



## **ONO PHARMACEUTICAL CO., LTD.**

Financial Results for the Fiscal Year Ended March 2022

May 12, 2022

### **[Number of Speakers]**

7	
Gyo Sagara	President and CEO
Toshihiro Tsujinaka	Senior Executive Officer/Executive Director, Corporate Strategy and Planning
Toichi Takino	Senior Executive Officer/Executive Director, Discovery and Research
Kiyoaki Idemitsu	Executive Officer/Executive/Director, Clinical Development
Satoshi Takahagi	Corporate Officer/Executive Director, Sales and Marketing, Primary Care Business Division
Kazuhiro Nagahama	Director of Finance and Accounting Department
Yukio Tani	Corporate Executive Officer, Head of Corporate Communications

# Revenue

Revenue	YoY Change
¥ 361.4 billion	+ 16.8 %

## Breakdown of Revenue

(Billion yen)

	FY 2020	FY 2021	YoY Change
Revenue of Goods and Products	214.5	246.0	+ 14.6 %
Royalty & other revenue	94.7	115.4	+ 21.8 %
<b>Total</b>	309.3	<b>361.4</b>	<b>+ 16.8 %</b>

**Sagara:** These are the results of FY2021. Revenue increased by JPY52.1 billion, or 16.8%, to JPY361.4 billion.

The breakdown is JPY246 billion from goods and products and JPY115.4 billion from royalty and other revenue. Revenue from goods and products increased by JPY31.5 billion and that of royalty and other revenue increased by JPY20.7 billion.

# Revenue

## Sales of Major Products

(Billion yen)

	FY 2020	FY 2021	YoY Change
<b>Opdivo</b>	98.8	<b>112.4</b>	<b>+ 13.8 %</b>
<b>Forxiga</b>	22.4	<b>36.7</b>	<b>+ 64.0 %</b>
<b>Glactiv</b>	25.5	<b>24.5</b>	<b>- 3.8 %</b>
<b>Orencia SC</b>	21.9	<b>22.9</b>	<b>+ 4.5 %</b>
<b>Parsabiv</b>	8.1	<b>8.9</b>	<b>+ 10.2 %</b>
<b>Kyprolis</b>	7.1	<b>8.4</b>	<b>+ 17.5 %</b>
<b>Velexbru</b>	2.1	<b>6.3</b>	<b>+ 204.1 %</b>
<b>Onoact</b>	4.7	<b>4.9</b>	<b>+ 4.5 %</b>
<b>Braftovi</b>	1.1	<b>2.7</b>	<b>+ 156.9 %</b>
<b>Mektovi</b>	1.0	<b>2.2</b>	<b>+ 124.7 %</b>
<b>Ongentys</b>	0.3	<b>2.9</b>	<b>+ 742.4 %</b>
<b>New Products (FY2021)</b>	—	<b>1.0</b>	—

 ONO PHARMACEUTICAL CO.,LTD. 3/14

Regarding revenue by product, revenue of Opdivo grows steadily in new indications, especially esophageal cancer, as well as in the first-line treatment of non-small cell lung cancer and gastric cancer. The revenue increased by JPY13.6 billion to JPY112.4 billion.

The revenue of Forxiga increased by JPY14.3 billion to JPY36.7 billion, due to expanded use for chronic heart failure and chronic kidney disease, in addition to diabetes.

The revenue of Glactiv decreased by about JPY1 billion, reflecting the sluggish growth of the market for this class.

Orencia and Parsabiv have competitive products and are facing a severe competitive environment in the market. However, we are doing our best to keep up.

Velexbru has seen steady sales growth. The market for Ongentys is also expanding steadily.

We have five new products launched in the last two or three years. Regarding Joyclu and Adlumiz, these have made a little slow growth from the start. As you are aware, there have been some unexpected adverse events with Joyclu, so we are taking various steps now to resolve this issue and then go ahead. Originally, we had planned to make JPY20 to JPY30 billion a year, but we got off to a late start.

# Revenue

## Sales of Long-term Listed Products

(Billion yen)

	FY 2020	FY 2021	YoY Change
Opalmon	5.5	4.7	- 13.4 %
Rivastach	6.6	2.9	- 56.6 %
Onon capsule	2.9	3.6	+ 22.0 %

As for long-term listed products, the revenue of Opalmon and Rivastach are decreasing as expected. Onon temporarily increased a bit, reflecting the short supply from generic manufacturers.

# Operating Profit

Operating Profit	YoY Change
¥ 103.2 billion	+ 4.9 %

## Costs, etc.

(Billion yen)

	FY 2021	YoY Change
• Cost of Sales	¥ 93.5	( + 9.3% )
• R&D Expenses	¥ 75.9	( + 21.6% ) ①
• SG&A Expenses	¥ 77.1	( + 11.3% ) ②
①+② Total	¥ 152.9	( + 16.2% )
• Other Income	¥ 1.0	( - 88.0% )
• Other Expenses	¥ 12.7	( + 557.3% )

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Operating profit increased by JPY4.9 billion, or 4.9%, to JPY103.2 billion. The cost of sales ratio dropped slightly, from 27.7% to 25.9%. The increase in the proportion of royalty was the main factor.

R&D expenses increased by JPY13.5 billion to JPY75.9 billion. SG&A expenses excluding R&D expenses increased by JPY7.8 billion to JPY77.1 billion. We plan to proactively invest in R&D and are proceeding accordingly.

Other income and expenses are quite irregular in FY2021. The other income included the front payment of the license agreement from Roche in the previous fiscal year. The reaction to this is that other income decreased significantly.

Other expenses included JPY7.3 billion that was balance with the reserve allowance accompanied with the settlement of the Opdivo patent lawsuit, as well as expenses related to contractual agreement with BMS, resulted in JPY12.7 billion, which exceeded JPY10 billion. For both factors, operating profit negatively affected.

## Profit for the Period (Owners of the Parent Company)

Profit for the Period (Owners of the Parent Company)	YoY Change
¥ 80.5 billion	+ 6.8 %

### Income tax expense

¥ 24.3 billion	( YoY Change - 4.1 % )
Statutory effective tax rate	30.6 % ( 30.6 % prior year )
Tax burden rate	23.2 % ( 25.2 % prior year )

### (Major change factors)

Increase in profit before tax

Profit for the period increased by JPY5.1 billion to JPY80.5 billion.

## Revenue (Forecasts)

Revenue	YoY Change
¥ 425.0 billion	+ 17.6 %

### Breakdown of Revenue

(Billion yen)

	FY 2021 (Result)	FY 2022 ( Forecast )	YoY Change
Revenue of Goods and Products	246.0	290.0	+ 17.9 %
Royalty & other revenue	115.4	135.0	+ 17.0 %
<b>Total</b>	361.4	<b>425.0</b>	<b>+ 17.6 %</b>

\* Assumed exchange rate 1 USD 110.00 yen

As for the forecasts for FY2022, revenue is expected to increase by JPY63.6 billion, or 17.6%, to JPY425 billion. Revenue of goods and products is expected to be JPY290 billion, and royalty and other revenue is expected to be JPY135 billion. They increased by JPY44 billion and JPY19.6 billion, respectively.

# Revenue (Forecasts)

## Sales Forecasts of Major Products

(Billion yen)

	FY 2021 (Result)	FY 2022 ( Forecast )	YoY Change
<b>Opdivo</b>	112.4	<b>155.0</b>	+ <b>37.8</b> %
<b>Forxiga</b>	36.7	<b>47.0</b>	+ <b>28.2</b> %
<b>Orencia SC</b>	22.9	<b>23.0</b>	+ <b>0.5</b> %
<b>Glactiv</b>	24.5	<b>23.0</b>	- <b>6.3</b> %
<b>Kyprolis</b>	8.4	<b>9.0</b>	+ <b>7.6</b> %
<b>Parsabiv</b>	8.9	<b>8.0</b>	- <b>9.9</b> %
<b>Velexbru</b>	6.3	<b>7.0</b>	+ <b>11.7</b> %
<b>Ongentys</b>	2.9	<b>5.0</b>	+ <b>73.6</b> %
<b>Onoact</b>	4.9	<b>4.5</b>	- <b>7.6</b> %
<b>Braftovi</b>	2.7	<b>3.5</b>	+ <b>27.4</b> %
<b>Mektovi</b>	2.2	<b>2.5</b>	+ <b>11.7</b> %

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Sales forecast by product is that Opdivo sales are expected to be JPY155 billion. The sale for the first-line treatment of non-small cell lung cancer and gastric cancer, adjuvant treatment of urothelial cancer, and cancer of unknown primary, etc. is expected to continue to expand in FY2022.

Use of Forxiga is also expected to grow for the treatment of chronic heart failure and chronic kidney disease, in addition to diabetes, and the revenue is expected to increase by JPY10.3 billion to JPY47 billion.

We also expect that the revenue of Ongentys, Velexbru and other products will continue to grow.



## Operating Profit (Forecasts)

Operating Profit	YoY Change
¥ 145.0 billion	+ 40.5 %

### Costs, etc.

(Billion yen)

	FY 2022 ( Forecast )	YoY Change
• Cost of Sales	104.0	( + 11.2 % )
• R&D Expenses	87.0	( + 14.7 % ) ①
• SG&A Expenses	88.0	( + 14.2 % ) ②
①+② Total	175.0	( + 14.4 % )
• Other Income	0.5	( - 49.0 % )
• Other Expenses	1.5	( - 88.2 % )

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Operating profit will increase by JPY41.8 billion, or 40.5%, to JPY145 billion. We expect a continuous downward trend for cost of sales ratio and are forecasting to be 24.5%.

R&D expenses are expected to increase by JPY11.1 billion to JPY87 billion. Naturally, the Opdivo patent cliff is expected to be in 2031, 10 years later from now in Japan, and royalties from overseas will gradually decline, so we are promoting proactive drug discovery activities and global development. This means that we will further promote joint research with academia.

As for SG&A expenses other than R&D expenses, co-promotion fees will increase because sales of Forxiga tablets will increase. We also expect an increase by JPY10.9 billion to JPY88 billion for investments in IT and digital-related infrastructure, as well as for the development and strengthening of our US business.

No significant other income or expenses are currently expected for FY2022.

The assumed exchange rate for FY2022 is JPY110 to 1USD. The sensitivity, or rather, the structure of the Company is such that a JPY1 depreciation will result in an increase of JPY800 million in profit.

## Profit for the Period /Owners of the Parent Company (Forecasts)

Profit for the Period (Owners of the Parent Company)	YoY Change
¥ 110.0 billion	+ 36.6 %

### Income tax expense

¥ 35.9 billion ( YoY Change + 47.5 % )

### (Major change factors)

Increase in profit before tax	¥ 41.0 billion
Increase in corporate tax	¥ 11.6 billion

Profit for the period is projected to increase by JPY29.5 billion, or 36.6%, to JPY110 billion.

The annual dividend was JPY56 per share for FY2021 and is expected to increase by JPY10 to JPY66 per share.

This is my report on our business performance.

# Reduction plan of Cross-shareholdings

(published on November 1, 2021)

## ➤ Reduction plan

- Period: October 2021 to March 2025 (3 and a half years)
- Details of reduction plan:  
30% reduction from the end of September 2021 (141.8 billion yen)  
※The company plans to reduce its cross-shareholdings to less than 20% of its net assets by the end of March 2022.

	End of September 2021	Expected at the end of March 2025	Plan	
			Reduction	Reduction rate
Market price at the end of September 2021	¥ 141.8 bil	¥ 99.3 bil	¥ 42.5 bil	-30.0%

## ➤ Medium-to long-term plan

We aim for the ratio of strategic shareholdings to net assets (on a balance sheet basis) to be less than 10%.

I will continue with an explanation of the status of reduction of cross-shareholdings.

By September last year, we had completed the first phase of our plan to reduce cross-shareholdings by about 30%. Then, after October, we started the second phase, a three-and-a-half-year period, with the goal of reducing a further 30%. The market price was JPY141.8 billion, and based on the price, our goal is to reduce it to JPY99.3 billion over three and a half years or reduce by JPY42.5 billion.

## Status of reduction of Cross-shareholdings

	End of September 2021	End of March 2022	Reduction*	Reduction rate
<b>Market price at the end of September 2021</b>	<b>¥ 141.8 bil</b>	<b>¥ 124.5 bil</b>	<b>¥ 17.3 bil</b>	<b>-12.2%</b>

\*Contain the growth investments after October 2021

(Reference )

	End of September 2021	End of March 2022	Change	Ratio of Cross-shareholdings to net assets
<b>Balance sheet accounting amount</b>	<b>¥ 141.8 bil</b>	<b>¥ 114.0 bil</b>	<b>¥ 27.9 bil</b>	<b>17.2%</b>

At the end of the six-month period, we reduced by JPY27.9 billion. The initial plan was to reduce 30%, but we have now reduced 12.2%, or the progression rate is approximately 40%, in six months. JPY124.5 billion is the current cross-shareholdings in the current market price.

We made a start, trying to keep the ratio to net assets below 20% in March this year, in part because of a request by our advisory firm in connection with the voting rights. As a result, we were able to advance to 17.2%. We will continue to work on the request of 10% or less

# ONO's History Timeline

A 300-Plus-Year History of Full Commitment to the Pharmaceutical Business



Since our foundation in 1717, we have made progress for more than 300 years in our commitment to relieving pain of patients and focus on their health improvement. "We believe there are new drugs that only we can develop." We still continue to unite our efforts in meeting the challenge of discovering our own innovative drugs.

※Only for FY1989 (ended on March31, 1990), the fiscal results are for four months from December 1, 1989 to March 31, 1990



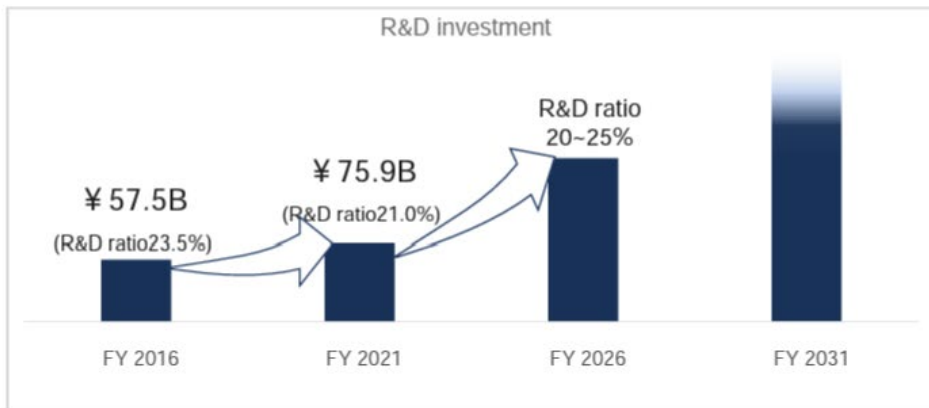
Finally, I would like to talk here about how Ono will continue to grow in the future. Here is "Ono's History Timeline."

We have been in business for over 300 years, but we have not been able to grow very much, and we are currently on a growth trajectory, thanks in part to the success of Opdivo, around the time when we celebrated our 300th anniversary.

From our point of view, each company has its own period of growth, and Ono has not been able to reach that period for a long time, but I feel that now is the right time for us. We want to make sure that we will continue to grow well.

# Key investment areas for growth

<p><b>Strengthen R&amp;D investment</b></p> <p>Approx. ¥ 600B (from FY 2022 to 2026) Additional strategic investment over ¥ 250B</p>	<p><b>Promote unique drug discovery research</b></p> <p>Strengthen pipeline</p>	<p><b>To the global market</b></p> <p>Global development Direct sales in Europe and the US</p>
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I will add a few words about the title, "Investment Strategy to Achieve Growth." First of all, it is a prerequisite to create unique and innovative new drugs.

There are two patterns. One is in-house development, where a product is created from the Company's own research laboratories, or development through joint research with academia from the research and drug discovery stages. Then there is the licensing activity, where Ono has been successful. The middle square shows the two pillars that all companies will naturally work on, and this is strengthening pipeline.

We have created and launched drugs in domestic market so far. However, we are now at the stage of implementing a new policy that we will do this at once globally. We started rather late -- Many Japanese companies have already been working on it -- but we do it this moment.

If the Japanese market size is 1, the US market is 5, and the European market is 2. Then, for example, a new drug that creates a revenue of JPY30 billion in Japan can generate JPY150 billion in the US, JPY60 billion in Europe, and eight times the revenue of the Japanese market. If we are able to use this revenue as a source of new R&D investment, then Ono will be able to grow further.

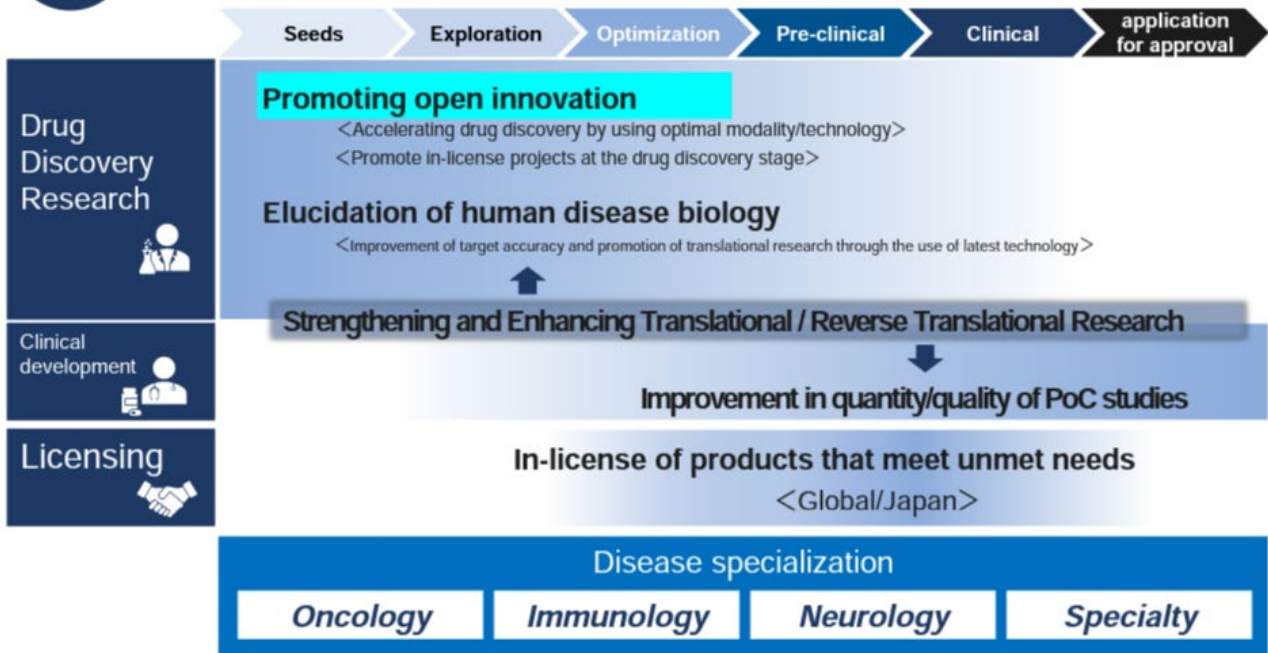
As for a big cliff of Opdivo, we will meet a big cliff at the time when about two-thirds of our sales, including royalties, will come from Opdivo, and so it will be a big cliff. In order to fill this cliff in that way, we would like to strengthen our investment in R&D, in addition to our regular investment in R&D.

We have not disclosed a mid-term business plan, but we have been proceeding with a five-year, three-phase mid-term plan starting from 2017, and this fiscal year marks the start year of the second phase.

# Strengthen development pipeline by promoting unique drug discovery research



Accelerate the development of new drugs that will change the world in collaboration with top scientists



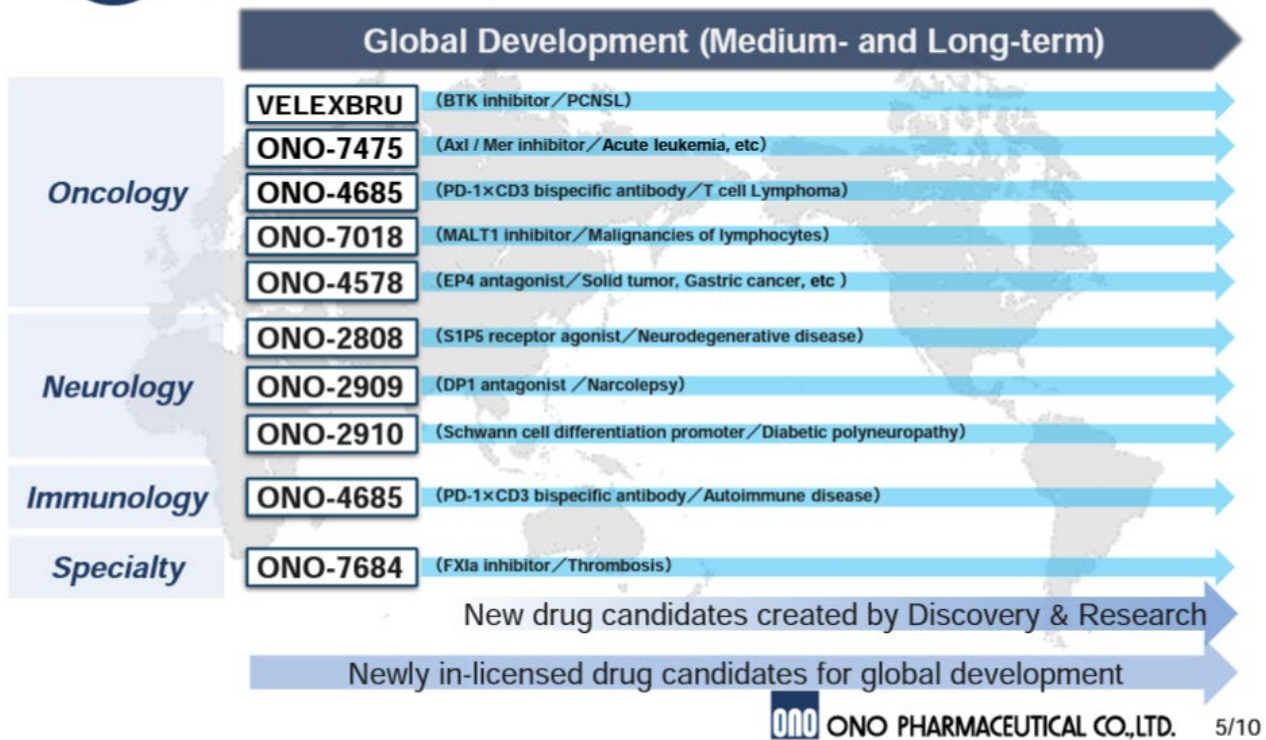
We are now focusing, as our strategic disease area, on Oncology, Immunology, Neurology, and Specialty.

We would also like to further advance open innovation, which has been our forte, even more aggressively. Beyond that, we are thinking of in-license, purchase of technology and compounds, or M&A of venture companies as further potentials.

# To the global market Continued expansion of global pipeline

Vision

Aiming to be a Specialty Pharma capable of competing globally, marketing new drugs in Europe and the US



We have now started global development of the compounds shown here. Currently, we are expecting Velexbu (ONO-4059) to be the first drug for which we will get approval in the US and Europe to sell by ourselves.

For other compounds, they are at Phase I or II, there are still some hurdles to establish PoC in the future. In addition, there are several compounds at a stage just before a compound number is assigned, which we will introduce to you all when that stage arrives.



# License/Discovery Alliance Partners

Cancer	Cancer Supportive Care	Immunology	Neurology	Specialty	
 <b>KYPROLIS® / Carfilizomib</b> MM (Japan)  <b>REPURE THERAPEUTICS</b> Polθ inhibitor Cancer  <b>GILEAD</b> <b>ONO-7913 / Magrolimab</b> Cancer (Japan, South Korea, Taiwan and ASEAN countries)  <b>ribon therapeutics</b> <b>ONO-7119 / RBN-2397</b> Cancer (Japan, South Korea, Taiwan and ASEAN countries)  <b>NUMA8 Drug Innovators</b> Biologics  <b>CANCER RESEARCH UK</b> Small molecule	 <b>BRAFTOVI® / Encorafenib</b> <b>MEKTOVI® / Binimetinib</b> mBRAF melanoma / CRC (Japan, South Korea)  <b>RAFAEL</b> <b>ONO-7912 / Devimistat</b> Cancer (Japan, South Korea, Taiwan and ASEAN countries)  <b>Chordia Therapeutics</b> <b>ONO-7018 / CTX-177</b> Cancer (Worldwide)  <b>Fote THERAPEUTICS</b> Biologics  <b>LifeArc</b> Biologics	<b>Merck</b> <b>EMEND®</b> <b>PROEMEND®</b> CINV (Japan)  <b>HELSINN</b> Building quality cancer care together <b>ADLUMIZ® / Anamorelin</b> Cancer anorexia / Cachexia (Japan, South Korea and Taiwan) <b>Bausch Health</b> <b>DEMSE® / Metyrosine</b> Pheochromocytoma (Japan)	 Bristol Myers Squibb® <b>ORENCIA®</b> RA (Japan) <b>Merus</b> Biologics  <b>ARIA PHARMACEUTICALS</b> AI-Drug <b>Vanderbilt Univ.</b> Ion Channel	 <b>NOVARTIS</b> <b>RIVASTACH® / EXELON®</b> AD (Japan)  <b>Bial</b> <b>ONGENTYS® / Opicapone</b> PD (Japan)  <b>SK biopharmaceuticals</b> <b>ONO-2017 / Cenobamate</b> Epilepsy (Japan)  <b>neurimmune</b> Human antibody therapeutics Biologics	 <b>AMGEN®</b> <b>PARSABIV® / Etecalcetide</b> SHPT (Japan)  <b>SEIKAGAKU CORPORATION</b> <b>JOYCLU® / SI-613</b> OA (Japan)  <b>DOMAİN THERAPEUTICS</b> Université de Montréal GPCR
<b>Undisclosed therapeutic area</b>					
 <b>Ligand®</b> Biologics  <b>MiraBiologics</b> Biologics  <b>SCHRÖDINGER.</b> Computational Chemist <sup>™</sup>  <b>PeptiDream</b> Peptide Drug Discov.  <b>healx</b> AI Drug Discov.  <b>IKTOS</b> Artificial intelligence Drug Discov. Design AI Drug Discov.					

This table shows our joint research and partnerships to date. Ono is still conducting more than 200 joint research projects. More than one-third are conducted overseas.

We will proceed by using our imagination and connoisseurship, although we will not know if we have it or not until we try.

# To the global market

## Establish the organizational structure and system in US and Europe

**Accelerate the construction of a self-sales organization in the US  
taking the launch of VELEXBRU into account**  
**Promote development and establish a self-sales organization in Europe**

ONO PHARMA USA 

Approx. 60 people at present → After 5 years, expand to more than 120 people having a self-sales organization



ONO PHARMA UK 

Approx. 50 people at present. Consider establishing a self-sales organization including marketing and sales etc. under the progress of development in Europe



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We are currently in the process of establishing development and sales bases in US and UK. Some of them have been established and are being enhanced, but we are currently creating the divisions I mentioned. Eventually, a commercial and sales department will be established.

# Qualitative Objectives

	FY2022~2026
Revenue CAGR※	late-single digit
R&D ratio	Maintaining 20-25%
Operating profit margin	Maintaining over 25%

※ Comparison with FY2021



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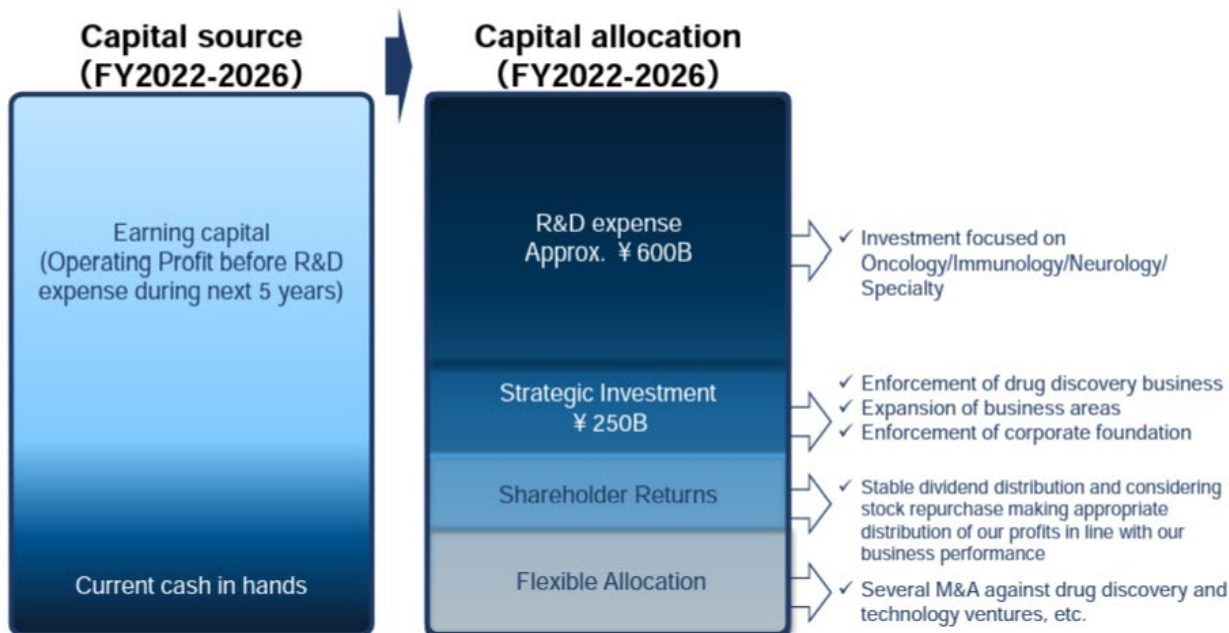
I will talk qualitatively how much growth we are projecting. We expect the late-single-digit average growth rate in the next five years.

Then, we would like to proceed with an R&D expenses ratio of about 20% to 25%, but we believe that we may temporarily implement a more aggressive R&D investment to get through the Opdivo cliff.

The operating profit margin also changes in conjunction with such expenses, but we have set a qualitative goal of maintaining an operating profit margin of 25% or higher.

# Investment policy for the next 5 years

Focus on R&D to overcome upcoming patent cliffs and achieve sustainable growth



In the process of new growth, cash will continue to flow out, and our first priority is to allocate it to R&D investments. Then, there may be investments in ventures related to this, and we would like to use the cash for our digital-related project, overseas operation and expansion of sales network.

As I mentioned before, we will invest JPY150 to 200 billion to strengthen drug discovery, and another JPY30 to 50 billion in business areas such as overseas, digital, and new healthcare-related businesses. In addition to the regular R&D investment, we expect to invest about JPY250 billion over the next five years.

In addition, we would like to make sure to return profits to shareholders.

This is a rough report and explanation on Ono's growth strategy for the next few years.

## **Development pipeline**

**Idemitsu:** First of all, for the materials, starting from page three to seven of the financial report, we describe the main progress of product development. Then, the supplemental material for the financial report shows the main progress of product development on pages 7 to 10. At this time, we will first use this supplemental material for the financial report to explain updates from 3Q of FY2021.

The materials are organized in the following order: first, oncology, and then non-oncology. Furthermore, they are listed in the order of the advanced development stage, i.e., Approved, Filed, Phase III, Phase II, and Phase I.

## I. Main Status of Development Pipelines (Oncology)

As of April 26, 2022

### <Approved>

\*) : "In-house" compounds include a compound generated from collaborative research.

Product Name / Development Code / Generic Name	Classification	Target Indication / Pharmacological Action	Dosage Form	Area	In-house*) / In-license
Velexbru Tablets / Tirabrutinib Hydrochloride	New chemical entities	Primary central nervous system lymphoma *1 / BTK inhibitor	Tablet	Taiwan	In-house
Opdivo Intravenous Infusion / Nivolumab	Additional indication	Urothelial carcinoma *2	Injection	Japan	In-house (Co-development with Bristol-Myers Squibb)
Opdivo Intravenous Infusion / Nivolumab	Additional indication	Colorectal cancer *3	Injection	S. Korea	In-house (Co-development with Bristol-Myers Squibb)

Changes from the announcement of financial results for the third quarter of the fiscal year ended March 2022

\*1: An application for Velexbru Tablets (BTK inhibitor) was approved in Taiwan for the treatment of recurrent or refractory primary central nervous system lymphoma.

\*2: An application for Opdivo was approved in Japan for the adjuvant treatment of urothelial carcinoma.

\*3: An application for the combination therapy of Opdivo and Yervoy was approved in South Korea for the treatment of microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer.

### <Filed>

\*) : "In-house" compounds include a compound generated from collaborative research.

Product Name / Development Code / Generic Name	Classification	Target Indication / Pharmacological Action	Dosage Form	Area	In-house*) / In-license
Yervoy Injection * / Ipilimumab	Additional indication	Esophageal cancer	Injection	Japan	In-license (Co-development with Bristol-Myers Squibb)

★: Combination with Opdivo.

### <Clinical Trial Stage>

<Opdivo>						
*) : "In-house" compounds include a compound generated from collaborative research.						
Product Name / Development Code / Generic Name	Classification	Target Indication / Pharmacological Action	Dosage Form	Area	Phase	In-house*) / In-license
Opdivo Intravenous Infusion / Nivolumab	Additional indication	Hepatocellular carcinoma	Injection	Japan S. Korea	III	In-house (Co-development with Bristol-Myers Squibb)
	Additional indication	Ovarian cancer	Injection	Japan S. Korea Taiwan	III	In-house (Co-development with Bristol-Myers Squibb)
	Additional indication	Bladder cancer	Injection	Japan S. Korea Taiwan	III	In-house (Co-development with Bristol-Myers Squibb)
	Additional indication	Prostate cancer	Injection	Japan S. Korea Taiwan	III	In-house (Co-development with Bristol-Myers Squibb)
	Additional indication	Pancreatic cancer	Injection	Japan S. Korea Taiwan	II	In-house (Co-development with Bristol-Myers Squibb)
	Additional indication	Virus positive / negative solid carcinoma	Injection	Japan S. Korea Taiwan	I / II	In-house (Co-development with Bristol-Myers Squibb)

First, the oncology area.

The top the table on page seven shows approved development products. Velexbru was approved in Taiwan this February for primary central nervous system lymphoma.

Below this, Opdivo received an approval in Japan this March for the adjuvant treatment of urothelial cancer.

Further down, this February, Opdivo was approved in South Korea in combination with Yervoy for the treatment of microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer.

<b>&lt;Others&gt;</b>						
*) : "In-house" compounds include a compound generated from collaborative research.						
Product Name / Development Code / Generic Name	Classification	Target Indication / Pharmacological Action	Dosage Form	Area	Phase	In-house*) / In-license
ONO-7913 / Magrolimab	New chemical entities	TP53-mutant acute myeloid leukemia / Anti-CD47 antibody	Injection	Japan	III	In-license (Gilead Sciences, Inc.)
	New chemical entities	Acute myeloid leukemia / Anti-CD47 antibody	Injection	S. Korea Taiwan	III	In-license (Gilead Sciences, Inc.)
Braftovi Capsules / Encorafenib	Additional indication	Thyroid cancer / BRAF inhibitor	Capsule	Japan	II	In-license (Pfizer Inc.)
Mektovi Tablets / Binimetinib	Additional indication	Thyroid cancer / MEK inhibitor	Tablet	Japan	II	In-license (Pfizer Inc.)
ONO-4059 / Tirabrutinib Hydrochloride	New chemical entities	Primary central nervous system lymphoma / BTK inhibitor	Tablet	USA	II	In-house
ONO-7475	New chemical entities	Acute leukemia / Axl/Mer inhibitor	Tablet	USA	I / II	In-house
	New chemical entities	EGFR-mutated non-small cell lung cancer / Axl/Mer inhibitor	Tablet	Japan	I	In-house
ONO-7913 / Magrolimab	New chemical entities	Solid tumor / Anti-CD47 antibody	Injection	Japan	I	In-license (Gilead Sciences, Inc.)
	New chemical entities	Myelodysplastic syndromes (MDS) / Anti-CD47 antibody	Injection	Japan	I	In-license (Gilead Sciences, Inc.)
ONO-4578	New chemical entities	Hormone receptor-positive, HER2-negative breast cancer / Prostaglandin receptor(EP4) antagonist	Tablet	Japan	I	In-house
ONO-4685	New chemical entities	T-cell lymphoma / PD-1 x CD3 bispecific antibody	Injection	USA	I	In-house

★: Combination with Opdivo.

Changes from the announcement of financial results for the third quarter of the fiscal year ended March 2022

\* With regard to Opdivo, phase II for the treatment of biliary tract cancer was conducted in Japan, but the project was removed from the pipeline as the application was abandoned due to strategic reasons.

\* Phase III of combination therapy for Opdivo and ONO-7701 (IDO1 inhibitor) for the treatment of bladder cancer was discontinued in Japan, South Korea and Taiwan due to strategic reasons.

\* Phase I/II of combination therapy for Opdivo and ONO-7807 (anti-TIM-3 antibody) for the treatment of solid tumor was discontinued in Japan due to strategic reasons.

\* Phase I of combination therapy for Opdivo and ONO-7911 (PEGylated IL-2) for the treatment of solid tumor was discontinued in Japan due to strategic reasons.

\* Phase III of ONO-7912 (cancer metabolism inhibitor) for the treatment of pancreatic cancer and phase III for the treatment of acute myeloid leukemia conducted by Rafael Pharmaceuticals, Inc. were not able to confirm anticipated efficacy. Based on these results, phase I for the treatment of pancreatic cancer in Japan was discontinued.

In the case of clinical development of the oncology drugs in the same indication, the most advanced clinical phase is described.

With regard to Opdivo, we had been conducting a Phase II study for biliary tract cancer, but we decided to abandon the application with its study result and removed it from the development pipeline.

In addition, we discontinued four other projects. First, the development of ONO-7701, an IDO1 inhibitor, which was in Phase III for bladder cancer, was discontinued for strategic reasons.

Next is ONO-7807, an anti-TIM-3 antibody, which was in Phase I/II for solid tumors in combination with Opdivo, but its development was also discontinued for strategic reasons.

We also suspended the development of ONO-7911, a PEGylated IL-2 antibody, in Phase I for solid tumors in combination with Opdivo in Japan for strategic reasons.

The expected efficacy of ONO-7912, a cancer metabolism inhibitor, was not confirmed in the Phase III study conducted for pancreatic cancer by Rafael, from which we in-licensed. So, we discontinued Phase I study conducted in Japan for pancreatic cancer.

## II. Main Status of Development Pipelines (Areas other than Oncology)

As of April 26, 2022

< Filed >

\*) : "In-house" compounds include a compound generated from collaborative research.

Product Name / Development Code / Generic Name	Classification	Target Indication / Pharmacological Action	Dosage Form	Area	In-house*) / In-license
Onoact for Intravenous Infusion / Landiolol Hydrochloride	Additional indication for pediatric use	Tachyarrhythmia in low cardiac function / Short-acting selective $\beta_1$ blocker	Injection	Japan	In-house

<Clinical Trial Stage>

\*) : "In-house" compounds include a compound generated from collaborative research.

Product Name / Development Code / Generic Name	Classification	Target Indication / Pharmacological Action	Dosage Form	Area	Phase	In-house*) / In-license
ONO-2017 / Cenobamate	New chemical entities	Primary generalized tonic- clonic seizures / Inhibition of voltage-gated sodium currents/positive allosteric modulator of GABA <sub>A</sub> ion channel	Tablet	Japan	III	In-license (SK Biopharmaceuticals)
	New chemical entities	Partial-onset seizures / Inhibition of voltage-gated sodium currents/positive allosteric modulator of GABA <sub>A</sub> ion channel	Tablet	Japan	III	In-license (SK Biopharmaceuticals)
Velexbru Tablets / Tirabrutinib Hydrochloride	Additional indication	Pemphigus *4 / BTK inhibitor	Tablet	Japan	III	In-house
ONO-2910	New chemical entities	Diabetic polyneuropathy / Schwann cell differentiation promoter	Tablet	Japan	II	In-house
ONO-4685	New chemical entities	Autoimmune disease / PD-1 x CD3 bispecific antibody	Injection	Japan Europe	I	In-house
ONO-7684	New chemical entities	Thrombosis / FXIa inhibitor	Tablet	Europe	I	In-house
ONO-2808	New chemical entities	Neurodegenerative disease / S1P5 receptor agonist	Tablet	Japan Europe	I	In-house
ONO-2909	New chemical entities	Narcolepsy / Prostaglandin receptor(DP1) antagonist	Tablet	Japan	I	In-house
Velexbru Tablets / Tirabrutinib Hydrochloride	Additional indication	Systemic sclerosis / BTK inhibitor	Tablet	Japan	I	In-house

Changes from the announcement of financial results for the third quarter of the fiscal year ended March 2022

\*4: Phase III of Velexbru Tablets (BTK inhibitor) was initiated in Japan for the treatment of pemphigus.

\* Phase II of Joyclu Intra-articular Injection (hyaluronic acid-NSAID) for the treatment of enthesopathy was conducted in Japan, but the project was removed from the development pipeline as it was not possible to achieve the primary endpoint.

Regarding the progress of products under development in non-oncology area, the second from the top of the table on page 10, Velexbru has entered Phase III for pemphigus in Japan.

Also, as you will see in the note below, we removed from the pipeline Joyclu, which was in Phase II study for enthesopathy, because it did not achieve the primary endpoint.



## Plan for Submissions in Japan

		OPDIVO	Non-OPDIVO Oncology	Non-Oncology	OPDIVO M=Mono C=Combo
<p>ONOACT&lt;Pediatric&gt; [Tachyarrhythmia in low cardiac function] Oct 2021</p>					
<p>[Cancer of unknown primary] investigator-initiated trial Apr 2021 (M)</p>					
<p>[1L-NSCLC] with Chemo and AVASTIN ONO-4538-52 Jun 2021 (Revision of labeling) (C)</p>					
<p>[1L-Esophageal cancer] with YERVOY / with Chemo CheckMate-648 Sep 2021 (C)</p>	<p>[Neoadjuvant-NSCLC] with Chemo CheckMate-816 Apr 2022 (C)</p>	<p>[Adjuvant-Gastric cancer] with Chemo ATTRACTION-5 (C)</p>	<p>[Adjuvant-RCC] with YERVOY CheckMate-914 (C)</p>	<p>[Adjuvant-Hepatocellular carcinoma] CheckMate-9DX (M)</p>	<p>[Perioperative Bladder cancer] With Chemo ONO-4538-86 (C)</p>
<p>[1L-Urothelial cancer] with YERVOY / with Chemo CheckMate-901 (C)</p>					
<p>2021 (results)</p>	<p>2022 (1H)</p>	<p>2022 (2H)</p>	<p>2023</p>		

As of Apr 26, 2022

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We will continue an explanation using the slide on the progress of the development pipeline, which can be found on our website. Please see the plan for submissions on page two.

First, regarding the results for 2021. We received approval for Opdivo for cancer of unknown primary in December last year, and for non-small cell lung cancer, we revised the package insert of Opdivo in June last year for the combination with Avastin (bevacizumab) for the first-line treatment of non-small cell lung cancer.

Next is the first half of FY2022. As for the neo-adjuvant treatment of non-small cell lung cancer, we submitted the application in April this year.

In the second half of FY2022, we will have the study results of Opdivo for adjuvant treatment of gastric cancer, renal cell carcinoma, and hepatocellular carcinoma. If the results are confirmed on schedule and in line with expectations, their applications will be filed as soon as the results are available. An application for the first-line treatment of urothelial carcinoma is also scheduled for this period.

Last, on the far right. The schedule for FY2023 is shown. As for Opdivo, the results of preoperative and postoperative adjuvant therapy for bladder cancer, as well as for the first-line treatment of MSI-H colorectal cancer will be available soon, and if the results meet our expectations, we will submit applications in sequence.

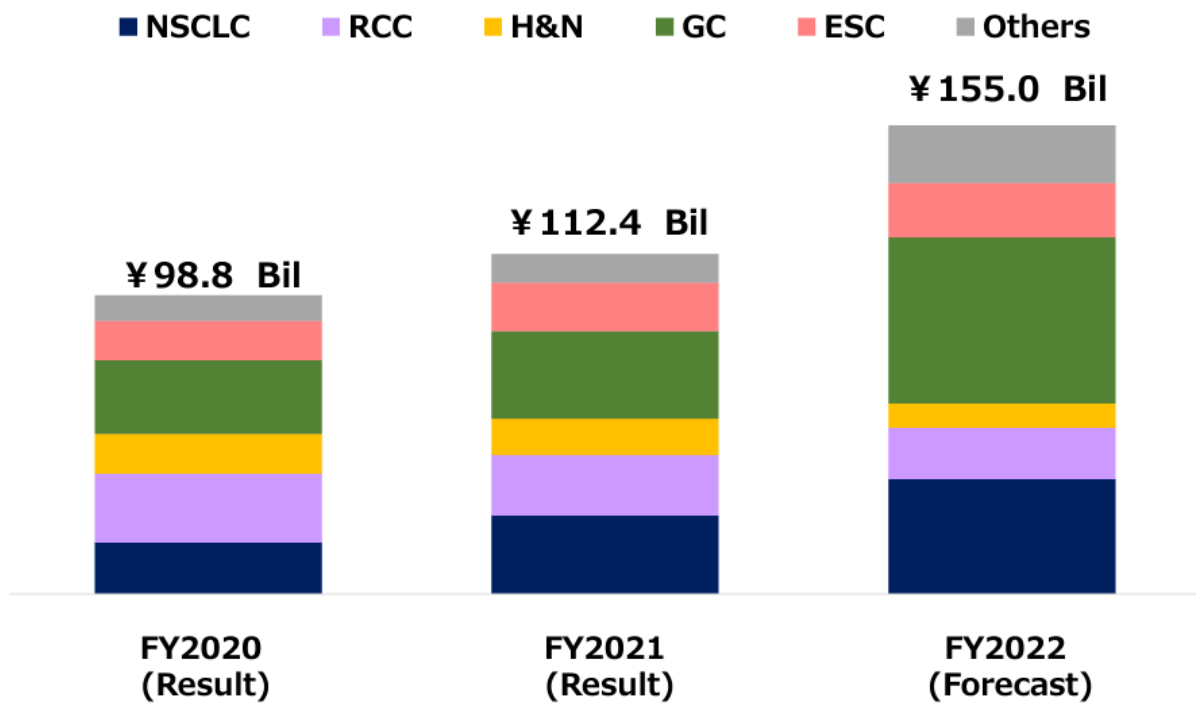
Then, regarding Braftovi/Mektovi, we will have the results for the second-line treatment of BRAF mutation-positive thyroid cancer.

We also plan to file Kyprolis for a once-weekly regimen KRd of Kyprolis, Revlimid and dexamethasone for the second-line treatment of multiple myeloma in 2023 based on the results of ongoing studies.

**Trend of Opdivo:**

**Takahagi:** I would like to introduce the general status of trend of Opdivo and the status by cancer type.

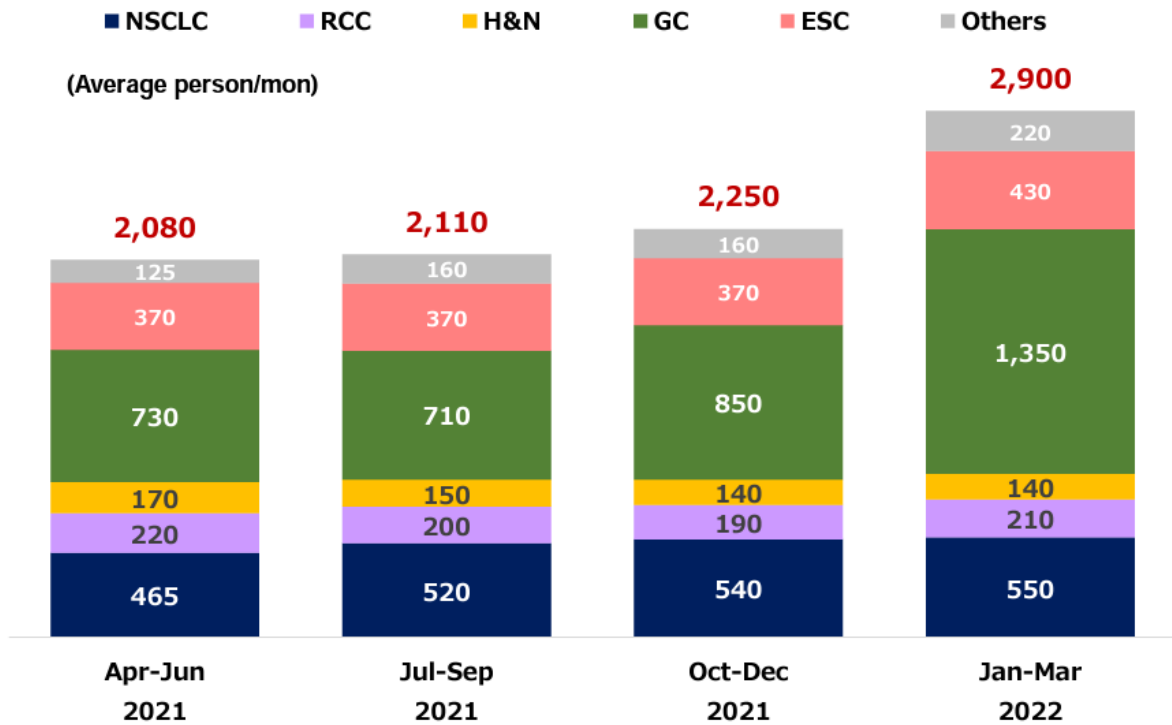
# Sales Trend of Opdivo by Each Cancer



Source: Estimation from external and internal data

**Takahagi:** First, we have Opdivo sales trend. Sales was JPY112.4 billion in the FY2021, and is forecast to reach JPY155 billion in the FY2022.

# Number of Patients Newly Prescribed with Opdivo by Each Cancer (Estimation)



Source: Estimation from external and internal data

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Bar graphs on number of patients newly prescribed with Opdivo by cancer type show average person/month quarterly from April-June 2021 to January to March 2022.

Although this is only an estimate, during the period from January to March 2022, 1,350 new prescriptions were for gastric cancer, 430 for esophageal cancer, and 550 for lung cancer.

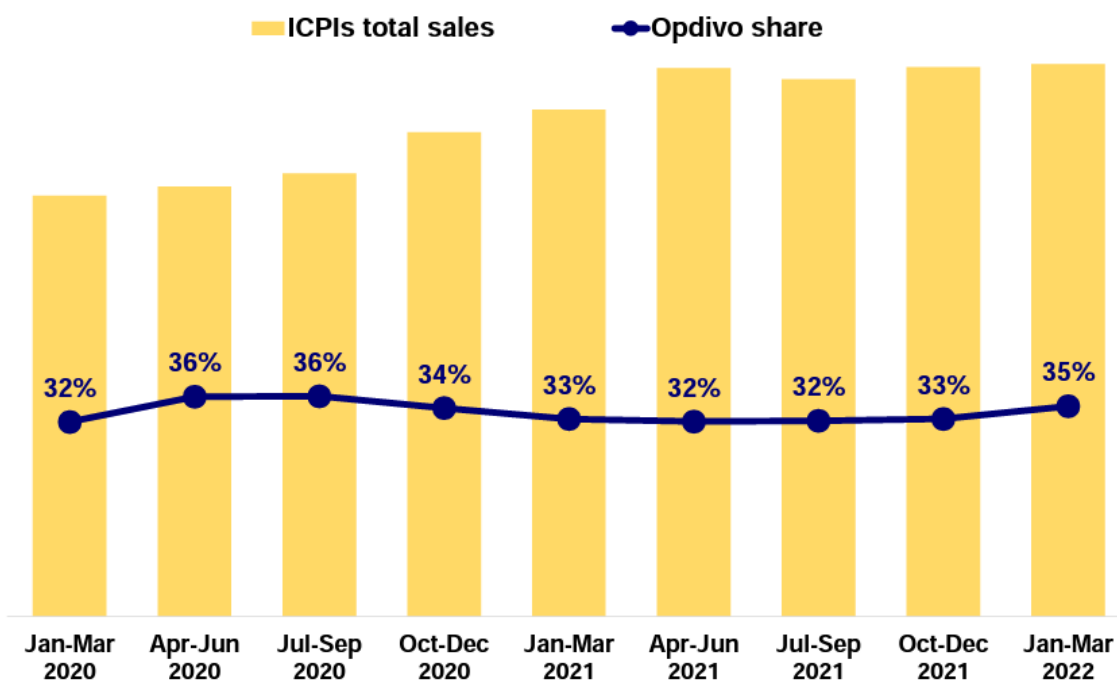
For the 1L treatment of lung cancer, which was approved in November 2020, more than 5,000 new prescriptions have been confirmed as of the end of March since the approval. In addition, we have confirmed about 420 prescriptions in the 1L treatment during the period from January to March this year.

In addition, the number of newly prescribed patients for the 1L treatment of gastric cancer, which was approved in November 2021, has exceeded 2,500 cases by the end of March since the approval. The average number of the 1L treatment cases for the period from January to March is expected to be approximately 670.

Furthermore, we expect 345 new prescriptions for adjuvant therapy of esophageal cancer, which was approved at the end of November 2021, by the end of March, and the average number of cases of the adjuvant treatment during the period from January to March is about 100 per month.

As for cancer of unknown primary, which was approved at the end of December 2021, the total number of newly prescribed cases is expected to reach 200 by the end of March.

# Trend of total sales of ICPIs and Opdivo share



Source: External data



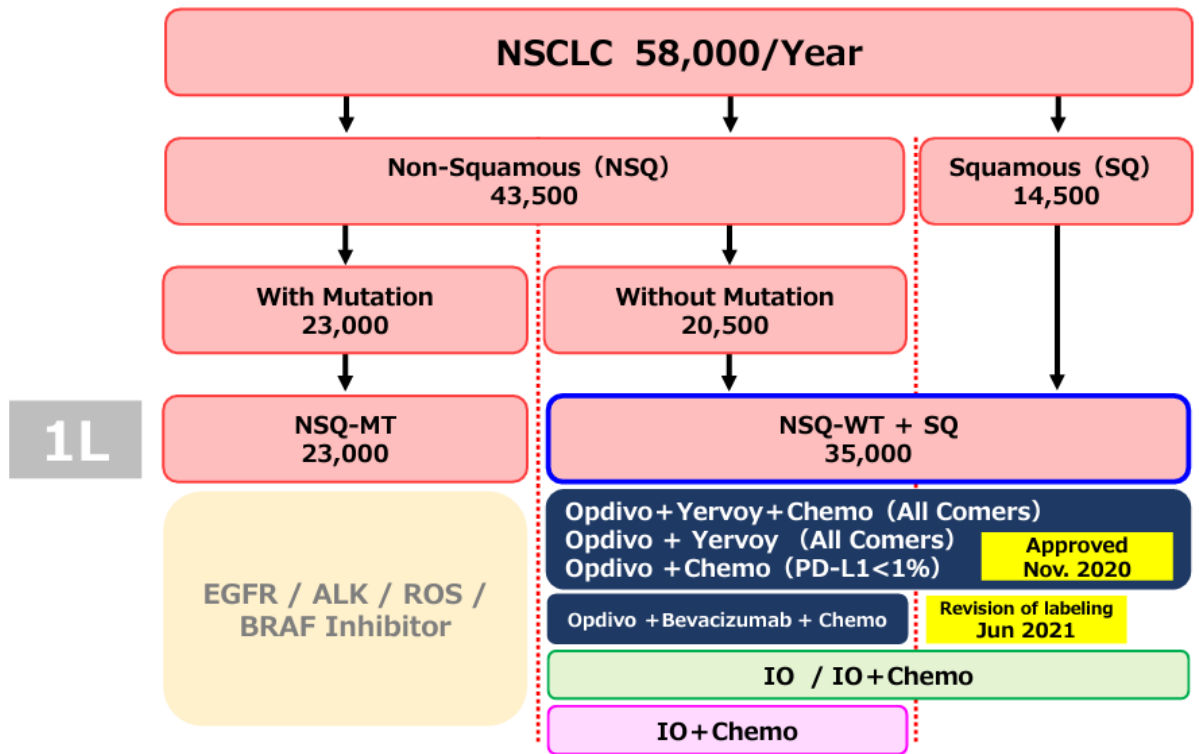
Here is the trend of total sales of all immune checkpoint inhibitors launched in Japan and Opdivo's market share.

The yellow bar graph shows the total sales of all immune checkpoint inhibitors and the dark blue line graph shows the share of Opdivo.

Overall sales of immune checkpoint inhibitors are increasing steadily. Despite the NHI price revision in FY2021, sales of all five products grew, with Opdivo's market share rising two percentage points, which we believe is a solid performance.

# Number of NSCLC\* Patients per year in Japan

\*: Unresectable Advanced or Recurrent NSCLC



Estimation based on internal survey (2021)

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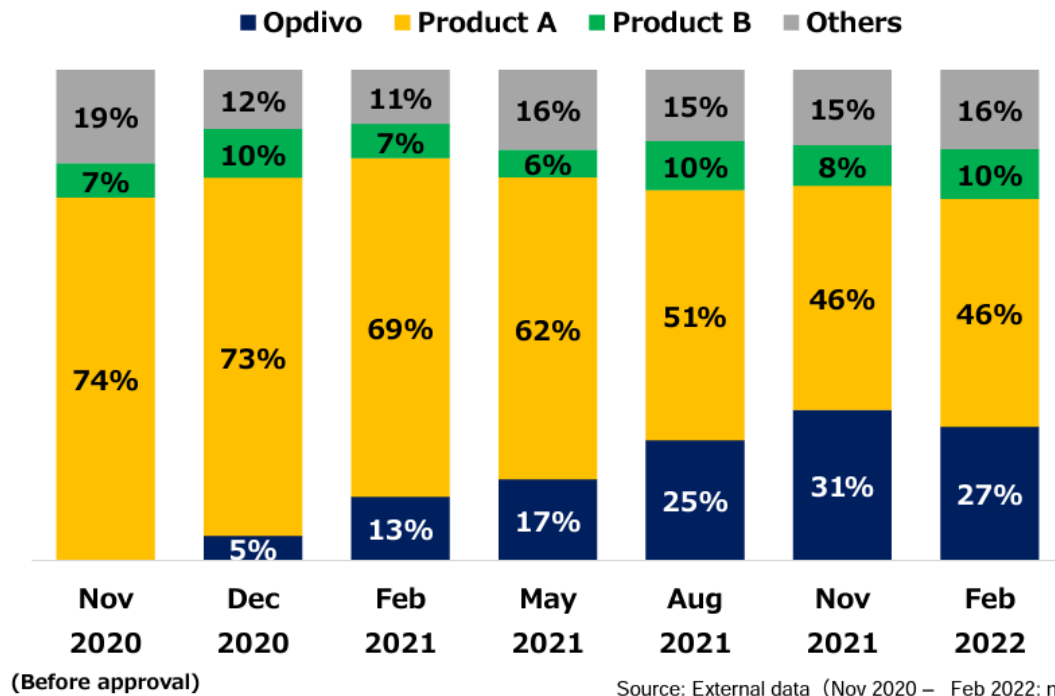
From here, we would like to explain it by type of cancer.

First, the lung cancer area. In the area of non-small cell lung cancer, we expect 35,000 patients per year to be eligible for the immune checkpoint inhibitors. This area is a very large market potential.

Currently, competition is very tough, and Opdivo entered the 1L therapy market in combination with Yervoy in November 2020, and was added in combination with bevacizumab in June 2021.

# Prescription Ratio in Patients Newly Treated for 1L NSCLC

※Patients starting 1L treatment within the last 1 month (Except Driver Mutation)



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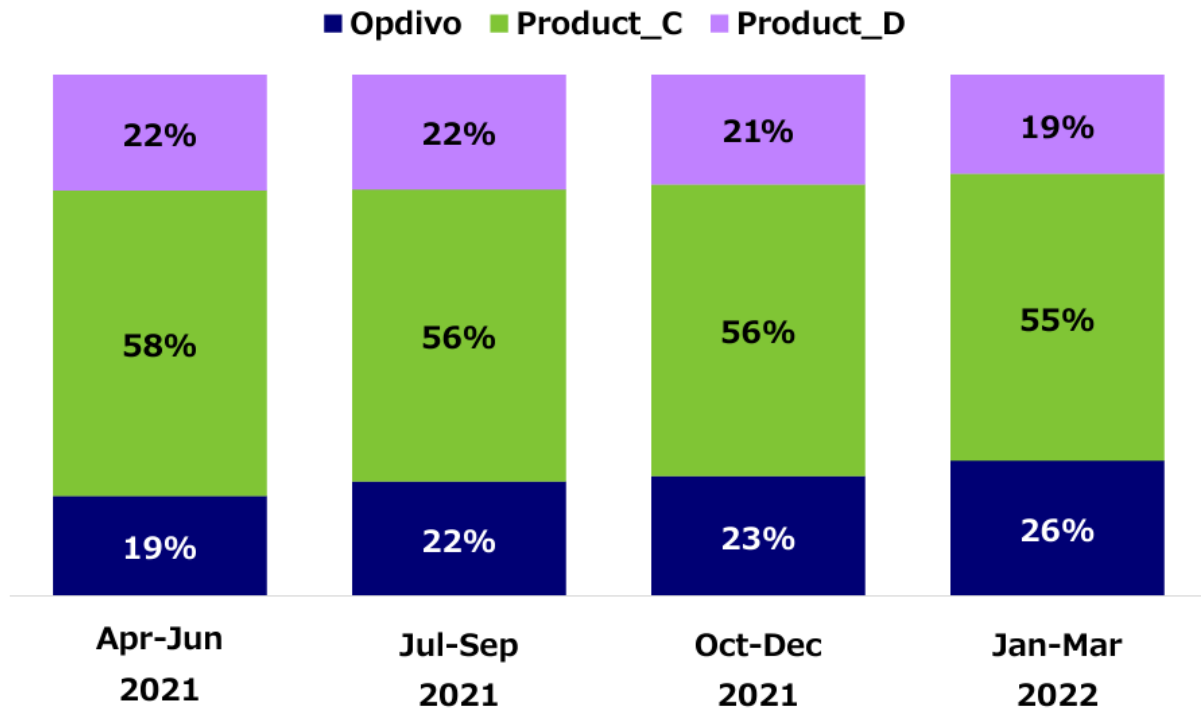
The table shows the change in prescription ratio in newly treated for the 1L treatment of lung cancer.

Opdivo's share of new patient prescriptions was 27% as of February. The evaluation of the Opdivo/Yervoy IO/IO combination therapy, which has not yet been available at the competitors, is gradually expanding, and we have confirmed 420 new prescriptions on average for the January-to-March period.

In the lung cancer field, PD-L1 is measured and the measurement value is divided into three groups; negative cases, weakly positive cases (1% to 49%) and strongly positive cases (50% or more). Each regimen is designed and administered for these groups accordingly. We are developing our activities with a particular focus for Opdivo on PD-L1 negative cases and 1% to 49% weakly positive cases.

In PD-L1 negative cases, the Opdivo combination regimen is already the top regimen in terms of new prescription share. However, prescriptions for this 1% to 49% market are still sluggish and stagnant, with a 27% share in the 1L treatment, and we would like to continue to promote the significance of IO/IO combination therapy.

# Sales Ratio of ICPIs in NSCLC (Estimation)



Source: External data

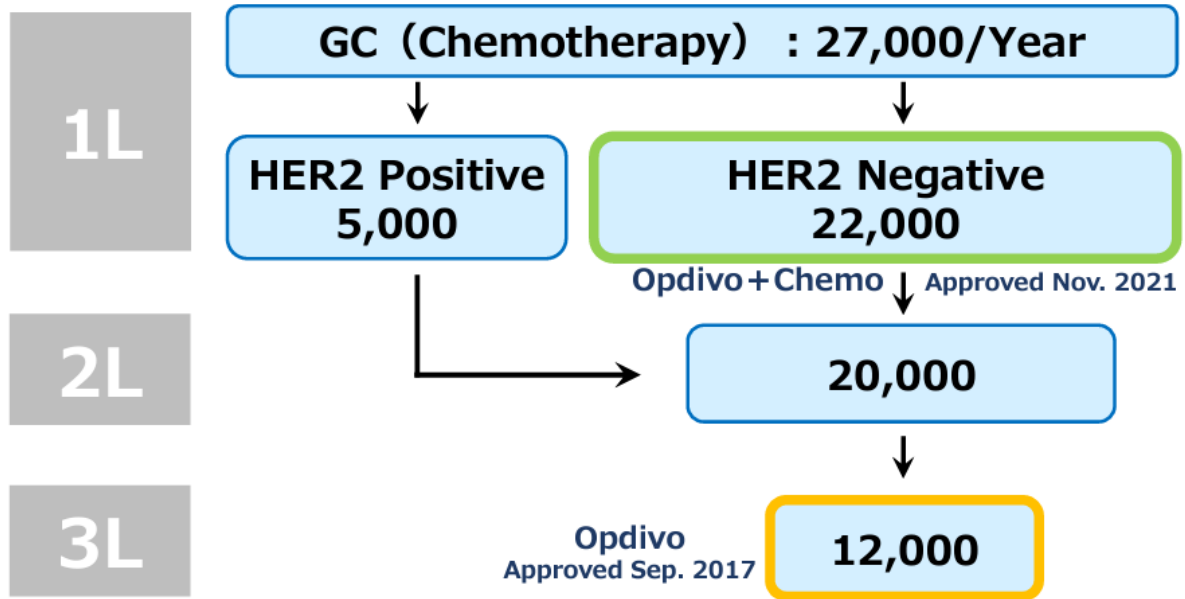
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This shows the sales ratio of immune checkpoint inhibitors for 1L and 2L treatments of non-small cell lung cancer. Data are shown quarterly. We are currently expanding the 1L treatment share, so the percentage has risen to 26%, and we will continue to aim for even higher percentages in the future.



# Number of GC\* Patients per year in Japan

\* : Unresectable Advanced or Recurrent GC



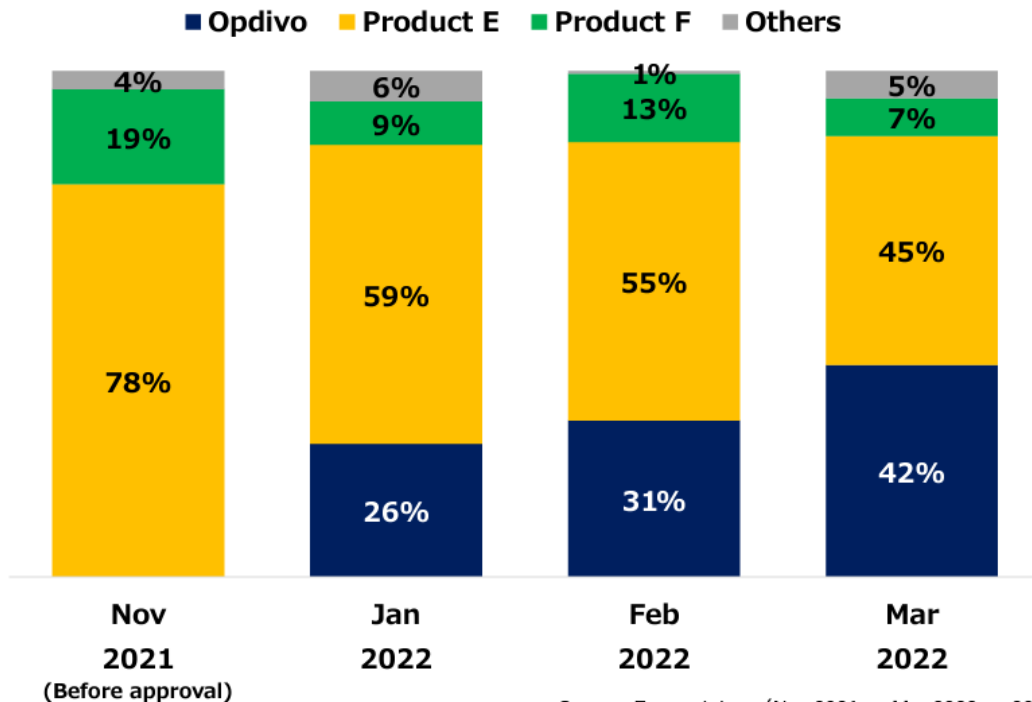
Estimation based on internal survey (2020)

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In the gastric cancer field, we entered the market in November last year with a combination regimen of Opdivo and chemotherapy for the 1L treatment of gastric cancer. In terms of the number of patients per year, the number of HER2-negative patients who are eligible for Opdivo is 22,000, which is a very large market.

# Prescription Ratio in Patients Newly Treated for 1L GC

※Patients starting 1L treatment within the last 1 month



Source: External data (Nov 2021 – Mar 2022: n=200~204)

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In this area, we are now firmly promoting the significance of Opdivo combination therapy, and we will show you the current share of new patient prescriptions. Opdivo's share of new patient prescriptions for 1L treatment is currently 42% and we believe it is growing steadily. We have confirmed the use at more than 80% of the facilities, which occupy the top 80% of the market.

As I mentioned earlier, we have confirmed 2,500 prescriptions as of the end of March since receiving approval, and we would like to further expand this number in the future.

We have been working on Opdivo in the area of 3L treatment of gastric cancer and 2L treatment of esophageal cancer. From the time of approval to 18 months of new prescription share, this slide lays out the portions of 3L treatment of gastric cancer and 2L treatment of esophageal cancer.

It is said that the peak time for new prescriptions of anti-cancer drug regimens generally takes about two years, but Opdivo has shown a rapid increase in the share of new prescriptions for 3L gastric cancer and 2L esophageal cancer treatment, reaching 70% of our target in 18 months.

As of four months after our entry into 1L treatment of gastric cancer, we have reached 42%, so we believe that we are doing our job in the gastrointestinal field as done before. We would like to continue to work hard here, as we hope to achieve 65% and 70% in the next 18 months.

Especially in 1L treatment of gastric cancer, we have received many opinions from key opinion leaders in Japan that Opdivo is a key drug for gastric cancer and must be administered in the treatment of gastric cancer. Until now, only about 40% of patients were eligible for Opdivo treatment because it was only indicated for 3L

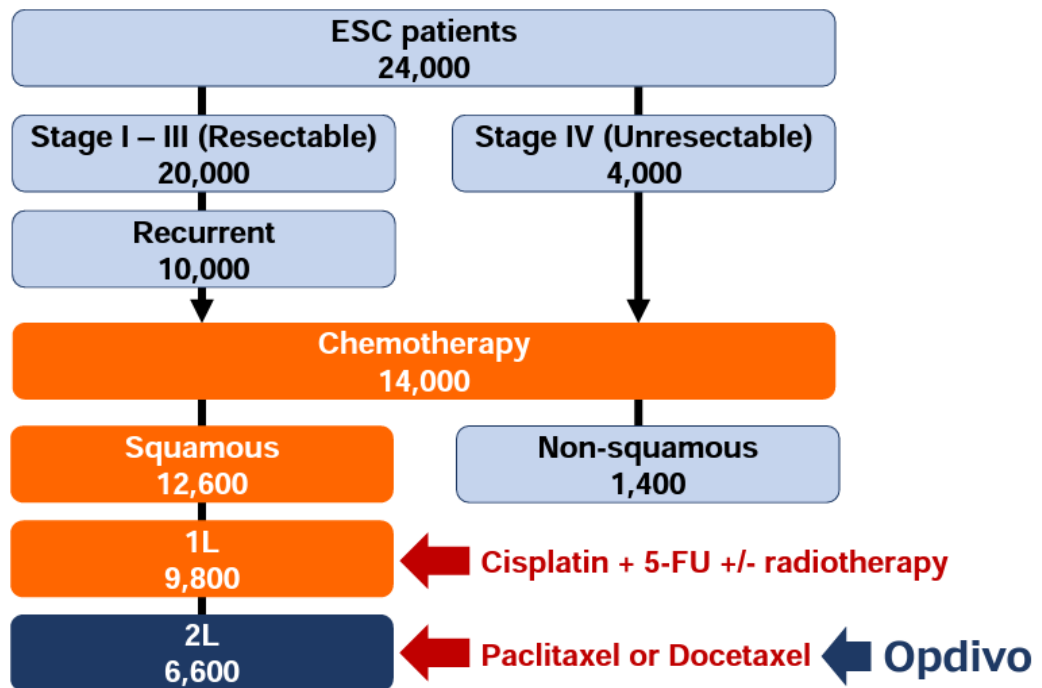
treatment, but now that it has been approved for 1L therapy, we have received many comments that more patients are now eligible for treatment. We will continue to value these opinions and ensure their proper use.

We would like to show the share of new patients in 3L treatment of gastric cancer. This graph shows the data from the approval of 3L treatment to November last year, and as I indicated earlier, we have maintained a 70% share in 3L treatment.

Since Opdivo was approved for 1L treatment this time, we also wanted to look at trends in prescriptions of Opdivo for 3L treatment and beyond, so we changed the survey method to one that combined 3L and 4L treatment, which look decreased share. However, looking back at past data, it was used approximately 60% in 3L and 4L treatments, and we believe that we have kept 70% today. We will focus our activities on 1L treatment, as the main area is the 1L treatment of gastric cancer.

# Number of ESC\* Patients per year in Japan

\* : Unresectable Advanced or Recurrent ESC

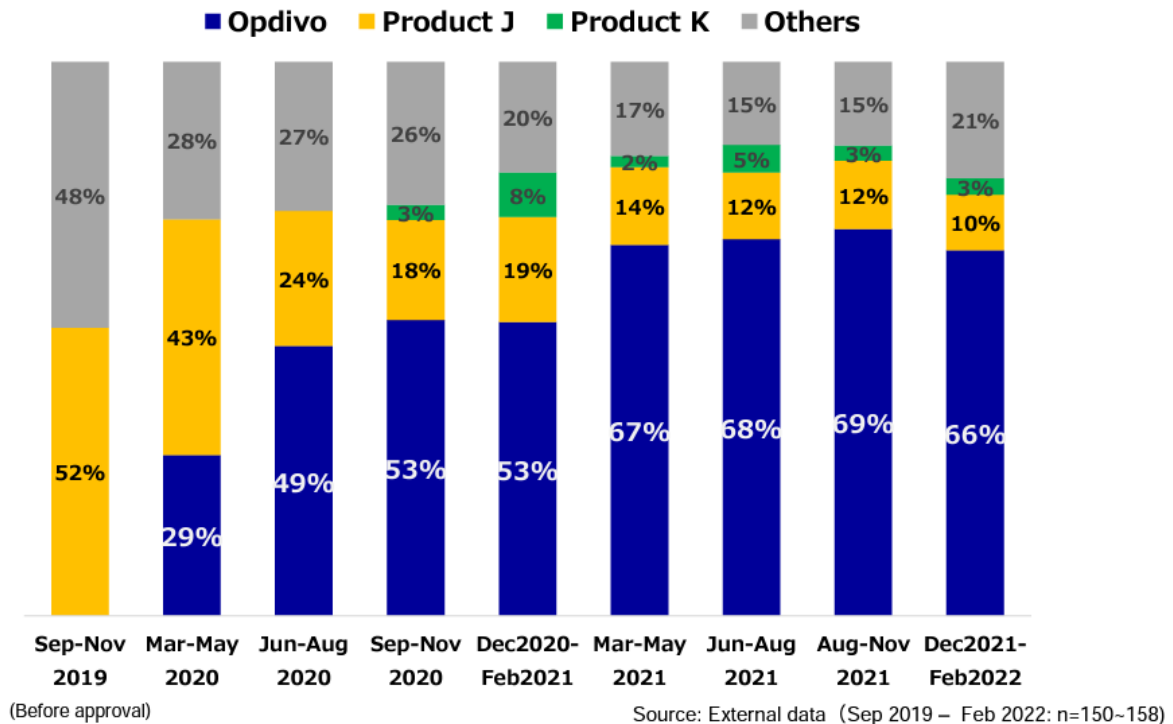


Estimation based on internal survey in 2020

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# Prescription Ratio in Patients Newly Treated for 2L ESC (Squamous Cell Carcinoma)

※ Patients starting 2L ESC within the last 3 months



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Regarding esophageal cancer, currently, we are working on 6,600 patients who are eligible for 2L treatment, and the current share of new prescriptions for 2L treatment is 66%.

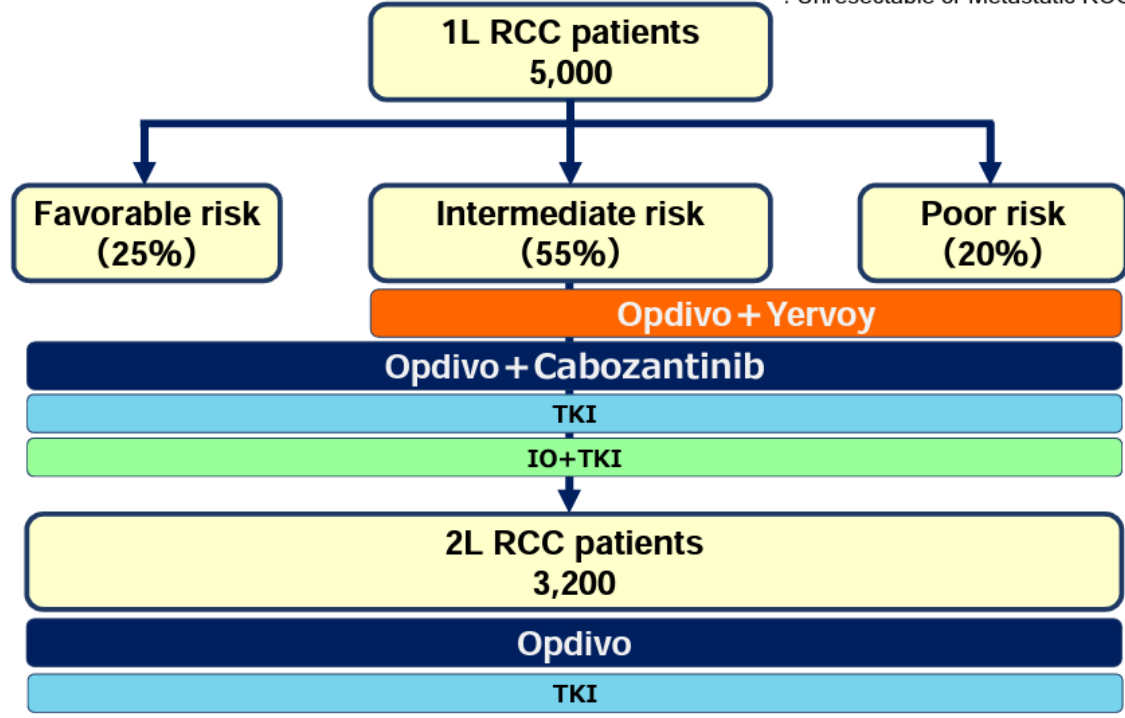
In addition, we have confirmed the use for the adjuvant treatment of esophageal cancer, which was approved in November last year, in 345 cases by the end of March since its approval. We are sorry that we are unable to present this information today, but we are aware that the current share of new prescriptions is approximately 30%.

Key opinion leaders of esophageal cancer have gradually recognized Opdivo as a safe and useful treatment option for patients who have received neoadjuvant CRT therapy and surgery, and failed in achieving pathological complete response. We will work hard to ensure that users consider the risks and benefits of implementing this treatment.

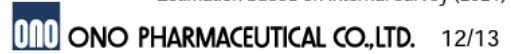
We will continue to firmly raise awareness of the usefulness of Opdivo for gastric cancer and esophageal cancer in this gastrointestinal field.

# Number of RCC\* Patients per year in Japan

\* : Unresectable or Metastatic RCC



Estimation based on internal survey (2021)

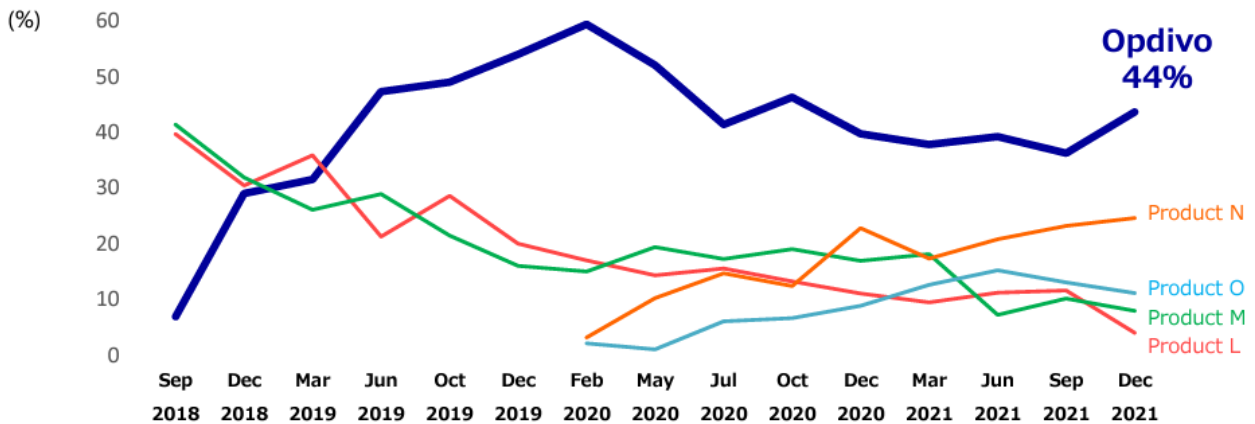


The last cancer type I would like to mention is renal cell carcinoma.

We have all the evidence for Opdivo in the Opdivo regimen, 1L treatment, 2L treatment, and beyond, and are currently working to make Opdivo available to all patients with renal cell carcinoma.

# Prescription Ratio in Patients Newly Treated for 1L RCC

	2018		2019				2020					2021			
	Sep	Dec	Mar	Jun	Oct	Dec	Feb	May	Jul	Oct	Dec	Mar	Jun	Sep	Dec
<b>Opdivo</b>	7	29	32	47	49	54	59	52	41	46	40	38	39	36	44
Product L	40	30	36	21	29	20	17	14	16	13	11	9	11	12	4
Product M	41	32	26	29	21	16	15	19	17	19	17	18	7	10	8
Product N							3	10	15	12	23	17	21	23	25
Product O							2	1	6	7	9	13	15	13	11



Source: External data (Sep 2018 – Dec 2021: n=46-110)



The chart shows the change in prescription ratio in patients newly treated for 1L treatment of renal cell carcinoma .

The prescription of IO combination therapy for 1L treatment is expanding rapidly, with the latest figures showing that 80% of patients have been treated with IO combination therapy.

The share of new prescriptions for the combination of Opdivo and Yervoy and the combination of Opdivo and TKI in 1L treatment is currently 44%, with 10% of patients at low risk, 40% at intermediate risk, and 70% at high risk being prescribed the Opdivo regimen.

We intend to continue to maintain our number one position in the 1L treatment of renal cell carcinoma.

In the last fiscal year, we received approvals for 1L treatment of gastric cancer, adjuvant therapy of esophageal cancer, cancer of unknown primary and adjuvant treatment of urothelial carcinoma. As I mentioned earlier, we have confirmed 200 new prescriptions as of the end of March for cancers of unknown primary that we were unable to show on the slides today.

The domestic key opinion leaders in this field of cancer of unknown primary, where the development is difficult, commented that the approval of Opdivo is of great significance in the field, and that Opdivo can be used regardless of the treatment history, and Opdivo should be used as soon as possible.

However, as a challenge, awareness of the disease itself is still low. Taking the opportunity of the approval of Opdivo for the treatment of cancer of unknown primary, we have made it our mission to promote the diagnosis and treatment of cancer of unknown primary.

As for adjuvant treatment of urothelial carcinoma, which was granted in March this year, so it has only been about one month since the approval. However, recurrence cases after resection of muscle-invasive urothelial carcinoma had a very poor prognosis, and there were no treatment options available. Therefore, the key opinion leaders consider a challenge is to avoid recurrence.

Some have commented that Opdivo shows great promise as a promising option for adjuvant therapy that improves disease-free survival and suppresses recurrence. We will work to increase our presence for urothelial cancer in the field of urologic oncology, along with renal cell carcinoma, which I mentioned earlier.

In addition, in this fiscal year, we plan to enter 1L treatment of esophageal cancer, so we will continue to promote proper use of the product and look forward to further expansion of its use.

Today, I explained Opdivo trends in general and by cancer type. We will continue to work to meet the unmet needs of cancer patients.



## Question & Answer

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**Questioner 1:** My first question is about Opdivo. You mentioned that the share in 2L treatment of esophageal cancer is now 66%. I understand that 1L is currently under application and will be completed in the future, but I would like to ask for confirmation that you are aiming at a position with 70% if you can obtain this as well.

**Takahagi:** In 1L esophageal cancer treatment, Keytruda first entered the market last year and its product is currently in use. For this reason, Keytruda is increasing in 1L treatment, and therefore, use of Opdivo in 2L is gradually decreasing. That has been a bit of a negative impact.

We will have to keep a close watch on how the number of these Keytruda patients increases in the future, but currently, we estimate that about less than 20% of the 1L treatment are using Keytruda. We will enter the market later. However, in this first-line therapeutic area, we believe that we can probably work with two regimens: a combination regimen of Opdivo with FP/chemo, like Keytruda, and a combination regimen of Opdivo and Yervoy, which they do not have.

Also, one more point, regarding the Keytruda regimen, it is a 3-week cycle, and we are on a 4-week cycle with Opdivo and chemo. I have heard that the conventional regimen used in Japan for chemotherapy is a four-week cycle, so we would like to work on considering the situation.

In the gastrointestinal field, I think there is a good chance that about 70% of patients will use IO regimen. We will compete well with Keytruda in this field and would like to work to somehow surpass them.

**Questioner 1:** As for the R&D expenses for this fiscal year, I understand that you are going to increase them since you mentioned it in the mid-term plan, but I think that the R&D expenses are quite high on top of the impairment in the previous fiscal year as well. Against this, the plan shows a significant increase in them this time. I wonder if this is something that can be used even with the actual development schedule, or if there is a possibility that the actual figure will be a little less than plan.

**Sagara:** We are, of course, planning to use them, but for this fiscal year. In the joint research section of the research department here, there are many areas that have increased this quarter only, so I think we are doing okay.

**Questioner 1:** Finally, you gave us a variety of information on the mid-term planning. I believe you gave us a list of pipelines that you are aiming to expand globally. Please explain to us a little bit more if there are any products to be candidates for next Opdivo among these that you think can go global?

**Sagara:** The product for which PoC is established is ONO-4059, Velembu, only. We hope to have more aggressive discussion when the results of the PoC are available in a little later. For example, if we have two or three compounds in success, we can fill the Opdivo gap, but just filling the gap is not quite attractive enough, we would like to grow further. So, I would like you to wait a bit for an answer to this question.

**Questioner 1:** Is it correct that you will give us updates when PoC is established in the future?

**Sagara:** Yes.

**Questioner 2:** I also have two questions about Opdivo, and research and development.

In your explanation about the annual number of patients with non-small cell lung cancer, you are now working very hard in this area. As for the IO/IO combination, when this was first discussed, I think there was some talk about whether doctors would really use IO/IO. I understand that there is no hesitation at all in the field of attacking with IO/IO, plus all-comer, and that Opdivo is now growing mainly in this area of non-small cell lung cancer. Is that correct?

**Takahagi:** First, hesitation of using IO/IO is really coming up in the form of trying to use, instead. However, it is an impression or comments of the Japanese doctors that we should carefully watch the balance between efficacy and safety.

Also, as far as whether it is an all-comer or not, there is a lot of data available on PD-L1 strong positive cases with a mono-therapy of competing product, including long-term five-year data, so it would be difficult to use IO/IO combination unless the data is superior to that. However, as to whether or not there are no cases in this area, we are of course working on prescriptions for this area, but we would like to establish a firm foundation for weakly positive and negative cases, and we are currently working on this area.

**Questioner 2:** May I understand that the addition of chemotherapy combination would be another strength, in a sense?

**Takahagi:** Yes. In terms of the percentage of prescriptions, 40% are Opdivo/Yervoy regimen used in 227 and 60% are Opdivo/Yervoy/chemo regimen used in 9LA. I have the impression that the doctors are more focusing on the regimen in 9LA.

**Questioner 2:** The next is adjuvant and neo-adjuvant treatment that I think we are going to see. I don't know how much will Opdivo be used for the neo-adjuvant treatment. As for adjuvant treatment, what is the average duration of administration? This may vary depending on the type of cancer, but do you have any reference values for this?

**Takahagi:** Referring to the data from the clinical trials, we estimate that the duration, for example, adjuvant therapy of esophageal cancer is about 6.8 months, and of urothelial cancer is also 6.8 months.

**Questioner 2:** Next, the data on adjuvant treatment of hepatocellular carcinoma is coming up, Isn't it?

**Idemitsu:** It is currently under trial.

**Questioner 2:** One last thing, regarding R&D, I hear that the president is very particular about JPY100 billion. With JPY100 billion, what can you do? What was not achieved before? Or do you mean this JPY100 billion is a benchmark, and when do you envision JPY100 billion?

**Sagara:** I cannot say I am not sticking to JPY100 billion, but I believe it is the first step. We would like to aim further JPY150 billion or JPY200 billion, and we would like to first aim for JPY100 billion considering our current capacity. Therefore, JPY100 billion is not a goal, and we are not obsessed with it; but rather, we want to aim JPY100 billion first. I think it would be a good idea that it would be about 20% to normal sales, however, it is okay to go over that when necessary. In light of the situation in which we are being told what to do with retained earnings, I think it is important to be able to allocate them to R&D investments when necessary. If we put the figure of JPY100 billion, we would like to make it an easy-to-understand figure to start with.

**Questioner 2:** May I understand that you have a variety of projects, if accumulated now, would not be enough with JPY100 billion?

**Sagara:** Basically, yes. I think we have enough work to do. JPY100 billion are allocated not only for in-house R&D but also for development and study of products obtained through licensing, some of which are large and require money.

**Questioner 3:** I have a question on your financial results and budget.

First, concerning the results. Regarding Opdivo, I understand that Opdivo is now gaining a significant share against Keytruda, and there is a gap between the two. I thought this was largely because of lung cancer. Looking at pages two, three, four, and seven in the presentation material, Trend of Opdivo, gastric cancer is a substantial contributor. This is the number of patients, so it is hard to connect it closely with sales. In February and March, Opdivo gained a lot, so can you say that the impact of gastric cancer is significant?

Furthermore, in your forecast for the current fiscal year, I can only see the picture, but can I assume that the proportion of this area will increase considerably?

**Takahagi:** We believe that the contribution of gastric cancer is significant. Since gastric cancer has been well treated in 3L treatment in the past, the number of cases administered has been accumulating, and 1L treatment of gastric cancer has been added to the number of cases. We believe that this contribution will increase in the current and next fiscal years. Considering this, use for gastric cancer treatment will further grow.

**Questioner 3:** Next is the budget, or rather, the forecast of performance. I thought this figure, when I look at sales, was quite strategic since it is a 17.6% increase in sales and 40.5% increase in operating income, but there is also the exchange rate and over JPY7 billion for Dr. Honjo and Kyoto University, so I wondered at what level they were. This means an increase of about JPY63.6 billion in sales. Simply looking at page 11 that you gave us, JPY42.6 billion for Opdivo and JPY10 billion for Forxiga, so these two alone is JPY60 billion. Since the royalty is JPY20 billion, I have the impression that it is not such a conservative or strategic figure as long as Opdivo grows properly. How do you think?

**Sagara:** It's not conservative, it's not challenging. The figure is objectively forecasted.

**Questioner 3:** You mentioned earlier JPY800 million by JPY1 weaker in the exchange rate.

**Sagara:** Yes.

**Questioner 3:** This means sales revenue, or top line, right?

**Sagara:** That's right.

**Questioner 3:** Since this is mostly royalties, can we assume that it is mostly directly related to profits?

**Sagara:** Yes. Sales equal profit.

**Questioner 3:** What kind of numbers are considered on the exchange?

**Sagara:** The exchange rate is JPY110, which is the value we currently expect.

**Questioner 3:** If it weakens by JPY1, JPY800 million will add to the positive, may I think like this?

**Sagara:** If the annual average is, say, JPY120, then 800 million multiplied by JPY10 would be added.

**Questioner 3:** So, it's a positive thing. I understand very well.

**Questioner 4:** The stock price dropped so much yesterday after the announcement that I was surprised at how much it dropped as well, but my question is also related to the dissolution of cross-shareholdings. When you see a sharp decline like this, I would be happy if you would do share buybacks, etc. Of course, I know that

the share price had risen considerably, but looking at the share price, did you consider the need for a buyback? I would appreciate your comments to the extent possible.

**Sagara:** After yesterday afternoon's decline, we are not thinking of any share buyback at all. We will make a decision after looking at various factors in the medium term, which is not something we can control, so we will therefore look at the situation over a period of time. But this does not mean that we will look at share-buy-backs in the medium term and think about them for a while after this one, but rather that we will not make an instant decision.

**Questioner 4:** One more thing about the Opdivo SC. You got the right in the previous term. One thing I would like to know is what you think of the development timeline. I don't think this will allow you to defer royalties, but please tell us what the payment relationship will be in Japan, for example, after the patent expires in 2031, and what is your idea of the economic terms.

**Idemitsu:** We are now discussing the development plan for the subcutaneous injection formulation, and we are currently working with BMS on a clinical trial plan to determine when we should release the product.

**Tani:** As for the economic conditions, we can't give you that. I'm sorry.

**Questioner 4:** Am I correct to assume that your company's profit margin ratio in Japan will not change significantly after 2031?

**Sagara:** Is that the profit margin ratio for the Company as a whole?

**Questioner 4:** No, it is the profit margin ratio of the Opdivo business in Japan. The point is, I think you are paying about 15% now, but I imagine that would be offset if the payment increases for the SC after the payment is eliminated.

**Sagara:** I can't answer that question right now. I may be able to answer it when it becomes clear. I'm sorry.

**Questioner 5:** I have a question about pages seven and eight of the slides, on strategies for continued growth. First of all, regarding page seven, the content is a little different between US and Europe. How much resources do you plan to invest in Europe and what level of return are you aiming for? Is it the same as in US or is it slightly different?

**Sagara:** I can give you a rough answer at the moment, but I think that the US is ahead, with the UK and Europe catching up behind. The US is now ahead of Europe in the development of maintenance and organization, but how they delay in Europe is not clear, but I hope you can see it that way.

**Questioner 5:** Also, I would like to know the details of the qualitative goal on page eight, which is to maintain an operating margin of at least 25%. I think that the profit structure of pharmaceutical companies means that even if sales grow, R&D and SG&A expenses do not increase so much in terms of variable costs, i.e., margins are likely to improve. If growth is in the low single digits, it would not be surprising to see an operating profit margin of 30% or 40%, as was once the case with your company. What kind of message are you sending to the market by maintaining more than 25%? Is this because the cost will increase considerably, or is it because you want to manage the Company with a certain degree of flexibility, so you may have such a case, but for the time being you would like to present only this level of information?

**Sagara:** To put it plainly, we are not sure if there will be years when expenses will increase, especially in R&D, but even in those years, we would like to secure at least 25%.

**Questioner 5:** So, you are considering the possibility that profits could be much higher than 25% for years other than those years?

**Sagara:** Possibly. Please understand that it will be possibly higher, and this is only possibility.

**Questioner 6:** I have two questions. One is on the forecast for Opdivo for this fiscal year on page two. I thought that sales of gastric cancer here were about one-third of the total, or JPY50 billion, which is quite large. I think you said that the first line will still grow in the next fiscal year, but what is the potential for gastric cancer in the first and third lines? The scale of sales should be approximately JPY50 billion, with different proportion of the first and third lines in the next fiscal year. Is there still more upside? This is my first question.

**Takahagi:** I believe that the first line will be the main focus in the future. The number of third line patients is 12,000, while the number of first line patients is 22,000, and the administration period is also about twice as long. I believe that if the first line becomes the mainstay in the future, we will be able to further expand sales in the gastric cancer field.

**Questioner 6:** This JPY50 billion is still a work in progress, and it will always grow again. Is this correct?

**Takahagi:** Yes. We will do our best to do so.

**Questioner 6:** My second question, slide eight, which shows continuous growth, shows sales growth from 2021 to 2026, which I think is about scale and loyalty. I understand that the drugs that will support the growth from 2026 to 2031 are under development and are not yet in sight, is my understanding correct? At that time, I had an image that some global products would probably be launched and grow from 2026 onward. How many global products do you think will be approved by 2026? If you have any numerical, quantitative targets, etc., could you please let us know?

**Sagara:** I can tell you now that one will be able to go by FY2026. As for after that, we will see if we can talk about whether the second one can go or not after we see the situation a little more.

**Questioner 6:** Am I correct in understanding that the growth from 2026 to 2031 will basically be supported by the marketed products that will come out from now on? Are you saying that Opdivo can support some growth here as well?

**Sagara:** Roughly, I think that would be fine.