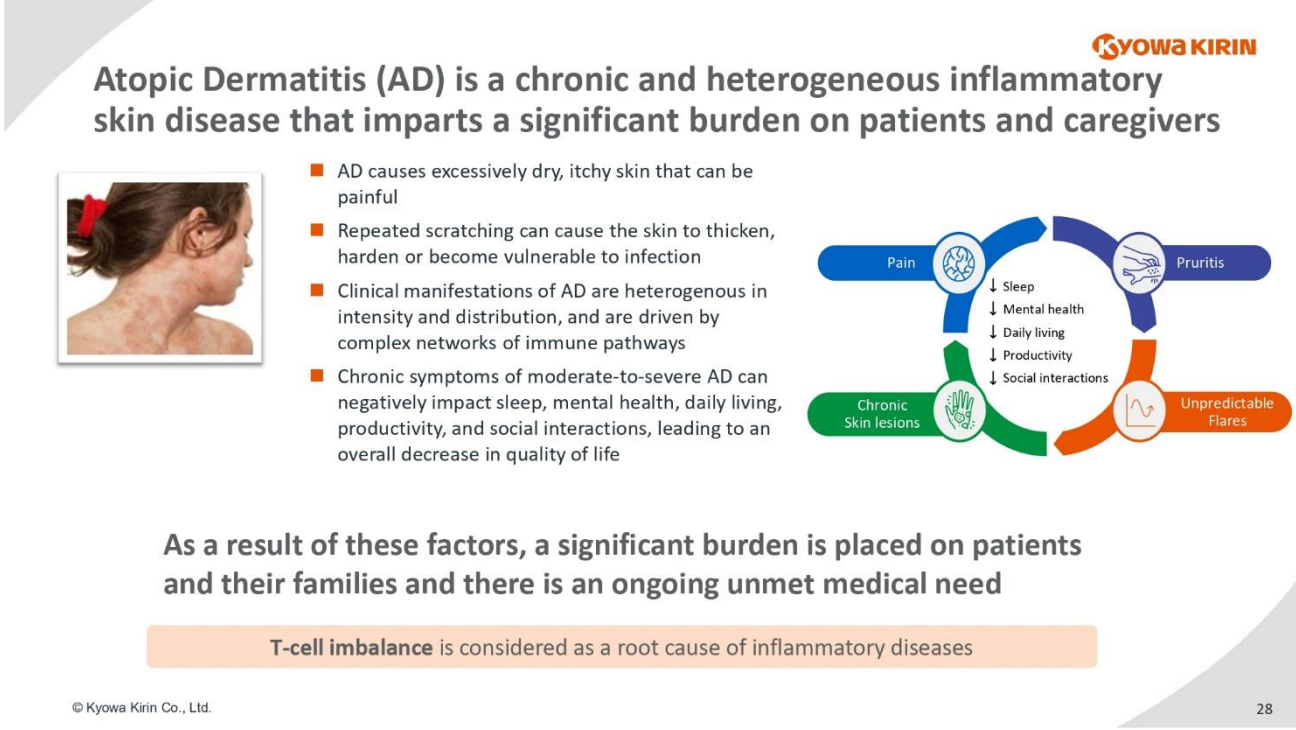
Next, the R&D update. I will focus on the changes from the previous financial statements.

First is rocatinlimab. For the ROCKET program, a Phase III study for atopic dermatitis, we plan to present detailed data from the HORIZON study in H1 of this year and top-line results from the SHUTTLE study in Q2 of this fiscal year. Further updates will be provided as data become available.

As for ziftomenib, we presented data from Phase Ia of the KOMET-007 study at a conference last December. In addition, top-line data from the Phase II section of the second-line single-agent KOMET-001 study was released yesterday. The KOMET-017 study for the first-line combination is scheduled to begin in H2 of this year. More details will be provided here as well.

We are currently preparing a Phase III study of infigratinib under the development code KK8398.

Finally, a Phase I study for KK8123 targeting XLH was initiated last November.

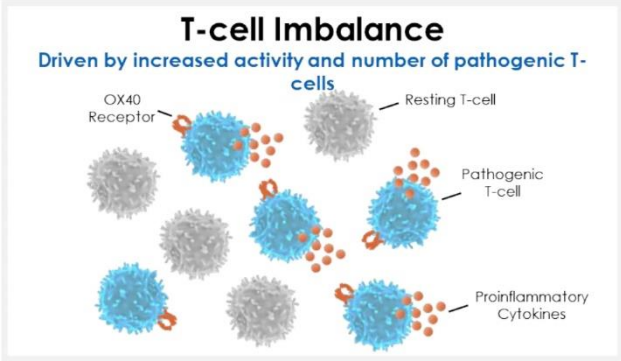


I would now like to explain rocatinlimab using slides. I would like to review the symptoms and unmet medical needs of the target disease, atopic dermatitis.

Atopic dermatitis is a chronic inflammatory disease, and it causes excessively dry, itchy skin with pain and more. Especially in patients with moderate-to-severe AD, it can negatively impact sleep, mental health, and social interactions, leading to an overall decrease in quality of life.

These are some of the unmet medical needs that place a heavy burden on patients and their families. These inflammatory diseases are thought to be caused, in part, by T-cell imbalance as a root cause.

T-cell Imbalance – a root cause of inflammatory diseases



- Atopic dermatitis is thought to be caused in part by **T-cell imbalance** due to the increase and enhanced activation of pathogenic T cells
- **T-cell imbalance** is one of the root causes of various inflammatory diseases

Atopic dermatitis is thought to be caused, in part, by T-cell imbalance due to the increase and enhanced activation of pathogenic T cells. T-cell imbalance is one of the root causes of various inflammatory diseases.

複数の病原性T細胞によるT細胞インバランスが、アトピー性皮膚炎の病態の慢性化と複雑性に寄与[1,2]

病原性エフェクターT細胞によって放出されるサイトカインにより多様な病態を引き起こし、病原性メモリーT細胞が疾患の持続性と慢性化を促進すると考えられている[1,3–5,8]

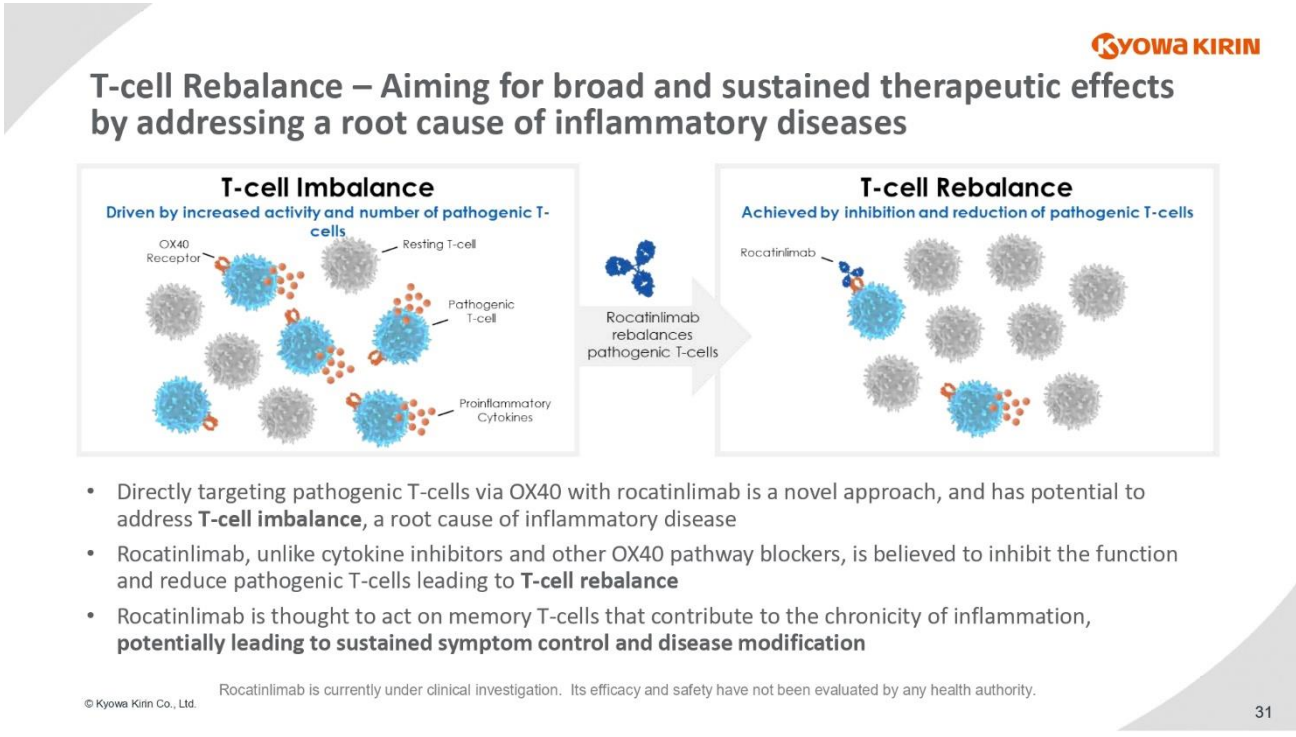
AD = atopic dermatitis. T_H = T helper. *OX40は T細胞が活性化されると一過性に発現する受容体であり、そのリガンドであるOX40Lとは区別される **1.** Fania L, et al. *Int J Mol Sci.* 2022;23:2684. **2.** Sadrolashrafi K, et al. Cells. 2024;13(7):587. **3.** Czarnowicki T, et al. *Allergy*. 2017;72:366-372. **4.** Carlier TDB, et al. *J Autoimmun.* 2021:120:102634. **5.** Croft M, et al. *Am J Clin Dermatol.* 2024;25(3):447-461. **6.** Bissonnette R, et al. *J Clin Med.* 2023;12:3805. **7.** Yew YK, et al. *J Am Acad Dermatol.* 2019;80:390-401. **8.** Chen L, et al. *Cell Mol Immunol.* 2020;17:64-75.

This is the mechanism of T-cell imbalance occurrence. The activation of naïve T cells, shown in the upper left corner, results in the transient expression of the receptor molecule OX40 on the cell, which, in turn, leads to differentiation into a variety of pathogenic T cells upon stimulation through this OX40-mediated pathway.

These include several effector T cells, such as Th2 cells, which are major players in atopic dermatitis, and memory T cells. This state of proliferation and activation of pathogenic T cells is referred to as T-cell imbalance.

At this time, various cytokines are released from effector T cells, causing diverse pathologies. Memory T cells, which are essentially immune memory cells, are also said to promote disease persistence and chronicity.

Thus, a T-cell imbalance occurs, which is thought to contribute to the diverse pathogenesis and chronicity of atopic dermatitis.



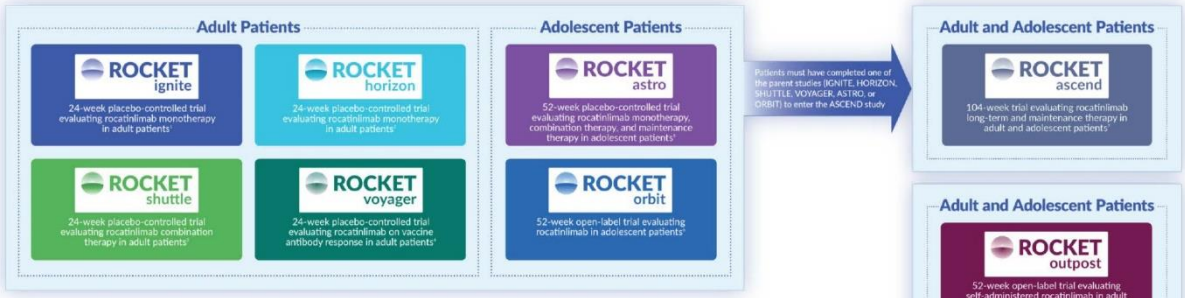
In contrast, directly targeting pathogenic T cells via OX40 with rocatinlimab is a novel approach and has the potential to address T-cell imbalance, a root cause of inflammatory disease.

Specifically, we believe that rocatinlimab can inhibit the function and reduce pathogenic T-cells leading to T-cell rebalance, unlike cytokine inhibitors and other OX40 pathway blockers.

In addition, rocatinlimab is thought to act on memory T cells that contribute to the chronicity of inflammation, potentially leading to sustained symptom control, as observed during the Phase IIb trial, and disease modification.

Rocatinlimab – Phase 3 the ROCKET Program

- Composed of eight global studies enrolling adult and adolescent moderate – severe AD patients
- To date, over 3,300 patients have been enrolled with seven studies having completed enrollment
- Studies were designed to examine long-term sustained efficacy and safety

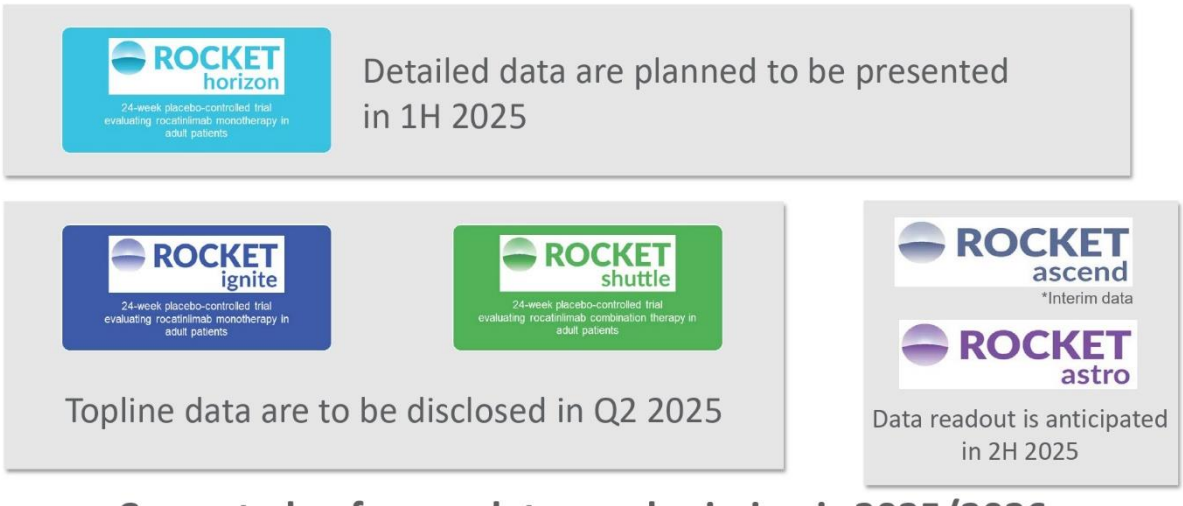


1. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT05398445. Accessed June 4, 2024. 2. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT05651711. Accessed June 4, 2024. 3. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT05724199. Accessed June 4, 2024. 4. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT05899816. Accessed June 4, 2024. 5. ClinicalTrials.gov. https://classic.clinicaltrials.gov/ct2/show/NCT05704738. Accessed June 4, 2024. 6. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT05633355. Accessed June 4, 2024. 7. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT05882877. Accessed June 4, 2024. 8. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT06224192. Accessed June 4, 2024.

I would like to reiterate the outline of Phase III, the ROCKET program. This is a large, global study consisting of eight studies enrolling adult and adolescent patients with moderate-to-severe AD.

To date, over 3,300 patients have been enrolled, with seven studies having completed enrollment. These studies, consisting of eight trials, were designed to examine long-term sustained efficacy and safety.

Rocatinlimab - Future Plans

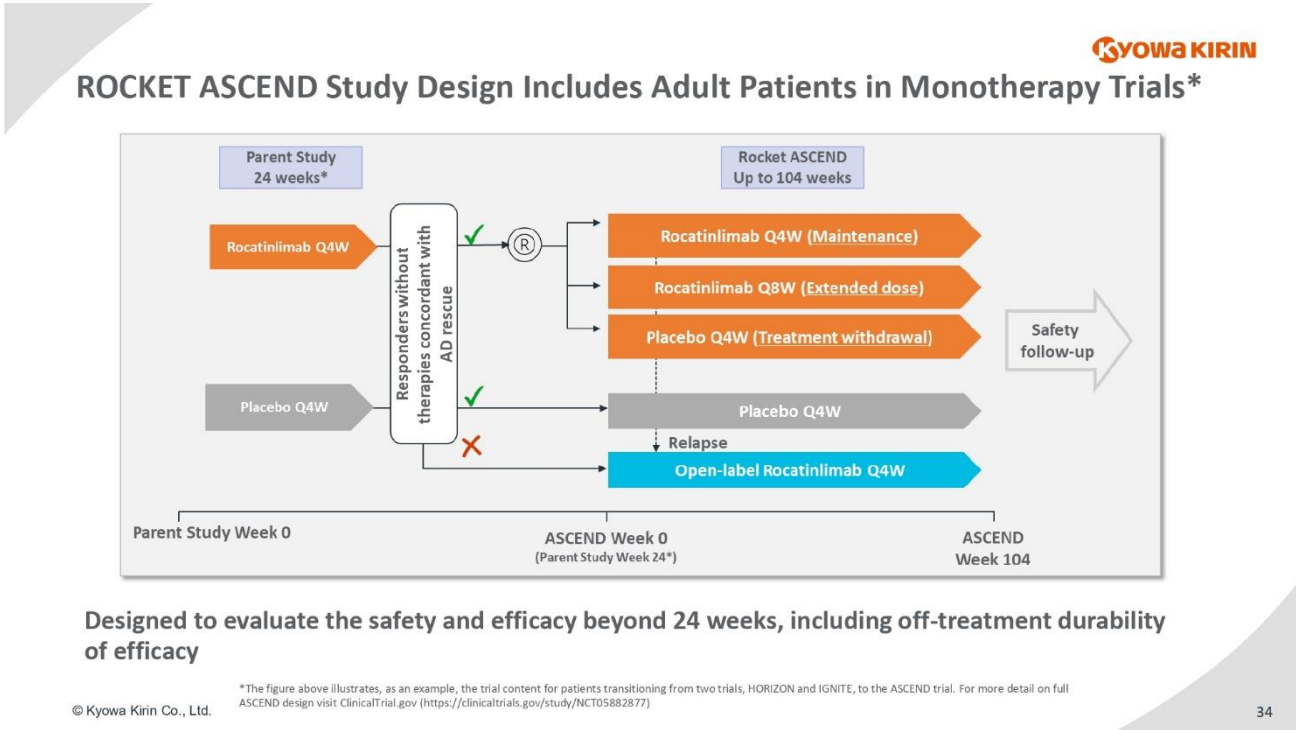


Current plan for regulatory submission is 2025/2026

Future plans. For the ROCKET and HORIZON studies, for which we announced the top-line results last year, we plan to announce detailed data in H1 of 2025.

Top-line data from the ROCKET IGNITE study for the single agent and the ROCKET SHUTTLE study for the combination topical application will be presented in Q2 of this year.

In addition, top-line data from the ROCKET ASCEND study, which evaluates the efficacy and safety of the drug in the medium to long term, and the ROCKET ASTRO study in adolescents are scheduled to be available in H2 of this year. We are aiming to achieve regulatory submission in 2025 or 2026.

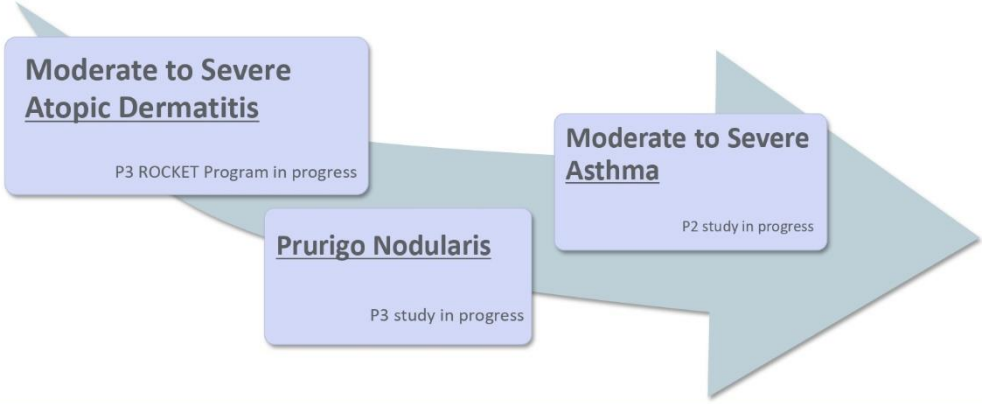


I want to introduce the ROCKET ASCEND study design, using an example of adult patients in monotherapy trials, which is marked in orange.

Patients who have completed other trials will participate in this ASCEND study. In this study, patients will be randomly assigned to cohorts receiving rocatinlimab either once every four weeks, once every eight weeks, or placebo once every four weeks. The study is designed to evaluate safety and efficacy beyond 24 weeks, including the off-treatment durability of efficacy.

Anti-OX40* antibody – Potential new treatment option for multiple inflammatory diseases

Future expansion into indications where "T-cell rebalancing" is expected to lead to reduced disease activity



We will continue our efforts to deliver Life-changing value to more patients in the future

*OX40 is expressed transiently on T cells when these become activated, and is distinct from its ligand, OX40L.

In addition to atopic dermatitis, we will continue to expand the indication to other diseases where T-cell rebalancing is expected to reduce disease activity.

We are currently conducting a Phase III study for prurigo nodularis and a Phase II study for moderate to severe asthma, and we will continue to pursue further possibilities with Amgen.

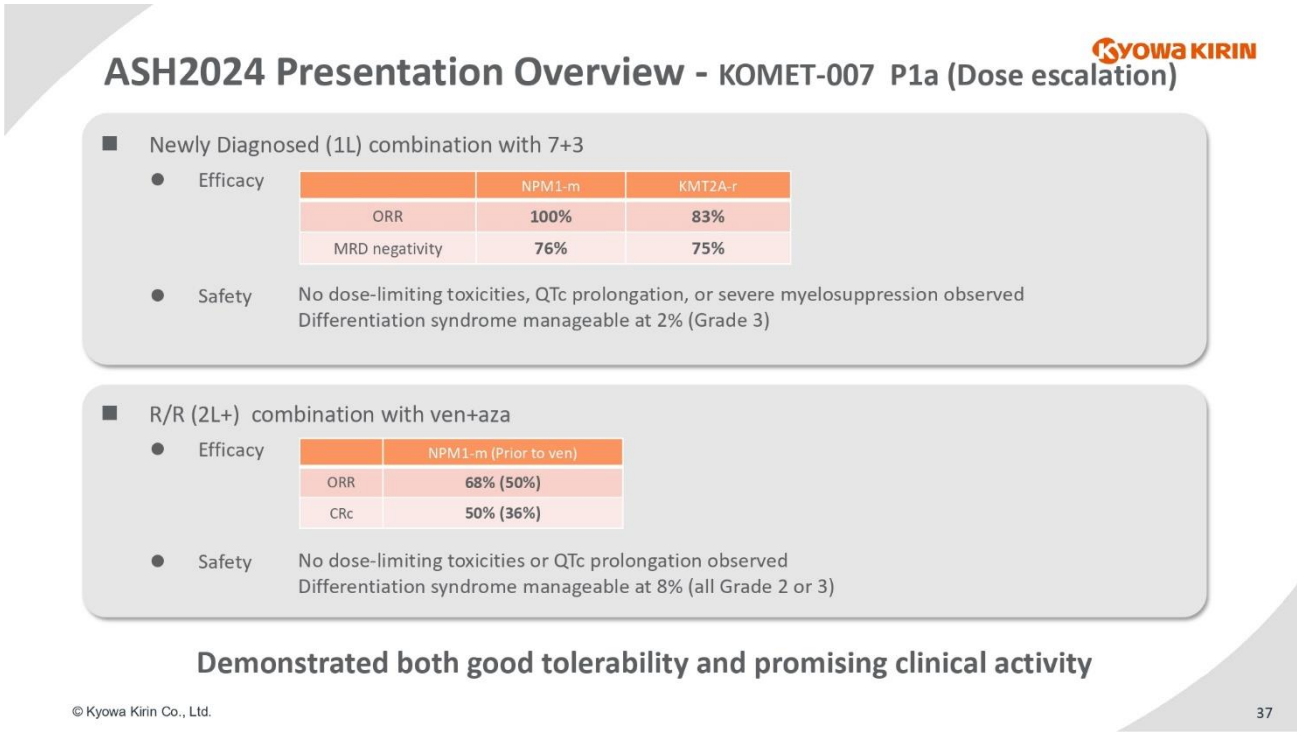
Overview of ziftomenib

- Selective Oral Small Molecule Menin Inhibitor
- Target Disease: Menin-dependent AML (NPM1 gene mutations and KMT2A gene rearrangements)
  - Up to 50% of AML cases are estimated to be menin-dependent (including NPM1 gene mutations and KMT2A gene rearrangements)
  - NPM1 gene mutation is one of the most common AML mutations, acting as a driver mutation via the menin pathway. It is observed in 30%-35% of cases.
  - AML with NPM1 gene mutations shows poor prognosis in relapsed/refractory AML and is attracting attention as a target for new treatments
- The only investigational therapy to receive Breakthrough Therapy Designation from the FDA for treatment of R/R NPM1-mutated AML
- Mechanism of Action: Inducing leukocyte blast differentiation by inhibiting the binding of menin and KMT2A (MLL)
- On November 21, 2024, announced entering into a global strategic collaboration with U.S.-based Kura Oncology for the development and commercialization of this product

Plan to submit New Drug Application (NDA) to the FDA for ziftomenib for the treatment of relapsed/refractory NPM1-mutant AML in Q2 2025

Ziftomenib is an oral small-molecule menin inhibitor, and its development indication is AML with an NPM1 gene mutation or KMT2A gene rearrangements.

In November of last year, we entered into a licensing agreement with Kura and plan to submit New Drug Application to the FDA for the treatment of relapsed/refractory NPM1-mutant AML in Q2 of FY2025.



This is a summary of the ASH 2024 presentation. These are the results of KOMET-007 combination trials. The first line showed good efficacy, and no safety issues were observed.

In the second line, there were no particular safety issues, and the efficacy was confirmed to be superior to that of conventional treatment, confirming both good tolerability and promising clinical activity.

Ziftomenib KOMET-001 Study Phase 2 Results

- Target Disease: R/R NPM1-Mutated AML
- Results: Primary endpoints (CR[1] and CRh[2]) were achieved, and safety and tolerability were consistent with previous reports.
- More detailed data presentation is scheduled at an upcoming medical conference in Q2 2025.

Future Plans

- 2L+ Monotherapy: Approval application to be submitted in Q2 2025
- 1L Combination: Phase 3 KOMET-017 is planned to start in 2H 2025
  - Consists of two trials: KOMET-017-IC and KOMET-017-NIC[3]
  - Randomized placebo-controlled trial (ziftomenib + standard of care vs. placebo + standard of care).

1. Complete response; 2. CR with partial hematological recovery ; 3. IC = intensive combination, NIC = non-intensive combination.

Additionally, we announced the results of the Phase II study of KOMET-001 yesterday, a second-line single agent. In conclusion, the primary endpoints were achieved, and safety and tolerability were consistent with previous reports. Detailed data will be presented at a conference in Q2 of this fiscal year.

Finally, here are the future plans for ziftomenib. For the second-line single agent, we are working to apply for approval in Q2, and if it is the fastest, we hope to obtain approval by the end of 2025.

In addition, a Phase III study, KOMET-017, is scheduled to begin in H2 of this year for the first-line combination. The trial is a randomized, placebo-controlled trial, consisting of a combination trial with two uses: intensive combination therapy and a non-intensive combination, as shown in the slide.

HSC-GT : Progress of OTL-203 development

Target Disease：MPS-IH - Disease snapshot

- Multisystemic neurometabolic condition affecting cognition, growth and skeletal function
- Diagnosed during first 2 years of life; life-expectancy up to 10 yrs.
- Current standard of care: Allogeneic HSCT w/ or w/o ERT as bridging/chronic therapy, both of which have significant limitations
- Incidence: ~1:100,000 live births; Hurler syndrome accounts for 60%[1]
- NBS established in some geographies, including U.S.

Engl J Med 2021; 385:1929-1940 DOI: 10.1056/NEJMoa2106596

Progress of "HURCULES" Registrational Study (equivalent to P3)

- Study Overview: A multicenter, randomized, active-controlled clinical trial to evaluate the efficacy and safety of OTL-203 in patients with MPS-IH compared to standard treatment with allogeneic hematopoietic stem cell transplantation (HSCT)
- Subject enrollment has progressed faster than planned and is nearing completion
  - **Evidence of the urgent medical need in MPS-IH**
- Primary endpoint analysis measured 2-year mark post-treatment ; data, if positive, to be used to support regulatory submissions
- **The current anticipated application timeline is for 2028, with potential U.S. approval planned in 2029 assuming priority review**

[1]Beck et al. The Natural History of MPS I: Global Perspectives from the MPS I Registry. *Genetics in Medicine* 2014, 16(10), 759

Finally, I would like to report on the development progress of OTL-203 with regard to hematopoietic stem cell gene therapy.

The target disease is MPS-IH, a rare disease for which multiple treatments currently exist, but each has its own concerns, and there are high hopes for new treatments.

The HURCULES study, a pivotal study, is currently underway, and enrollment has progressed faster than planned and is nearing completion. The existence of an urgent unmet medical need in MPS-IH can be seen in this circumstance.

The primary endpoint analysis is measured at the two-year mark post-treatment. If data is favorable, we will move on to regulatory submissions. The current anticipated application timeline is for 2028, with potential US approval planned in 2029, assuming priority review.

The new updates since last year are listed on page 40 and beyond. Page 44 onward contains updates since the previous announcement.

I will skip going into details, but we will promote a group-wide, global approach to research, production, sales, and other functions, as well as the human resources and DX infrastructure that support them, based on our medium- to long-term growth strategy, steadily growing our business.

In 2025, we plan to transition to a new CEO and COO structure, and we will continue moving forward with efforts to realize our vision under the new structure.

That is all for our explanation.

Question & Answer

Nakamura [M]: We will now move to the question-and-answer session.

Yamaguchi [Q]: My name is Yamaguchi from Citigroup Global Markets.

The first question: I understand that last year's actual result of 95.4 billion yen includes various special factors, and adjusting for all of them could make things quite complicated. However, from an external perspective, it's difficult to grasp how this year's forecast of 80 billion yen compares in terms of underlying performance when excluding these special factors. Could you provide some insights on this?

Kawaguchi [A]: As Mr. Yamaguchi mentioned, there are various factors involved in the JPY80 billion forecast for this fiscal year, and it is difficult for me to provide an exact basis for the forecast.

However, as you know, the first special factor last year is the one-time earnings of JPY13.1 billion in EMEA due to the transfer of three brands. Additionally, there was milestone income of JPY1.6 billion from Tostran. Together, these represent a special factor of JPY14.7 billion.

In contrast, we plan to transfer one brand this fiscal year, but the scale size will be one of three brands. So, the biggest factor was a decrease in sales and profit of at least JPY10 billion.

And then there is the APAC region. Regarding the business transfer here, overall sales would drop significantly but only slightly in terms of profit under the scheme.

When it comes to the 2024 comparison, the restructuring implemented in 2024 has become a positive factor in terms of profit. We entered a new scheme in October and, by clearing inventories, achieved sales that exceeded the plan by more than JPY1 billion.

Therefore, there was already a considerable decrease in expenses after October 2024, which are JPY3 to JPY4 billion. In contrast, sales have been decreasing since the start of this fiscal year, and expenses have also been decreasing, but the decrease in expenses was only effective for nine months.

So, when compared to the previous year, this has become a significant decreasing factor. These are the special factors.

I am not sure if this should include as special factors, but the biggest impact was the termination of the Dovobet sales partnership at the end of last year, which had JPY7.9 billion in sales and an undisclosed profit.

Another point is exchange rates. Although the current exchange rate may be considered a bit conservative, we are looking at JPY145, which will have an impact of JPY11.4 billion on sales and JPY4.4 billion on profit. If you remove those impacts, you will see the actual line.

Yamaguchi [Q]: My second question is about the top line of Kura. They just issued a release without details, so I do not know much about it.

Kura’s stock price is going up and down. I would appreciate your thoughts or comments, including whether this is good or bad in relation to the plan. Maybe I should wait for the conference presentation, but I would be grateful if you could share something now.

Miyamoto [A]: I will get more details from Yamashita later, if there is anything else.

We, as an entire company, believe that the data itself is as planned, or rather, it is data that we can move forward with confidence. More details will be available at the conference, but would you like to add anything?

Yamashita [A]: Regarding the content, we are highlighting that the results met expectations and were successful. This announcement serves to communicate that success. Since this is a small study, disclosing the data now would reveal most of its contents. Therefore, we plan to present a comprehensive report at the conference and will limit the disclosure for now, refraining from announcing the full details. We hope you understand.

Yamaguchi [Q]: Is this announcement for Q2, ASCO?

Yamashita [A]: We have not disclosed that part yet either.

Yamaguchi [M]: Not disclosed. I understand. Thank you very much.

Wakao [Q]: My name is Wakao from JP Morgan Securities. Thank you for taking my questions.

I would like to ask about the operating profit of JPY80 billion for this fiscal year. Based on your explanation, a direct comparison with the previous year's profit level is not straightforward, given the influence of certain primary factors on last year's results. However, looking at these figures, the stock price has declined, which suggests an impact on market perception.

Considering these numbers, the outcome may have been somewhat predictable. That said, I would like to understand the extent of rationalization factored into these figures. Based on your explanation, these figures reflect rationalization efforts while accounting for the necessary investments in growth. I would like to understand the specific rationalization measures implemented and how these figures were calculated.

If this represents the post-rationalization structure, it seems that the profit level may remain relatively unchanged in the coming fiscal years. Could you share your insights on this?

Miyamoto [A]: I, Miyamoto, will explain overall, and Kawaguchi will add comments if he has any.

You are right, and as I mentioned earlier in my presentation, we are making various reforms to achieve our vision and to grow beyond it. The first step we took was the divestiture of established medicines in Europe. Then, we reorganized APAC operations last year, followed by rationalization measures, such as reducing small molecules and shifting toward the new modality side, which we are now doing in a sense.

In this regard, we have not yet completed rationalization or muscling up our operations, and we will continue these efforts, as this will likely be an ongoing process.

However, there are various special factors that come into play, some of which are difficult to see and some of which may result in extraordinary losses. I hope for your understanding in this regard. Based on this, we would like to build strength in having excess ability to grow globally as well as having excess investment capacity.

As you mentioned, it remains uncertain whether profits will see a V-shaped recovery this year and next. However, from a medium-term perspective, we believe we are well-positioned to sustainably elevate profit levels.

This year, for example, we are making a company-wide, global effort to enhance digital transformation, which will require increased investment in this area while scaling back in others.

Additionally, we will work on improving efficiency, and we are entering a phase of conducting a strategic review of our pipeline portfolio, carefully distinguishing between projects that drive growth and those that may be deprioritized.

From a medium- to long-term perspective, while R&D inherently carries uncertainties, if we execute our strategy effectively, we are confident that we can achieve a sustainable growth trajectory on a global scale. This is the focus of our current efforts.

Kawaguchi-san, do you want to add anything?

Kawaguchi [A]: As I mentioned earlier, with the announcement of our Vision 2030, we have already clearly defined the areas where we will focus and those where we will pursue collaborations with partners. We are allocating resources to invest firmly in the focused areas, which led to the changes we mentioned earlier.

While we have a certain level of planning in place for this fiscal year, we cannot put plans into place for some areas due to various factors. Regarding our future earnings growth potential, I can say with confidence that we are making firm, strategic investments toward 2030, as outlined in our capital allocation plan.

I have to say that some short-term profits have been partially impacted as a result of this long-term investment strategy. However, it does not mean accepting a decline in overall profit levels. Instead, we are working to balance cost reductions with maintaining stability while executing our growth strategy. At this stage, we are beginning to see steady growth beyond 2030.

Last year, we faced some concerns due to impairment losses and other factors. However, our 2030-focused investments have made steady progress in 2024, strengthening our confidence in achieving our long-term goals for 2030.

Wakao [Q]: The second question is about capital allocation. In terms of capital allocation and its return to shareholders, both were implemented in the last fiscal year. Now, the president has explained that you will be directing toward business investment in the current fiscal year. I didn't see the term "shareholder return," and I would like to understand better.

I believe you will continue to invest in growth, but did you mean that you will shift the focus to investment in growth rather than shareholder returns this year? I would like to know if the intention is to invest in growth first and then return profits to shareholders later.

In terms of growth investments, Orchard and ziftomenib are expanding. It would be helpful if you could share your insights on what additional measures are needed to achieve our 2030 goals.

Miyamoto [A]: We believe that the first priority is investment in growth, so we would like to focus on that first. Of course, regarding share buybacks, Kawaguchi and I regularly discuss taking a flexible approach based on factors such as stock price movements and cash position. While we cannot commit to a definitive course of action, we also do not rule it out entirely.

Then, as for what we need to do further toward 2030, as you pointed out earlier, we believe there are still areas that need to be made more muscular, as you pointed out. This is something we need to address on a global basis to determine the best situation. For growth by 2030, we need to invest in R&D and then increase production capability.

We will also consider larger license-ins in a flexible manner, depending on the status of the development portfolio review. As Kawaguchi mentioned earlier, we will consider various possibilities in line with the growth story, in a flexible manner. In any case, we believe that growth investment is the top priority.

Hashiguchi [Q]: My name is Hashiguchi from Daiwa Securities.

Where are the remaining challenges in building a muscular structure? My own take on it is that it may be necessary to redefine the nature of the Japanese business.

Are you considering the possibility of some kind of initiative to boldly change the product portfolio, as was done in APAC and EMEA? I would like to know about that.

Miyamoto [A]: Thank you.

As you say, and as you can see from the figures from last year, Japan already accounts for about 30% of total sales. Naturally, everyone is thinking that the Japanese business cannot continue as before.

Nothing concrete has been decided yet, but I think a shift will be necessary in terms of what we do with the Japanese business, even as we look at our portfolio and pipeline for the future. So, I think you're right, and there is still much to be done.

Hashiguchi [Q]: I think you mentioned that there is a possibility of incurring impairment losses for some. Do you have any potential costs planned related to the Japanese business?

Miyamoto [A]: As I said, nothing specific has been decided. So, there is nothing in particular that we have identified and included in this plan.

Hashiguchi [Q]: Is it the same even if it is not limited to the Japan business?

Miyamoto [A]: In general, we still include a certain number of estimates in the other things we do, but I don't think we have incorporated anything specifically targeting Japan.

Hashiguchi [Q]: One more point regarding the situation of Lenmeldy in the US: in the last quarter, you were unable to treat a single case. What has changed since the acquisition compared to your initial expectations? You might say that things are on track, but how do you evaluate the progress made so far? If there are areas for improvement, what do you think those areas are?

Miyamoto [A]: When we acquired the company, we expected that we would be able to secure FDA approval around last April and set a reasonable price, and we anticipated that there would be a significant number of patients. In fact, we thought we might be able to treat several cases within the last year. Unfortunately, many of the patients identified last year had already advanced symptoms and were not feasible candidates for this treatment, so we were unable to provide treatment.

Although these efforts have been ongoing for a long time, the key priority is establishing a system to screen newborns as early as possible, before symptoms appear. Ideally, this would allow for early identification and timely access to treatment.

Many of the patients being identified now are discovered through family screening, as parents become concerned about their younger children after an older sibling is diagnosed. Unfortunately, in many cases, they choose to have their second or third child tested before symptoms appear, and a significant number of these children end up entering treatment.

I think newborn screening is important. For example, Illinois is the only state in the US that includes MLD in newborn screening. If this is the case, we are currently working to have it recommended by the federal government. I think that once we receive a federal recommendation, we will be able to advocate for its inclusion in each state. If we continue that activity and start in each state, I think we will identify more patients.

In any case, while it's difficult to say whether it is fortunate that we were able to identify a patient this year, from a business perspective, we have already treated one case in January. Moving forward, we remain committed to expanding these efforts to identify and support patients as early as possible, ensuring that we can help as many individuals as we can.

Hashiguchi [Q]: I think diseases are basically the same in Europe and the US, but having gained some experience in Europe before coming to the U.S., what differences have you observed between Europe and the U.S.?

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

In terms of the project in Europe, the history is a little longer, and the approval was granted in 2022. So, it has been approved as an established treatment, and in that sense, a network to identify patients has already been established in Europe. In that sense, I think we are already seeing momentum in Europe regarding this treatment, and we are starting to see signs of it in the US as well.

As just one example, there are six facilities in Europe that have received this certification and are qualified. There are also facilities with accreditation. Additionally, five facilities in the US have received accreditation by the end of the year. Along with this, we have applied for newborn screening and hope to receive more positive feedback on our application.

If we receive such supportive feedback, I believe that identifying newborn patients will be developed as a routine. In that sense, I would say that the prospects for this business are still bright.

I would like to make one more comment on MPS I, Hurler's syndrome. Miyamoto just explained the HURCULES test. This newborn screening for MPS I is currently being discussed in the US, and we are in the process of enrolling patients in our clinical trials.

Therefore, I hope that you will see the contents I have just explained as a tailwind for our business model.

Hashiguchi [M]: Thank you very much.

Sakai [Q]: My name is Sakai from UBS Securities. I would like to ask you two questions about development.

First, you know that there was an earlier generation drug prior to ziftomenib in the US, which is Syndax's Revuforj .

If you look at page 38, you'll see the interest from American biotech analysts yesterday, or rather in the last few days. It says that you have not disclosed the primary endpoints here, CR and CRh, referring to complete remission or complete remission with partial hematologic recovery. Syndax has reported a 23% rate, and how your results compare to that will be a key factor in this evaluation.

Are these figures being reported to your company, and what Dr. Yamashita just mentioned, is it based on those figures? I want to confirm that the rug is not being pulled out from under you.

Company Representative [A]: Thank you for your question.

I will refrain from disclosing specific information at this time. However, as I mentioned earlier, the key point I wanted to emphasize is that, while you referenced a comparison with Syndax's drug, the indications for which Syndax has obtained approval differ from those we are currently seeking.

Specifically, Syndax's drug is approved for patients with KMT2A rearrangement, whereas we are targeting AML patients with NPM1 mutations, for which no drug is currently available. This means that this will be the

first drug. Naturally, we have established an endpoint that demonstrates the significant value of this drug, and we are confident in our ability to meet it.

Sakai [Q]: So, you are certain that CR and CR2h are the evaluation items, right?

Yamashita [A]: Yes, that's right.

Sakai [Q]: Given the nature of this disease, that is certainly the primary endpoint. Of course, I ask this knowing that there is no head-to-head studies, but thank you.

Another one is about rocatinlimab. I believe it was on page 26 that you mentioned T-cell imbalance. I wonder if the value of this product ultimately comes down to this. In other words, based on the ROCKET study, the initial perception seemed to be that it did not perform as well as competing products. However, President Miyamoto has stated that he believes it was a success.

Regarding T-cell imbalance, do you think this can be demonstrated directly in clinical trials, or would it require further investigation through translational research? How would you position the characteristics of this drug?

Miyamoto [A]: If there are any additional comments, they will come from Yamashita, but I think we probably need both of them.

Clinical trials alone are not enough, and translational research alone is not enough either. So, I think it is necessary to show how patients' situations have changed by using rocatinlimab, for example.

Yamashita [A]: What we are presenting here is not just a fantasy, but is based on science, and we are presenting it in a way that shows we are sure this is what is happening. Then, how can this be verified? We could do so through clinical studies, such as biomarker analysis, or by evaluating specimens for further assessment in the clinical area.

However, the most important part is how this concept will lead to therapeutic effects. Rocatinlimab not only blocks or neutralizes incoming cytokines but also suppresses the cells that release them. I believe differences may emerge in aspects such as the onset of efficacy and persistence, distinguishing it from antibodies that target cytokines. From this perspective, I also think we can further solidify the concept behind this approach.

Sakai [M]: Okay. Thank you very much.

Wada [Q]: Thank you very much. My name is Wada from SMBC Nikko Securities. I would like to ask questions about the pipeline, too.

Following up on Mr. Sakai’s current question, I would like to ask about the ROCKET study. Since this pertains to atopic dermatitis, I would like to understand how you perceive the remaining unmet needs. Additionally, on page 34, you mention the ASCEND study. I interpret this as the target of your efforts.

Dupixent is used quite a bit in the market. Maybe as an unmet need, there are about 20 or 30% of patients for whom Dupixent does not work, so I am looking at that as the first potion.

The second is that among the patients who respond to Dupixent, since it is a remission induction therapy, I believe that remission is inducted and can be divided into three categories.

Patients who stop taking Dupixent after about six months but maintain remission even after stopping the administration, I wonder if there are some patients who are essentially cured, where there is no need for this therapy anymore.

I think there are probably about three types of patients: those who cannot stop taking Dupixent and maintain remission after six months, and those who continue to take the drug but relapse. I would like to know what percentage of these patients you are seeing in the field.

Miyamoto [A]: We are not in a position to explain such detailed figures. Of course, we are looking at all the details of what kind of strategy to attack the market in considerable detail with Amgen, but we are not in a position to unveil that here and now.

Wada [Q]: I understand that the three groups in the ASCEND study shown on page 34 represent patients who will likely either continue with maintenance dosing or transition to an extended dosing interval, along with the placebo group, which has already discontinued treatment. Is this interpretation correct in terms of assessing how long the effects can be maintained?

Miyamoto [A]: That is part of it, as I explained earlier. We want to see long-term efficacy and safety, and then sustainability.

Wada [Q]: One more point, ziftomenib. You mentioned earlier that you are going to get an indication for NPM1, but I would like to ask how you see the second-line KMT2 mutation. I believe that you take both NPM1 and KMT2 rearrangement for the first line, but can you comment on this concept, including the data you have?

Yamashita [A]: As for the second-line KMT2A rearrangement, as I mentioned earlier, Syndax has already been approved as a single agent. We are also considering the possibility of using a combination of drugs instead of a single drug. We are in the process of continuing such studies.

Then, as for the first line, we are proceeding to target both of those two genetic mutations and rearrangement.

Wada [M]: Thank you very much.

Ueda [Q]: My name is Ueda from Goldman Sachs.

First, I would like to know about your approach to mid-term planning. You indicated that the KPI achievement period will be after FY2026.

In terms of the KPIs you have presented so far, could you tell us which areas you place particular emphasis on as the business environment changes, and what the time frame is for achieving these KPIs? In addition, what are your thoughts on the need to re-set KPIs in a changing environment?

Miyamoto [A]: Thank you.

As you say, the world has changed considerably, and our surroundings have also changed dramatically. So, we are currently discussing internally how to set these KPIs. In particular, we are trying to figure out what the best way is to present the medium-term. In any case, Kawaguchi always says that ROE is important, so naturally, we will be looking at that area as well.

I may sound like I'm making excuses, but if we need to reconsider the KPI itself, we will have to talk about when the KPI we are showing here will be achieved at the same time. Though, I might even say to just forget about this altogether.

Ueda [Q]: Second, I would like to know your thoughts on business investment. The question is, how is the current pipeline being evaluated? Last year, you introduced some of your brand products in the early stages of development and made progress in bringing in later-stage assets as well.

How do you assess the current situation? If further reinforcement is needed, what are your thoughts on the development phase and therapeutic areas to prioritize? Additionally, considering the current cash position, how much investment do you anticipate can be allocated?

Miyamoto [A]: First of all, I think the current view of the pipeline is basically quite complete. In particular, rocatinlimab and ziftomenib are in the late stage, and we have near-global rights to those as well. So, I think the situation is quite different from what it was two or three years ago.

In addition, we are quite encouraged by the fact that we have seen quite a few of our own products come up in the early stage. The most important point is ensuring that our drug discovery efforts translate into actual products.

In that regard, the number of candidates that entered clinical trials last year has increased significantly, with several more waiting. Looking at this progress, I believe our portfolio is becoming much more robust.

However, if you ask me if I am satisfied with this, I have learned from the past that you never know what will happen in R&D, so I would like to continue aiming to enhance the pipeline, especially in what we call our focus areas.

While we have the cash available for investment, each new asset introduced not only requires a one-time licensing fee but also leads to increased development costs significantly. We need to carefully balance these factors.

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

Muraoka [Q]: This is Muraoka of Morgan Stanley. Thank you very much.

I don't want to ask a question that catches the edge of the word, but just a few minutes ago, President Miyamoto commented that we never know what will happen in R&D. Now, I want to ask you: If the results of ASCEND show that the drug is working but not commercially viable, what action do you think is necessary?

Miyamoto [A]: That's a hard question to answer. Internally, we are considering various scenarios, of course, but there is little that we can disclose here and now. Of course, there is also the question of how to consult with Amgen. If we can get approval, then we will go for it. So, we have scenarios internally, but to be honest, I cannot answer that question at this time.

Muraoka [Q]: I know this is difficult to answer, but if, for example, zifto is the only available product in the late stage, do you have to go and buy a late-stage product? Or perhaps, by that time, your own products will have progressed, allowing you to manage without acquiring late-stage products. I'm curious about which risk scenario is more likely. What probability should I consider?

Miyamoto [A]: This largely depends on the availability of data, particularly for our early-stage products. As we have clearly stated, we are also seeking partnerships for products outside our core focus areas. The situation may vary depending on whether sufficient data is available and whether we have successfully identified the right partners. We believe it is essential to remain flexible in evaluating this landscape.

So, the answer for now is that both can be options.

Muraoka [Q]: With the recent decline in stock price, I have been considering ways to bring it back. I am hopeful that the financial results in three months will be strong, but I anticipate a rebound for Crysvita in the US. However, Q1 last year was not particularly strong, apart from a one-time BI payment, making YoY comparisons go less easy.

Regarding the Q1 outlook in three months, it would be helpful if you could provide some insights on whether I should expect a stronger or weaker performance.

Miyamoto [A]: Since you have been following closely, I was listening and thinking, hmm… It's already been a month into the year, so we will have to see how things unfold. That said, Crysvita in the US has historically had a slow start in Q1 due to seasonal trends.

At the end of last year, we saw a healthy level of inventory in specialty pharma, though not an excessive build-up. Given that, I expect Q1 to start slow, but things should pick up to some extent.

As for any special factors, I can't comment definitively at this stage. However, I believe the overall trend will likely align with your expectations, Mr. Muraoka, and things should progress smoothly.

Muraoka [Q]: If possible, it would be very helpful if you could release a set of information on SHUTTLE and IGNITE around May when the Q1 results come out.

That is all. Thank you very much.

Miyamoto [A]: Thank you.

Everyone is paying attention to this, and I hope we can discuss the timing of disclosure of data in this area with Amgen.

Muraoka [Q]: Thank you very much.

Speaking additionally, it would be very helpful if you could set up a call that is somewhat satisfactory, rather than the indigestible one you had last time, when the SHUTTLE and IGNITE information become available. This is a request from me.

Yamashita [A]: Thank you.

I think there may have been a misstep last time, including in terms of timing. Therefore, we intend to move forward with this project, ensuring that there are gaps, as we have carefully coordinated with Amgen. Thank you for your questions.

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

Matsubara [Q]: My name is Matsubara from Nomura Securities.

First, tell us about KHK4083. I understand that the focus of this material is on T-cell rebalancing rather than a direct effect on skin cells, which supports its potential for long-term efficacy. Given this, I expect that ASCEND, ORBIT, and ASTRO will demonstrate effectiveness at 52 weeks.

In this context, what is your company's current assessment of the results from IGNITE and SHUTTLE, as well as the 24-week trial? Specifically, I noticed that the HORIZON trial appeared to show slightly lower efficacy compared to the Phase II trial. Based on this, how does your company view the results of IGNITE and SHUTTLE in the current situation?

Miyamoto [M]: Dr. Matsubara, current situation.

Matsubara [Q]: For example, there are various factors, such as the patient's background and phenotype. Could you tell us how you are considering this now? Of course, I know you don't know the results and cannot disclose them, but could you please share your considerations in this context?

Miyamoto [A]: Okay. I believe it is challenging to gain a complete picture from top-line data alone, including HORIZON, so it would be best to wait for the disclosure of the detailed data.

As you mentioned, it is crucial to examine the patient background, concomitant medications, and specific data on who responded well and who did not. Given the large patient population in these studies, we expect to gain valuable insights moving forward.

Additionally, as mentioned in the previous question, we will continue to learn more about the real-world potential of this product in the actual market. For now, the best approach is to wait for further data disclosures.

Without data, we believe that we cannot evaluate the actual its value. We are eager to see the detailed analysis, including the results from IGNITE, SHUTTLE, and other studies, and look forward to the insights that will emerge.

Dr. Yamashita, do you have anything to add?

Yamashita [A]: I think that as more data is accumulated, we will be able to show you more clearly what we are expecting. I am also hopeful that the characteristics of rocatinlimab obtained in Phase II will be sufficient data to introduce such a point.

Also, I am hoping that we will be able to present much more clearly when we are able to disclose data from longer trials, as you mentioned earlier.

Matsubara [Q]: As Mr. Muraoka requested earlier, we would be grateful if you could disclose the details of your analysis as well. Thank you very much.

The second point is Crysvita. I know it has bumpy trend, and I think there were some issues with medication compliance in Q3. Have you had any such updates, like an improvement regarding to compliance?

Miyamoto [A]: Excuse me, what is your question about Crysvita's patient?

Matsubara [Q]: Any updates on medication compliance.

Miyamoto [A]: Update. I understand. Abdul knows this area better. I will let him speak as much as he can share.

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

Currently, this adult new patient population in the US is at a 75% level. These symptoms are different than before, but sustainability is quite different compared to children. Over the past couple of months, we have reorganized our patient services structure to follow up on our adult patients. The system is designed to help adult patients better understand how important it is to continue taking the medication.

Then, we started hiring new people, clinical educators. These people are medical professionals, and their role is to educate patients about this disease and answer patients' questions. In that sense, I believe that compliance issues, such as ensuring that people take their medications properly, can be resolved through these efforts.

What we consider very promising is the very large number of adult patients, the number we have been able to recruit, compared to the number of pediatric patients.

That is all. Thank you very much.

Matsubara [M]: Thank you very much.

Wakao [Q]: I have three questions. The first one, I would like to know in a simple format, yes or no: Are there any more one-time revenue items in your plans for this fiscal year? I know that Grünenthal royalties will be included, but other than that, are there any other one-time profits included that you have not announced so far? It could be the other way around, though.

Kawaguchi [A]: It's not in particular.

Wakao [Q]: The second question is about Crysvita. From your explanation, I understand that compliance is improving. However, when looking at your fiscal year plan, it seems slightly more conservative compared to the previous trend. I would like to understand the reasoning behind this projection.

If we simply apply the YoY increase in US dollar terms and local currency terms from FY2023, the expected figure should be somewhat higher. Additionally, since your explanation suggests that the overall trend has not changed, I feel the absolute amount can align with past trends. However, the projected growth appears to be relatively modest.

Could you clarify the background on this? Is the projection being kept conservative due to overstretched expectations in the past, or is it because compliance improvements are still in progress and some challenges remain?

Kawaguchi [A]: Regarding Crysvita, we do not disclose the 2025 projections by region, so I will address the figures collectively as overseas.

Globally, the number of patients was 7,000 in 2024, and our plan for this fiscal year is to steadily increase that by 1,000, reaching 8,000. Please understand that we aim to maintain the same volume growth trajectory this year. As the denominator goes up, the growth rate percentage may appear lower, but in terms of volume, we are maintaining a steady pace.

Another key point in comparing growth rates between 2023 and 2024 is that, in 2023, Europe underwent a price correction, bringing prices significantly lower than in previous years. As a result, when comparing 2024 to 2023, Europe shows a much higher growth rate.

On the other hand, in 2025, Europe will see a lower pricing impact due to adult approval in the UK. The growth rate may appear weaker, primarily due to the pricing effect in the UK market.

Additionally, the exceptionally high growth rate last year makes this quarter’s growth appear lower in terms of the pricing impact against volume. These mixed factors contributed. Then there is the exchange rate. While there are notable currency fluctuations impacting planning, our volume growth remains unchanged in our plans.

Wakao [Q]: I wanted to know in absolute terms. I think that is true in terms of the percentages, as you mentioned. But in absolute terms, even if you only consider the US, I feel that it is not enough to apply the growth in that area. Now, I was wondering if the same number of patients is incorporated. I thought you factored in those who discontinue treatment or drop out. Is that not the case?

Kawaguchi [A]: No, it is not.

Wakao [Q]: Just one more question. Ziftomenib must be best-in-class, I thought, based on the data I saw when your company first announced the partnership with Kura. On the other hand, looking at the data for Sumitomo Pharma's enzomenib that came out later at ASH, I thought this was best-in-class.

Now, if you are able to comment on your company's evaluation of Sumitomo Pharma, we would appreciate your insights. However, if you cannot comment on another company's product, could you instead elaborate on the factors that make your product best-in-class?

Yamashita [A]: On your first point, we are not familiar with Sumitomo Pharma's drug, so we will refrain from commenting on it.

As mentioned earlier, Syndax has already entered the market with a menin inhibitor, but even within this class, there are distinct segments. We are the first to advance in the NPM1.

Additionally, NPM1 mutations are present in a significant percentage of AML patients, making this a key opportunity for the potential future expansion of our drug. Our drug is, of course, effective as a menin inhibitor, but its differentiated profile sets it apart. For instance, existing products may have prolonged QTc effects, which could limit their use.

Furthermore, certain concomitant therapies, such as venetoclax, are metabolized by CYP3A4. If there is an inhibitor of this metabolic enzyme, it could make combination use difficult.

However, our drug has a favorable drug interaction profile and strong safety profiling. Rather than focusing too much on comparisons with other companies, we believe we are well-positioned to move forward with minimal obstacles and establish a leading position in this space.

Wakao [Q]: If that is the case, should we assume that during your partnership negotiations with Kura, you did not consider Sumitomo's enzomenib data and that it was not a key factor in your decision?

Yamashita [A]: We are aware that such a drug has been developed, but information was very limited. Of course, we have been negotiating the partnership on the assumption that such a drug exists.

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

Wada [Q]: One point: I understand that a new pipeline has entered Phase I for the same indication as Crysvita, similar to KK8123. I would like to know whether its mechanism of action is the same and how you position this drug within your portfolio. Additionally, what is your strategy for its development? May I have your comments?

Miyamoto [A]: I'm not in a position to make any further disclosure on that. Sorry.

Nakamura [M]: Any other questions? Thank you very much.

Nakamura [M]: Now we will take questions from the press attending the meeting.

Sakaguchi [Q]: My name is Sakaguchi from Iyaku Keizai Sha.

With regard to the rationalization of the Japanese operations, how many voluntary retirements in the R&D were counted last year?

Miyamoto [A]: We are trying to downsize the small-molecular study, so we solicited voluntary retirement for specific job functions, resulting in 122 applicants.

Sakaguchi [Q]: How would you evaluate the number of 121?

Miyamoto [A]: As we made the strategic decision to scale down our small molecule study and shift toward new modalities, 121 individuals chose to pursue other career paths. While parting ways with colleagues is

always an emotional moment, we remain committed to honoring their contributions and staying focused on advancing in new modalities with determination.

Sakaguchi [Q]: Thank you very much.

Relatedly, in terms of improving the efficiency of your Japanese operations in the future, do you have any plans to implement a voluntary retirement program for other divisions as well?

Miyamoto [A]: Nothing is set in stone right now. As I explained earlier, it is very important how we grow globally and as a company as a whole. So, we are always thinking about shifting or reducing the number of heads, if necessary, not only in the Japanese business. Nothing is set in stone right now.

Sakaguchi [M]: Okay. Thank you very much.

Sakata [Q]: Thank you. My name is Sakata from Yakuji Nippo.

I would like to ask about the new management structure. To put it bluntly, I wonder if there was a need to reiterate it now.

Second, I would like to ask Dr. Mullick. You mentioned that the new organization will be focusing on the vision. How do you see your mission and your aspirations?

The third is the new mid-term plan starting in FY2026 and the challenges that you envisage. What is your view on those initiatives? You mentioned that the first priority is to invest in growth, and that you will also review the company's structure to build more muscle. I would appreciate your thoughts on that area, and my three questions.

Miyamoto [A]: I will answer the first and third questions. I'll leave the second to Abdul.

I think your question is why we are now in a CEO/COO structure. Since I was appointed president, we have been able to launch two global products during my time, and the mid-term management plan has been in place since 2021.

In addition, for example, AstraZeneca made a great effort to expand Fasenra, which we developed, on a global scale. We are now conducting strong global clinical trials with Amgen for rocatinlimab, an antibody we have developed. From the pipeline side, we have a relatively good foothold in the global market.

Additionally, the organization has transitioned from a structure where overseas subsidiaries were expanded from the Japanese headquarters to a truly global company structure.

Therefore, as I previously explained, we have issued the Story for Vision 2030, our vision for 2030 and beyond, to build more muscle and prioritize pipeline development. We are making a lot of progress toward this goal, but we need to accelerate this progress.

Rather than having me alone oversee and control everything, I thought it would be better to have a CEO and COO structure with separate roles to accelerate this operation and the overall structure of the company. Since it has been seven years since I was appointed, and since we have great talent in our company, I think it would be best for us to adopt this structure. We will implement it from the next fiscal year.

Then we are talking about what to do in the next year and beyond, and we are discussing this quite a bit internally right now. We will discuss it with you when the time comes. The Story for Vision 2030 and Vision 2030 will not change, so I think the most important thing is how strongly we advance this toward 2030.

During this period, our focus will be on advancing the pipeline you mentioned earlier. I believe that if its progress remains smooth, we will be positioned on a significant growth trajectory. To achieve this, we must establish a structured process moving forward to ensure its successful execution.

Now, the aspirations from Abdul.

Mullick [A]*: I consider myself very lucky. In other words, my mission is to execute the stories clearly outlined for Vision 2030. I believe there are three important factors. We have been able to successfully launch drugs that provide life-changing value, and we have successfully developed the infrastructure to deliver them.

We have learned a lot from it, but along with that, we want to keep improving and deliver our medicine to more patients. With that in mind, it becomes evident that Crysvita and Poteligeo are currently reaching only a small percentage of the patients who could benefit from them. Therefore, our journey to expand access continues.

Secondly, and I am sure you are well aware of the level of investment we are making in R&D, it is extremely important that we take this project further while utilizing the infrastructure we have put in place worldwide.

Thirdly, it is important for us to maintain our unique presence as a united J-GSP and Kyowa Kirin. We have employees all over the world, and Miyamoto just introduced the KABEGOE principles for how they should behave. It is important that employees act in accordance with the principles.

I have highlighted key aspects of our mission that we must fulfill to deliver life-changing medications and bring smiles to more patients' faces.

Thank you very much.

Sakata [M]: Thank you very much.

Nakamura [M]: Thank you very much. Thank you all for your valuable questions.

This concludes the question-and-answer session, and the Zoom streaming has now ended. Thank you to everyone who participated online.

[END]