Conference on FY2022.12 3Q Financial Results

CHUGAI PHARMACEUTICAL CO., LTD.

24 October 2022

Important Reminder

Forward-Looking Statements

This presentation may include forward-looking statements pertaining to the business and prospects of Chugai Pharmaceutical Co., Ltd. (the “Company”). These statements reflect the Company’s current analysis of existing information and trends. Actual results may differ from expectations based on risks and uncertainties that may affect the Company’s businesses.

Core Results

Chugai discloses its results on a Core basis from 2013 in conjunction with its transition to IFRS. Core results are the results after adjusting non-recurring items recognized by Chugai to IFRS results. Chugai’s recognition of non-recurring items may differ from that of Roche due to the difference in the scale of operations, the scope of business and other factors. Core results are used by Chugai as an internal performance indicator, for explaining the status of recurring profits both internally and externally, and as the basis for payment-by-results.

Note:

- Amounts shown in this report are rounded to the nearest 0.1 billion yen
- Variance and % are calculated based on the amounts shown

Conference on FY2022.12 3Q Financial Results

Agenda

01	FY2022 Q3 Overview	**Dr. Osamu Okuda** President & CEO
02	FY2022 Q3 Consolidated Financial Overview (Core)	**Toshiaki Itagaki** Director, Executive Vice President & CFO
03	Overview of Development Pipeline	**Tetsuya Yamaguchi** Executive Vice President, Head of Project & Lifecycle Management Unit

FY2022 Q3 Overview

Dr. Osamu Okuda

President & CEO

Financial Overview

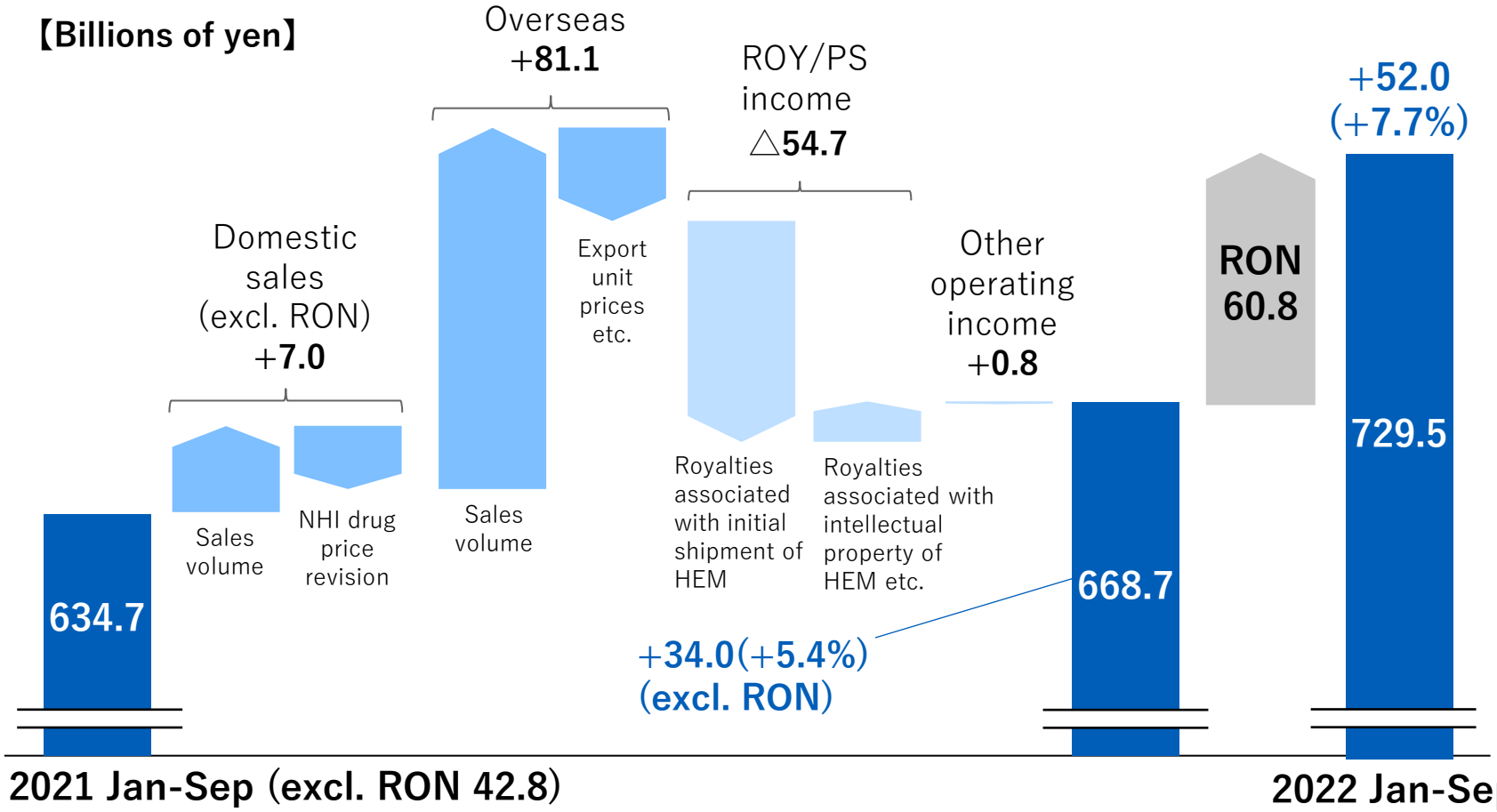
- **Increases in revenues and profits driven by favorable penetration of new products and growth of exports to Roche, which significantly outperformed the decrease in ROOI**
- **As core businesses in Japan and overseas are growing steadily, the company will continue aiming to achieve its initial forecast**

Core (billions of JPY)	2021 Jan - Sep actual	2022 Jan - Sep actual	Growth		2022 Jan - Dec forecast	Progress (%)
Revenues	**677.5**	**729.5**	**+52.0**	**+7.7%**	**1,150.0**	**63.4%**
Domestic sales	362.6	387.6	+25.0	+6.9%	646.3	60.0%
Overseas sales	176.0	257.1	+81.1	+46.1%	385.2	66.7%
ROOI	138.8	84.9	-53.9	-38.8%	118.5	71.6%
Operating profit	**290.7**	**299.0**	**+8.3**	**+2.9%**	**440.0**	**68.0%**
Operating margin	42.9%	41.0%	-1.9%pts	-	38.3%	-
Net income	**209.7**	**213.0**	**+3.3**	**+1.6%**	**312.5**	**68.2%**
EPS (yen)	**127.45**	**129.48**	**+2.03**	**+1.6%**	**190.00**	**68.1%**

- Domestic sales grew as expected due to the favorable market penetration of new products and the steady performance of Hemlibra despite the impact of the NHI drug price revision and other factors. Ronapreve is scheduled to be delivered to the government by the end of the year as initially forecasted
- Overseas sales increased mainly due to Hemlibra and Actemra exports to Roche. Progress on the export of Actemra was delayed due to manufacturing timing
- Regarding ROOI, royalties associated with initial shipment of Hemlibra significantly decreased. Progress was more favorable than expected
- Costs and operating expenses partially increased due to factors including high energy prices caused by the Russian/Ukraine situation. Limited impact on development activities

Topline Overview

- **Domestic sales (excl. Ronapreve) increased due to increases in new products and sales volume**
- **Overseas sales significantly increased as volume growth far exceeded the decline in export unit prices**
- **The decrease in royalty income was offset by an increase in overseas sales as expected**



- Domestic sales (excl. Ronapreve) increased as market penetration of new products such as Evrysdi, Polivy, and Enspryng, and sales growth in Hemlibra exceeded the impact of generics and NHI drug price revision
- Overseas sales increased significantly due to the full-scale Hemlibra exports to Roche at regular shipment unit price and the contribution of Actemra exports
- Royalties associated with overseas' local sales of Hemlibra increased despite a substantial decrease in royalties associated with initial shipment of Hemlibra

Hemlibra: Trends of domestic hemophilia A patient share

'22Q3 28.5%, '22Q2 27.3%, '22Q1 26.3%, '21Q4 24.7%, '20Q4 20.0%, '19Q4 14.4%, '18Q4 2.2%

R&D Overview

■ Steady progress in R&D, including in-house projects

- Progress in early-stage in-house projects including out-licensing of NXT007 to Roche and initiation of DONQ52 development
- Multiple phase III studies were initiated. The regulatory filing for crovalimab was accepted in China, and Mitchga has launched in Japan

Letters in blue: in-house related projects

P1/P2 (Early-stage development)

1) DONQ52 (Celiac disease /P1)
2) pralsetinib (Solid tumors/P2)
3) RG6330[KRAS G12C inhibitor]+ RG6433[SHP2 inhibitor] (Solid tumors/P1)

P3 (Late-stage development)

1) Enspryng (AIE)
2) Enspryng (MOGAD)
3) Polivy + RG7828[mosunetuzumab] (r/r aNHL)

Regulatory filing

1) crovalimab (PNH/China's NMPA* accepted the filing in Q3)
2) Actemra(SSc-ILD/Filed in EU/August)
3) RG6264(fixed-dose subcutaneous combination of Perjeta and Herceptin**) (Japan/Filed in September)

Launch/Additional indication

1) Polivy (Previously untreated DLBCL/Additional indication approved in August)
2) Mitchga (Itching associated with atopic dermatitis/Japan/ launched in August)

*National Medical Products Administration
**Fixed-dose subcutaneous combination of pertuzumab and trastuzumab (same monoclonal antibodies as in Perjeta and Herceptin)

Licensing Agreement

- NXT007 (Hemophilia A) : Out-licensed to Roche
- PRIME CAR-T Tech : In-licensed from Noile-Immune Biotech, Inc.

Notable Readout within the year

- Gantenerumab : GRADUATE1/2 trials (Alzheimer's Disease)
  - To be presented at Clinical Trials on Alzheimer's Disease (CTAD) in San Francisco, US. (local time: November 30)

FY2022 Q3 Consolidated Financial Overview(Core)

Toshiaki Itagaki

Director, Executive Vice President & CFO

IFRS and Core Results Jan - Sep

(Billions of JPY)	IFRS results	Non-core items		Core results
		Intangible assets	Others	
Revenues	**821.5**		**-91.9**	**729.5**
Sales	644.7			644.7
Royalties and other operating income	84.9			84.9
Other revenue	91.9		-91.9	-
Cost of sales	-263.3	+0.9		-262.4
Operating expenses	**-174.3**	**+0.5**	**+5.7**	**-168.1**
M&D and G&A *	-69.9		+2.8	-67.1
Research and development	-104.4	+0.5	+2.9	-101.0
Operating profit	**383.8**	**+1.4**	**-86.2**	**299.0**
Financial account balance	-1.9			-1.9
Income taxes	-110.0	-0.4	+26.3	-84.1
Net income	**272.0**	**+1.0**	**-59.9**	**213.0**
EPS (JPY)	165.29			129.48

Non-Core items

(Billions of JPY)

Intangible assets

Amortization	+1.1
Impairment	+0.3

Others

Lump-sum income related to settlement agreement with Alexion Pharmaceuticals, Inc., etc.	-90.7
Restructuring expenses, etc.	+4.5

* M&D: Marketing and distribution, G&A: General and administration

FY2022 Q3 Consolidated Financial Overview (Core)

P/L Jan - Sep(Year on Year)

(Billions of JPY)	2021	2022	Growth	
Revenues	**677.5**	**729.5**	**+ 52.0**	**+ 7.7%**
Sales	538.7	644.7	+ 106.0	+ 19.7%
Domestic	362.6	387.6	+ 25.0	+ 6.9%
Overseas	176.0	257.1	+ 81.1	+ 46.1%
Royalties and other operating income	138.8	84.9	- 53.9	- 38.8%
Royalty and profit-sharing income	135.4	80.7	- 54.7	- 40.4%
Other operating income	3.4	4.2	+ 0.8	+ 23.5%
Cost of sales	**-225.7**	**-262.4**	**- 36.7**	**+ 16.3%**
(cost to sales ratio)	41.9%	40.7%	-1.2%pts	-
Operating expenses	**-161.1**	**-168.1**	**- 7.0**	**+ 4.3%**
M&D and G&A	-66.9	-67.1	- 0.2	+ 0.3%
Research and development	-94.1	-101.0	- 6.9	+ 7.3%
Operating profit	**290.7**	**299.0**	**+ 8.3**	**+ 2.9%**
(operating margin)	42.9%	41.0%	-1.9%pts	-
Financial account balance	-1.9	-1.9	0.0	-
Income taxes	-79.2	-84.1	- 4.9	+ 6.2%
Net income	**209.7**	**213.0**	**+ 3.3**	**+ 1.6%**
EPS (JPY)	127.45	129.48	+2.03	+ 1.6%

Domestic sales
Increase due to sales growth of new products as well as mainstay products

Overseas sales
Significant increase in sales of Hemlibra and Actemra

Royalty and profit-sharing income
Significant decrease in royalty income for initial shipping inventory of Hemlibra

Other operating income
Increase in one-time income

Cost of sales
Cost to sales ratio improved due to a change in product mix, etc.

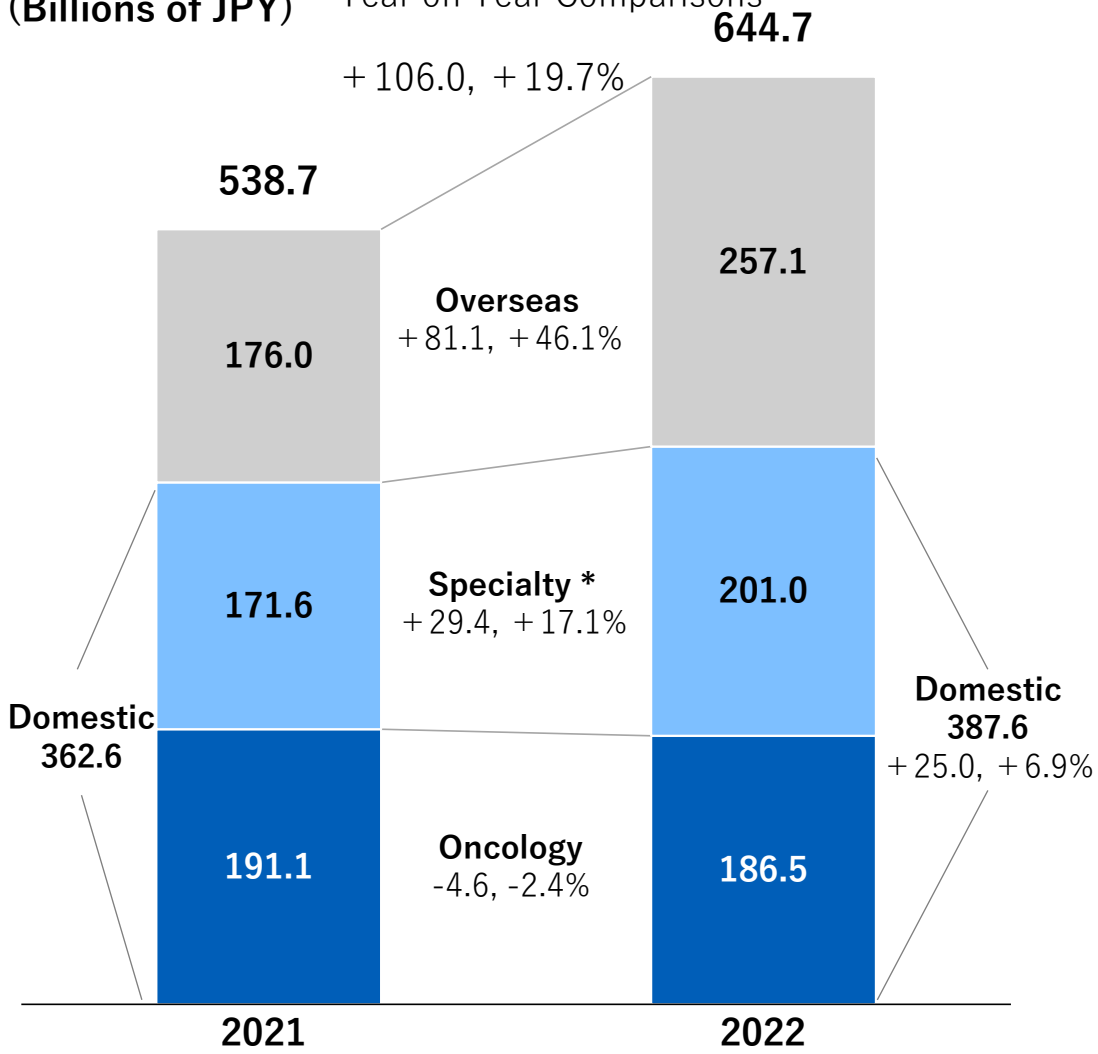
Operating expenses
Increase due to progress of development projects and impact of yen depreciation on costs denominated in foreign currencies, etc.

Operating profit
Growth mainly due to increase in sales

Sales Jan - Sep(Year on Year)

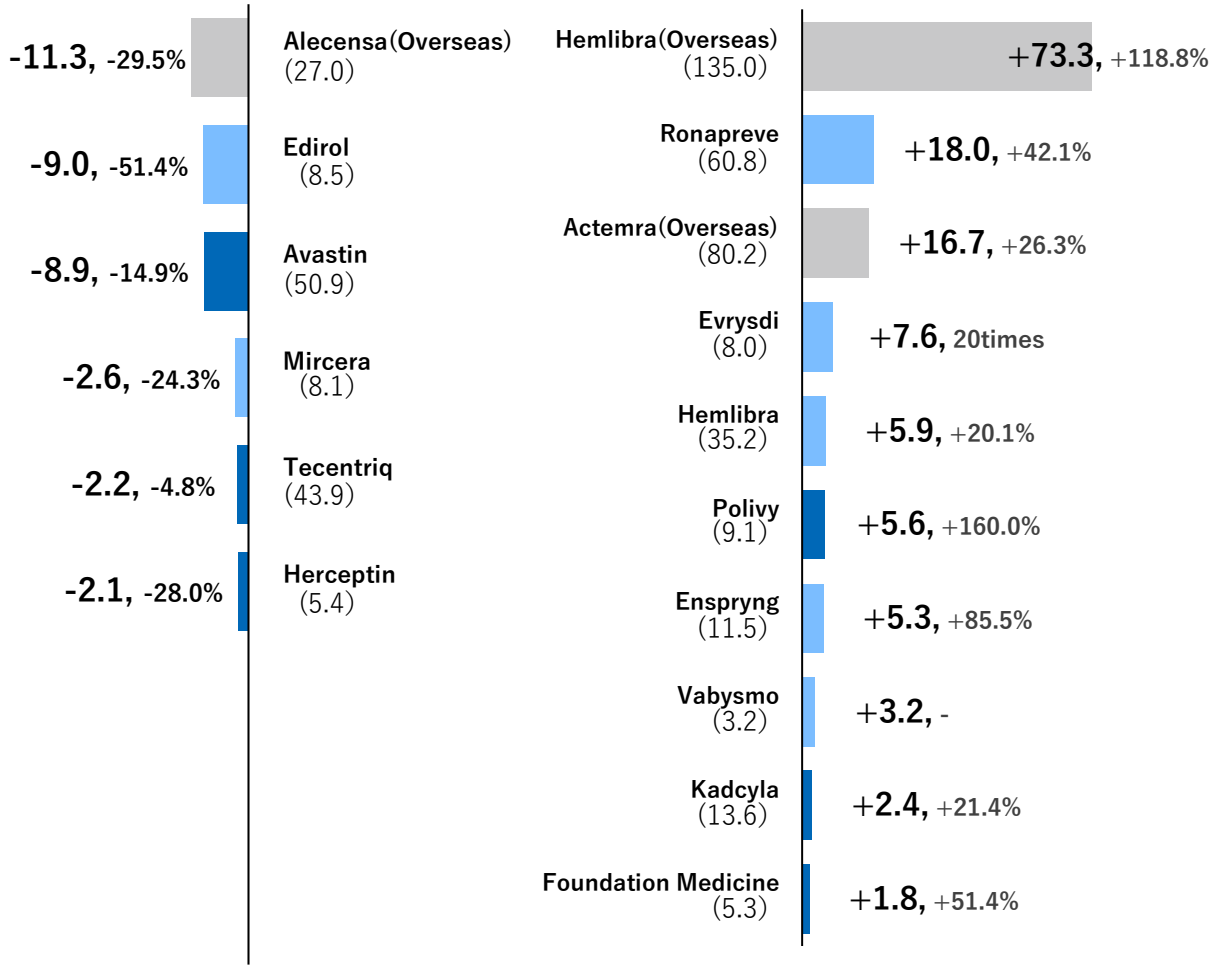
Sales by Disease Area,
Year on Year Comparisons

(Billions of JPY)



Sales by Products,
Year on Year Changes

( ): Actual sales in FY2022
%: Year-on-year percentage change

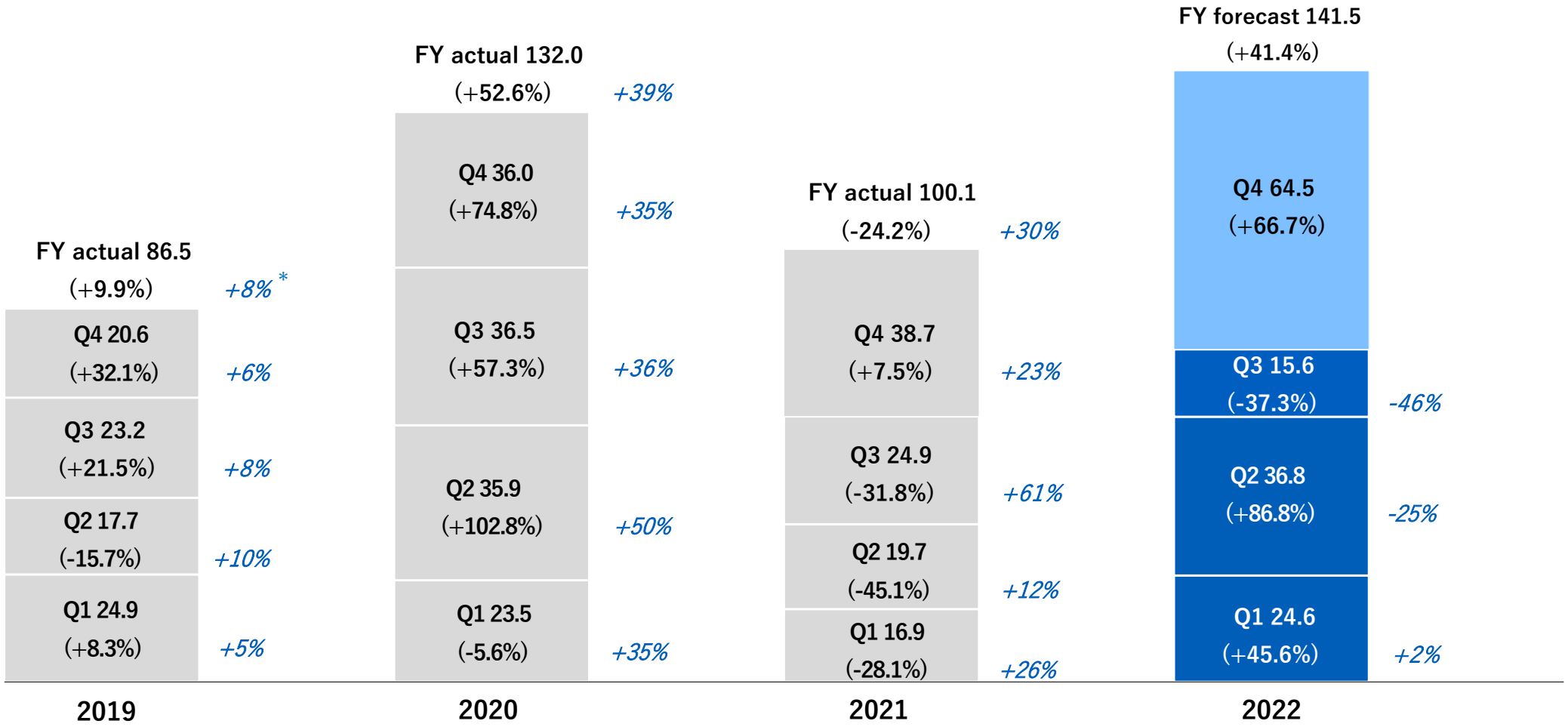


*"Primary" used as the name of disease area is replaced with "Specialty" from July 2022

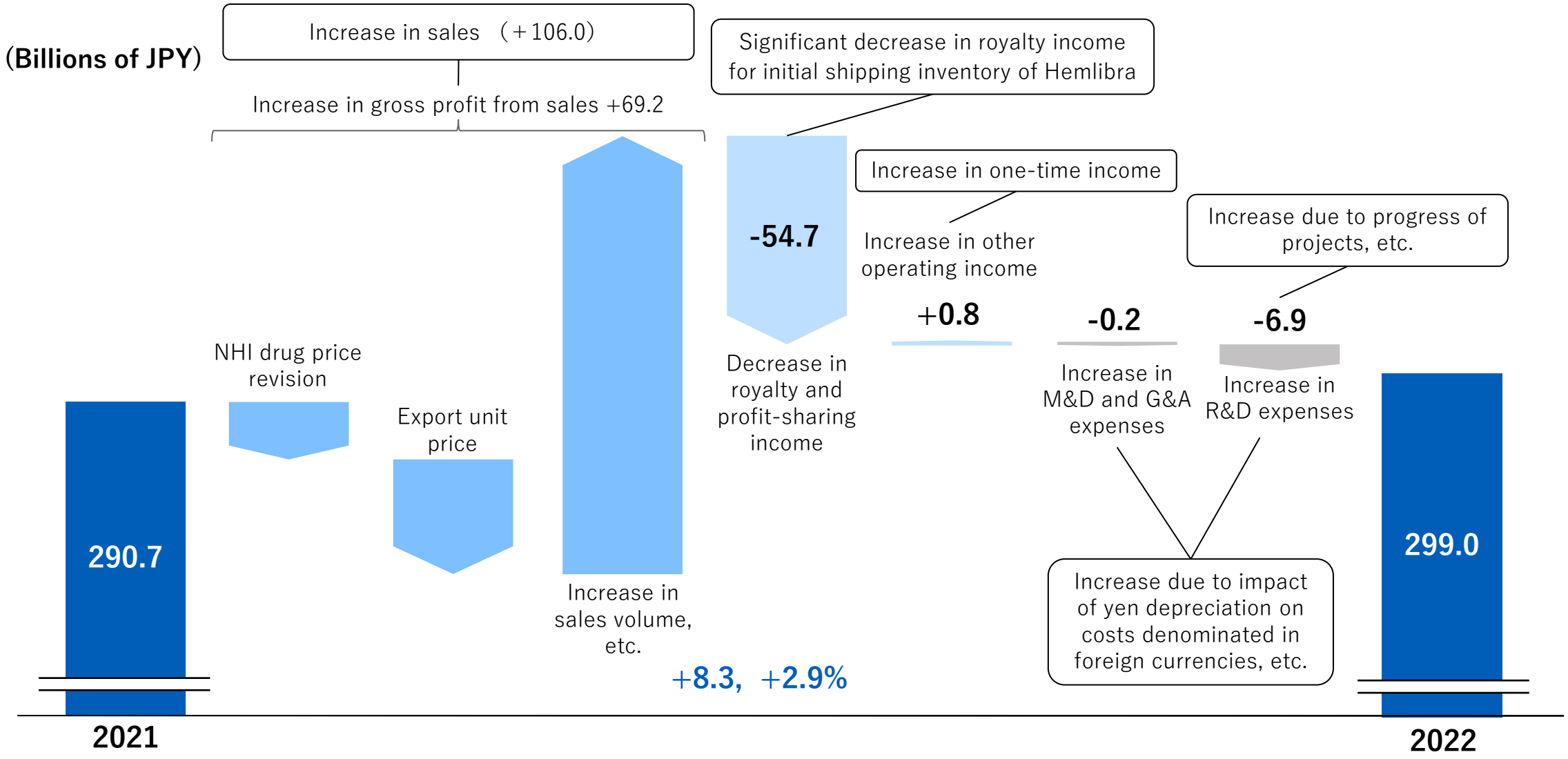
Export of Actemra to Roche

%: Year-on-year percentage change
black: Chugai sales to Roche
blue*: Roche sales excluding Japan (for reference)
*Growth rates in blue are calculated with the effects of exchange rate fluctuations eliminated.

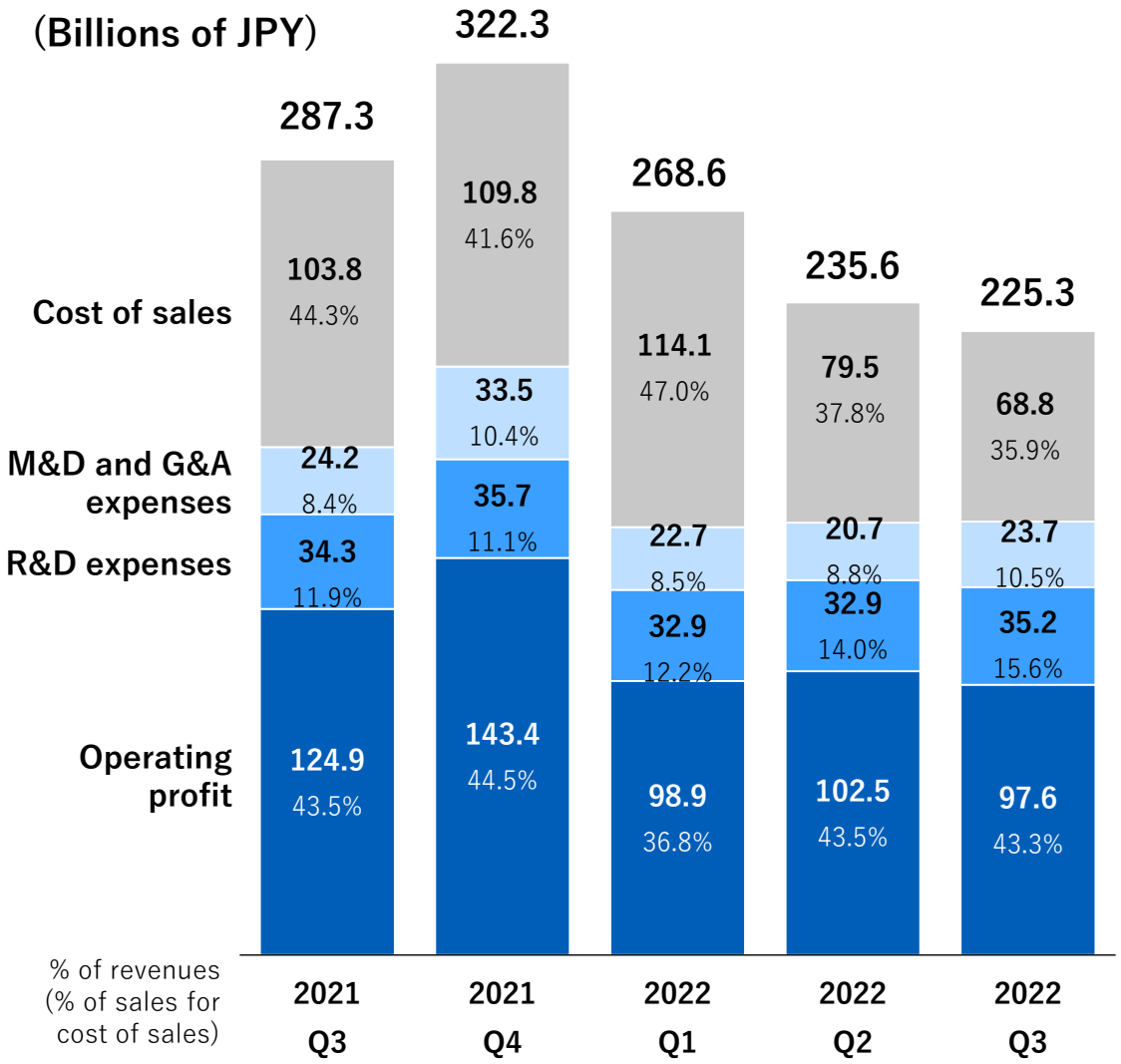
(Billions of JPY)



Operating Profit Jan - Sep(Year on Year)



Structure of Costs and Profit by Quarter



Year on Year (2021 Q3)

Cost of sales ratio: improved due to a change in product mix, etc.

R&D expenses: increase due to impact of yen depreciation on costs denominated in foreign currencies and progress of projects, etc.

Operating profit: -27.3, -21.9%

Quarter on Quarter (2022 Q2)

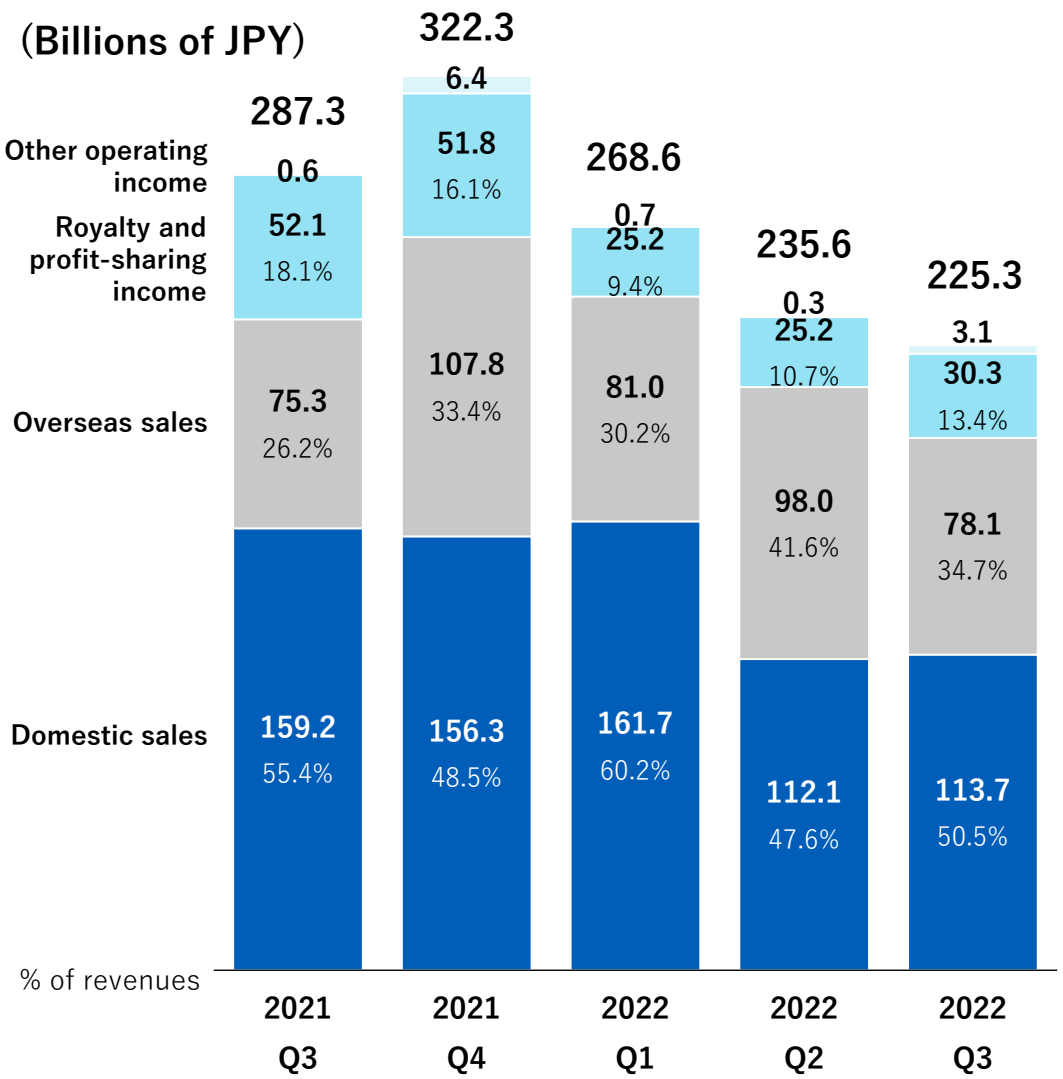
Cost of sales ratio: improved due to a change in product mix, etc.

M&D and G&A expenses: increase due to gain on sales of property, plant and equipment in the second quarter, etc.

R&D expenses: increase due to progress of projects, etc.

Operating profit: -4.9 , -4.8%

Structure of Revenues by Quarter



Year on Year (2021 Q3)

Domestic sales: decrease due to the absence of supply of Ronapreve to the government, etc.

Overseas sales: significant increase in sales of Hemlibra

Royalty and profit-sharing income: significant decrease in royalty income for initial shipping inventory of Hemlibra

Quarter on Quarter (2022 Q2)

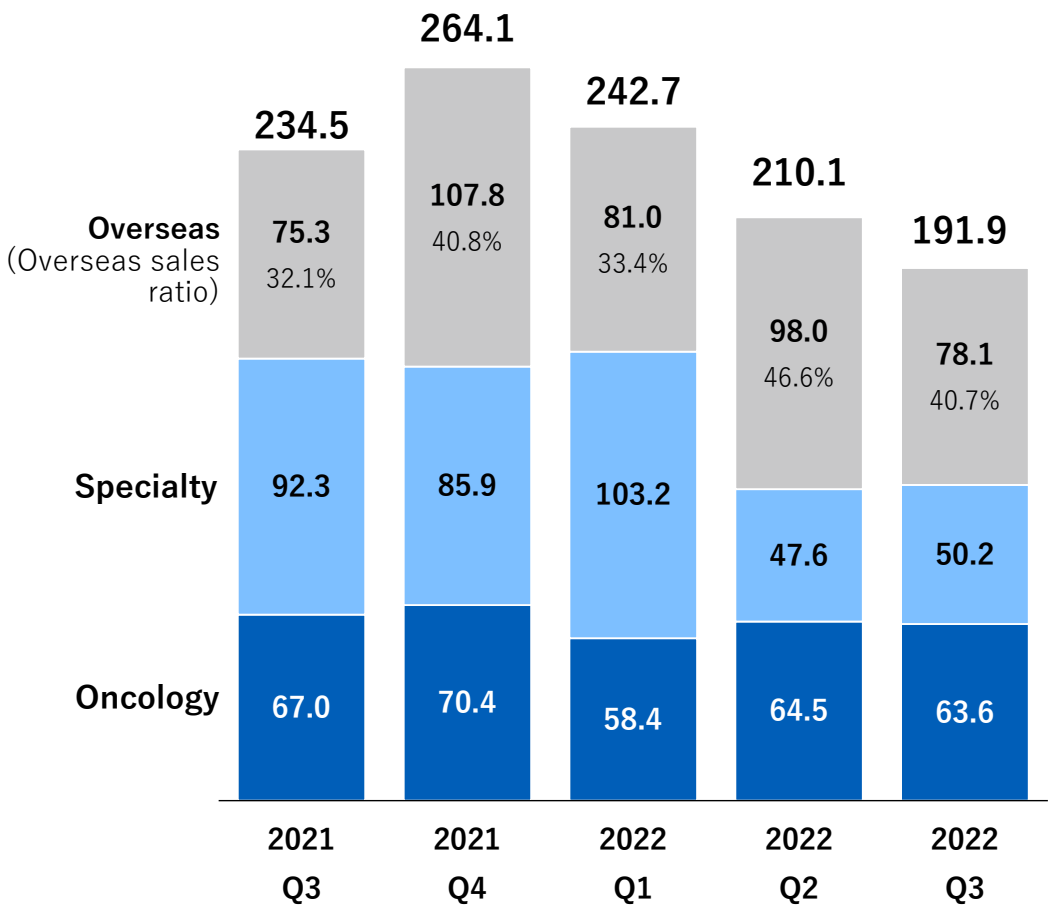
Domestic sales: increase due to sales growth of new products as well as mainstay products

Overseas sales: decrease mainly due to variance in timing of exports from quarter to quarter, etc.

Royalty and profit-sharing income: Increase in royalty income related to intellectual property rights of Hemlibra

Structure of Sales by Quarter

(Billions of JPY)



Year on Year (2021 Q3)

Oncology	Avastin:	-3.9	Herceptin:	-0.6
	Polivy:	+0.9	Kadcyla:	+0.6
Specialty	Ronapreve:	-42.8	Edirol:	-7.4
	Evrysdi:	+2.7	Hemlibra:	+2.5
	Vabysmo:	+2.3	Enspryng	+1.8
Overseas	Hemlibra:	+15.5	Actemra:	-8.8
	Alecensa:	-4.8		

Quarter on Quarter (2022 Q2)

Oncology	Avastin:	-1.0	Polivy:	+0.6
Specialty	Vabysmo:	+1.4	Hemlibra:	+1.0
Overseas	Actemra:	-20.9	Hemlibra:	-2.3
	Alecensa:	+3.0		

FY2022 Q3 Consolidated Financial Overview (Core)

P/L Jan - Sep(vs. Forecast)

(Billions of JPY)	Actual 2022 Jan - Sep	Forecast 2022 Jan - Dec	Progress	2021 Progress*
Revenues	**729.5**	**1,150.0**	**63.4%**	**67.8%**
Sales	644.7	1,031.5	62.5%	67.1%
Domestic	387.6	646.3	60.0%	69.9%
Overseas	257.1	385.2	66.7%	62.0%
Royalties and other operating income	84.9	118.5	71.6%	70.5%
Royalty and profit-sharing income	80.7	114.0	70.8%	72.3%
Other operating income	4.2	4.5	93.3%	34.7%
Cost of sales	**- 262.4**	**- 460.0**	**57.0%**	**67.3%**
(cost to sales ratio)	40.7%	44.6%	-	-
Operating expenses	**- 168.1**	**- 250.0**	**67.2%**	**70.0%**
M&D and G&A	- 67.1	- 100.5	66.8%	66.6%
Research and development	- 101.0	- 149.5	67.6%	72.5%
Operating profit	**299.0**	**440.0**	**68.0%**	**67.0%**
(operating margin)	41.0%	38.3%	-	-
Net income	**213.0**	**312.5**	**68.2%**	**67.3%**
EPS (JPY)	129.48	190.00	68.1%	67.3%

Domestic Sales
Overall progress nearly in line with forecast
Ronapreve supply to the government expected in the fourth quarter

Overseas sales
Export of Actemra was delayed due to manufacturing timing

Royalty and profit-sharing income
Progress steady in view of forecast

Other operating income
Progress nearly in line with forecast

Cost of Sales
Cost to sales ratio nearly in line with Jan to Sep forecast

Operating expenses
Overall progress slightly lower than forecast

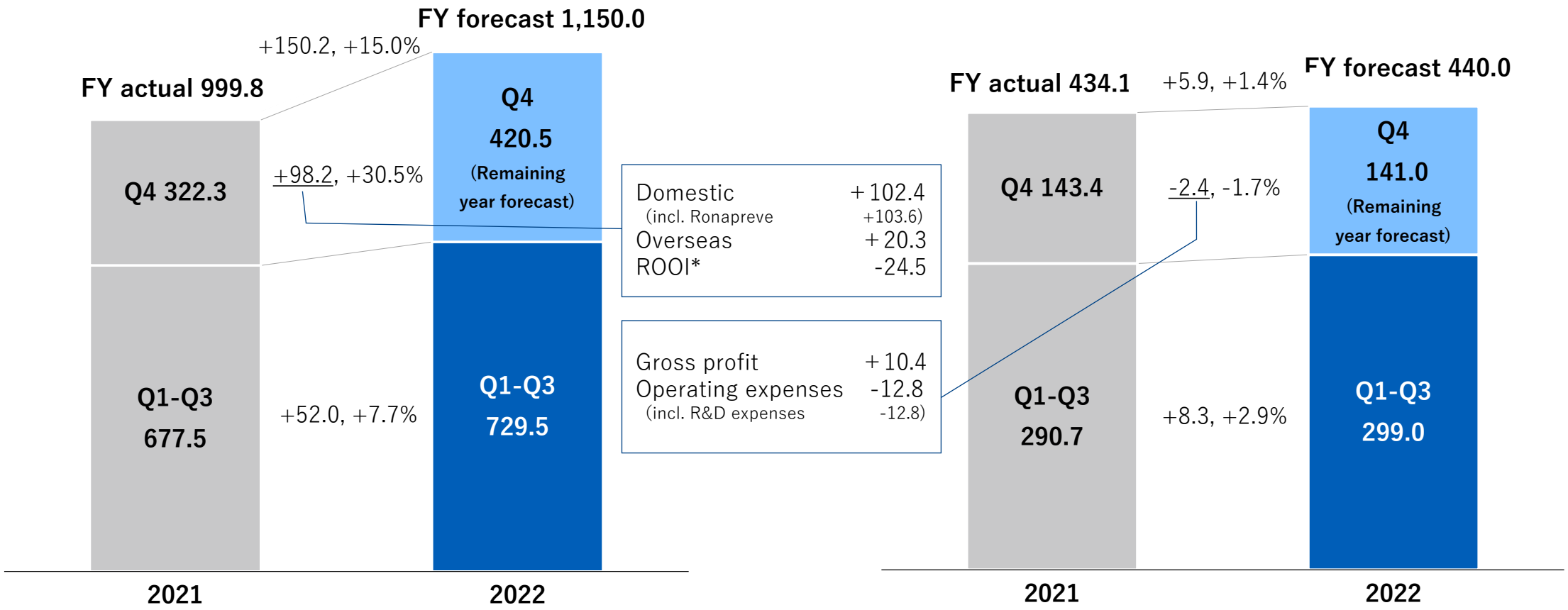
Operating profit
Progress nearly in line with forecast

* Jan - Sep progress versus Jan - Dec

Jan-Sep Actual and Remaining Year Forecast (Year on Year)

(billions of JPY)

* ROOI: Royalties and other operating income



Sales Jan - Sep(vs. Forecast)

(Billions of JPY)	Actual 2022 Jan - Sep	Forecast 2022 Jan - Dec	Forecast Progress	2021 Progress *
Sales	**644.7**	**1,031.5**	**62.5%**	**67.1%**
Domestic	**387.6**	**646.3**	**60.0%**	**69.9%**
Oncology	**186.5**	**260.5**	**71.6%**	**73.1%**
Avastin	50.9	69.4	73.3%	73.9%
Tecentriq	43.9	62.0	70.8%	74.1%
↓ Perjeta	23.5	33.7	69.7%	73.9%
Alecensa	20.9	28.7	72.8%	72.6%
↓ Polivy	9.1	16.2	56.2%	51.5%
↑ Kadcyla	13.6	16.0	85.0%	71.3%
↓ Herceptin	5.4	8.3	65.1%	76.5%
↓ Gazyva	3.1	5.4	57.4%	71.1%
Rituxan	3.3	4.1	80.5%	70.6%
↓ Foundation Medicine	5.3	9.1	58.2%	68.6%
Other	7.7	7.5	102.7%	75.9%

(Billions of JPY)	Actual 2022 Jan - Sep	Forecast 2022 Jan - Dec	Forecast Progress	2021 Progress *
Specialty	**201.0**	**385.8**	**52.1%**	**66.7%**
Ronapreve	60.8	199.0	30.6%	55.3%
Hemlibra	35.2	51.8	68.0%	70.4%
Actemra	31.2	41.9	74.5%	73.8%
Enspryng	11.5	16.7	68.9%	63.9%
Edirol	8.5	10.8	78.7%	78.5%
Mircera	8.1	10.2	79.4%	74.3%
↑ Evrysdi	8.0	8.8	90.9%	17.4%
CellCept	5.8	7.4	78.4%	73.8%
Bonviva	5.3	7.0	75.7%	74.4%
Oxarol	4.1	5.1	80.4%	74.2%
↑ Vabysmo	3.2	4.6	69.6%	-
Other	19.2	22.5	85.3%	67.8%
Overseas	**257.1**	**385.2**	**66.7%**	**62.0%**
Hemlibra	135.0	186.0	72.6%	54.0%
↓ Actemra	80.2	144.4	55.5%	61.8%
Alecensa	27.0	34.1	79.2%	76.4%
↓ Enspryng	2.0	4.6	43.5%	80.0%
Neutrogin	6.7	8.8	76.1%	74.7%
Edirol	0.0	0.1	0.0%	-
Other	6.2	7.4	83.8%	74.2%

↑ exceed forecast
↓ below forecast

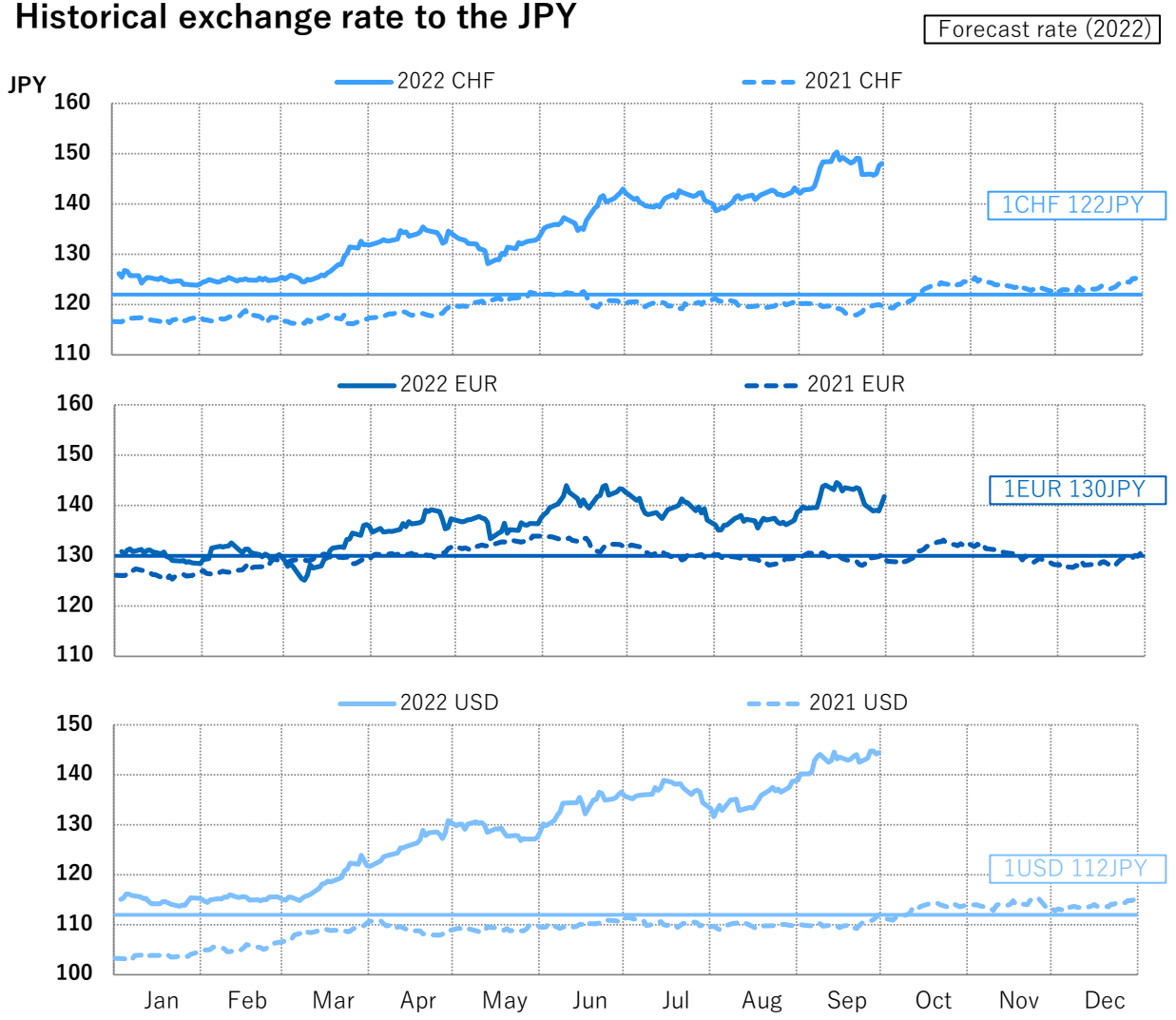
* Jan - Sep progress versus Jan - Dec

Impact from Foreign Exchange Jan - Sep

(billions of JPY)	vs. 2021 Actual	vs. 2022 Assumption
Revenues	**+20.6**	**+5.1**
Sales	+13.8	+2.4
Royalties and other operating income	+6.8	+2.7
Cost of sales	**-7.6**	**-0.6**
Operating expenses	**-3.3**	**-2.1**
Operating profit	**+9.7**	**+2.4**

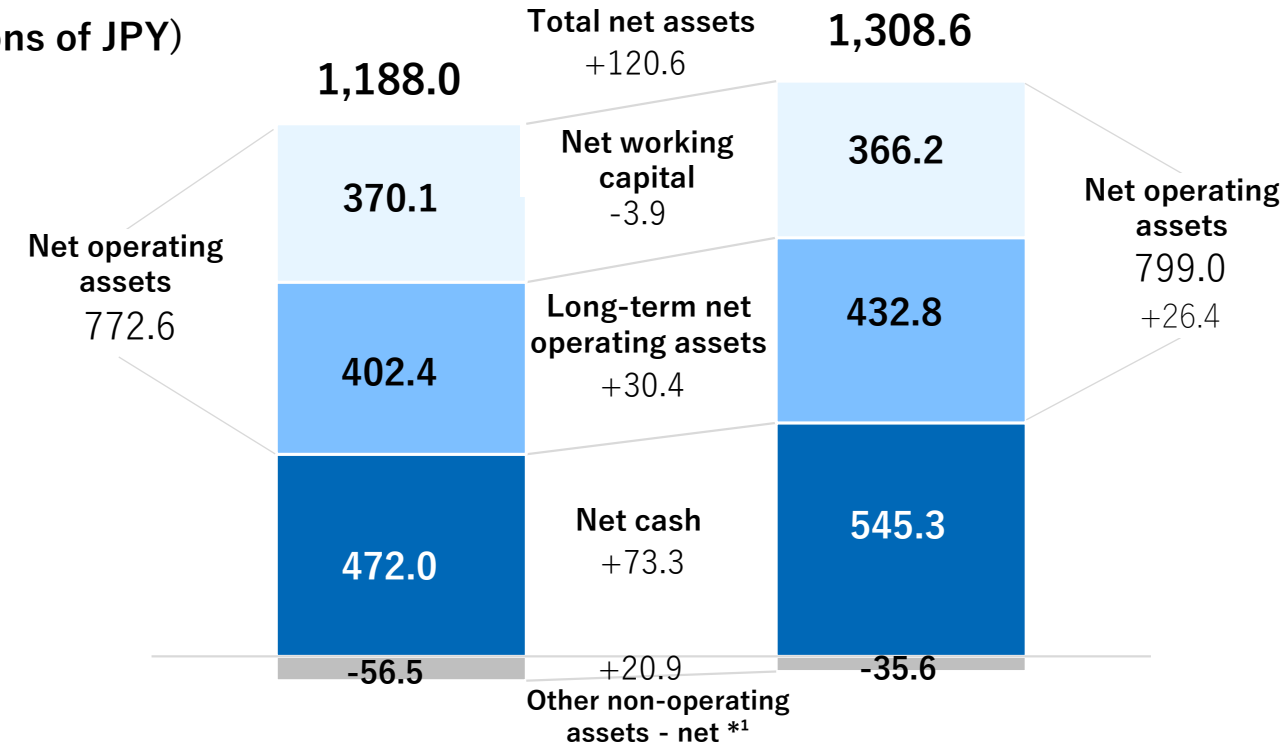
Market average exchange rate(JPY)	2021 Actual	2022 Assumption	2022 Actual
1CHF	119.03	122.00	134.54
1EUR	129.77	130.00	136.10
1USD	108.45	112.00	128.01

Historical exchange rate to the JPY



Financial Position (vs. 2021 Year End)

(Billions of JPY)



	2021 Dec		2022 Sep
Total assets	1,538.7	+162.1	1,700.8
Total liabilities	-350.7	-41.5	-392.2
Total net assets	1,188.0	+120.6	1,308.6
Ratio of equity attributable to Chugai shareholders	77.2%	-0.3%pts	76.9%

Decrease in net working capital

Decrease mainly in trade accounts receivable

Increase in long-term net operating assets

Increase in property, plant and equipment due mainly to the following investments
- Chugai Life Science Park Yokohama
- New manufacturing building for APIs*2 (FJ2) at Fujieda Plant
- Biopharmaceutical APIs manufacturing building (UK4) at Ukima Branch

Increase in net cash

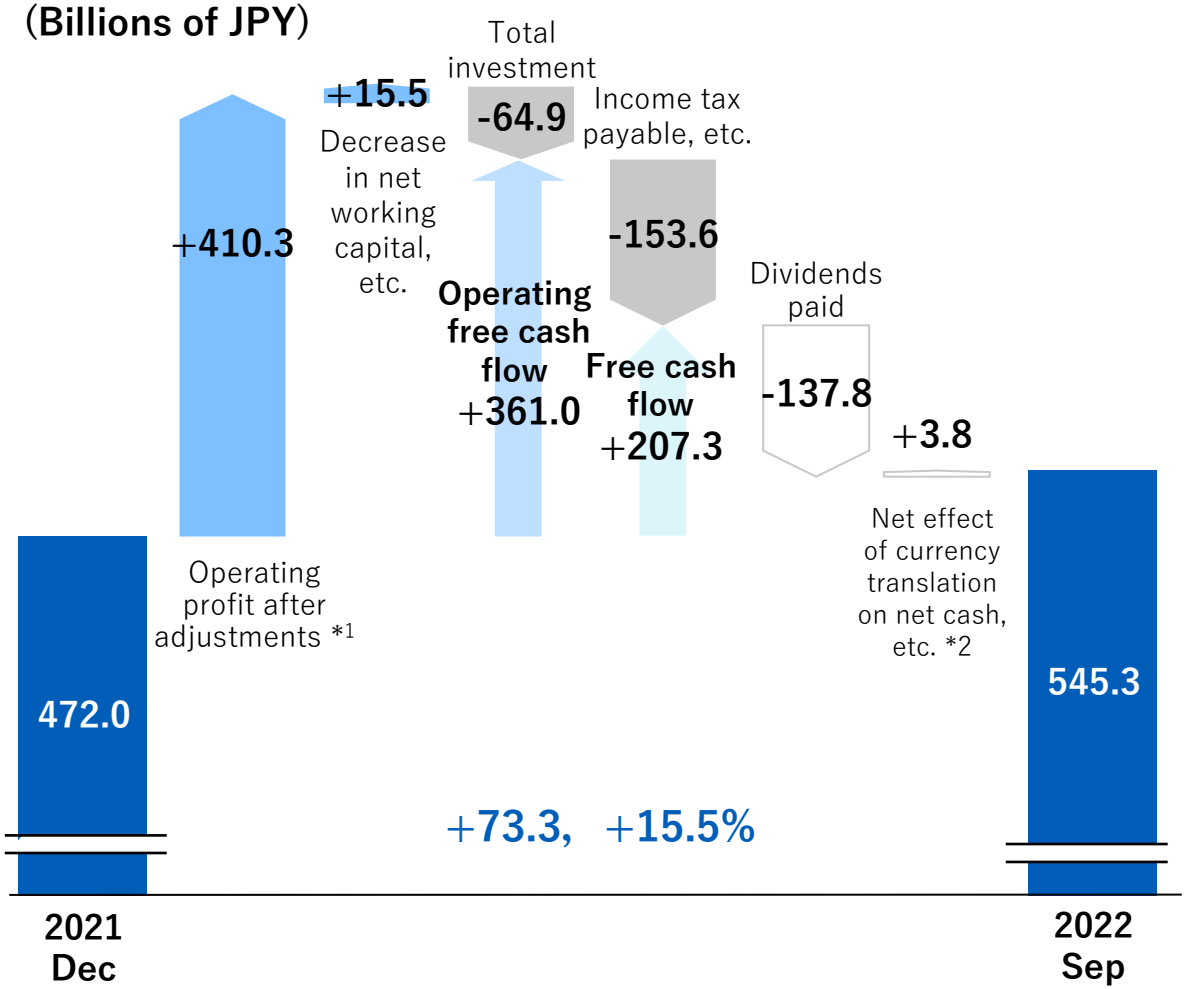
(See next slide)

Increase in other non-operating assets – net

Decrease mainly in current income tax liabilities

* 1 E.g., deferred income tax assets, accrued corporate tax, etc.
* 2 APIs: active pharmaceutical ingredients

Net Cash (vs. 2021 Year End)



Operating profit after adjustment [*1]	**+410.3**
Operating profit [*1]	+383.8
Depreciation, amortization and impairment [*1]	+22.6
Decrease in net working capital, etc.	**+15.5**
Total investment	**-64.9**
Property, plant and equipment	-50.7
Payment for lease liabilities	-5.7
Intangible assets	-8.6
Operating free cash flow	**+361.0**
Income tax payable, etc.	**-153.6**
Income tax payable	-151.1
Free cash flow	**+207.3**
Dividends paid	**-137.8**
Net effect of currency transaction on net cash, etc. [*2]	**+3.8**

*1 Including Non-Core (IFRS results)
*2 Net effect of currency translation on net cash, etc. = Transaction in own equity instruments + Purchase of non-controlling interests + Net effect of currency translation on net cash(*3)
*3 Results from using different types of exchange rates when consolidating overseas subsidiaries in financial statements, i.e. net cash using end of period exchange rate and free cash flows using average exchange rate. (Chugai defines this term based on International Accounting Standard (IAS) 7 and IAS 21)

Current Status / Plan for Major Investments

Production

Fujieda Plant: Construction of a new synthetic manufacturing building to accelerate the development of small- and mid-size molecule active pharmaceutical ingredients (FJ2)

2019-22: 19.1 billion JPY (19.8 billion JPY)

Fujieda Plant: Construction of a manufacturing building for active pharmaceutical ingredients to cover late-stage clinical development and early commercial production of small and mid-size molecule drugs (FJ3)

2021-24: 55.5 billion JPY (17.1 billion JPY)

Ukima Branch: Construction of biopharmaceutical APIs manufacturing building for early-stage clinical development (UK4)

2021-23: 12.1 billion JPY (3.2 billion JPY)

Research and development

CPR (Singapore): Accelerate creation of clinical candidates utilizing proprietary antibody technologies

2012-21: 476 million SGD (437 million SGD),
incl. capital investments of 61 million SGD (70 million SGD)

2022-26: 282 million SGD (44 million SGD),
incl. capital investments of 21 million SGD (2 million SGD)

Chugai Life Science Park Yokohama: Building of state-of-the-art R&D site to create innovative new drug candidates

Purchase of business site 2016-18: 43.0 billion JPY

Construction of laboratory 2019-22: 128.8 billion JPY (113.0 billion JPY)

Comprehensive collaboration in research activity with **IFReC**

2017-27: 10.0 billion JPY (6.7 billion JPY)

( ): Cumulative amount at the end of Sep, 2022

Overview of Development Pipeline

Tetsuya Yamaguchi

Executive Vice President, Head of Project & Lifecycle Management Unit

Overview of Development Pipeline

Q3 Topics

Letters in orange：in-house projects (global development)　**Letters in blue**：in-licensed from Roche (development and distribution in Japan)

As of October 24, 2022

Launched	Mitchga*	Itching associated with atopic dermatitis (only when existing treatment is insufficiently effective) (JP)	August 2022
Approved	Edirol	Edirol tablet (Additional dosage form)	August 2022
	Polivy	Previously untreated DLBCL	August 2022
Filed	SKY59/crovalimab	PNH (China) (priority review designation)	Q3 2022
	Actemra	Systemic sclerosis with interstitial lung disease (EU)	August 2022
	RG6264**	HER2-positive breast and colorectal cancer	September 2022
	FoundationOne Liquid CDx cancer genomic profile	Expanded use of the results in the detection of genetic alterations “copy number alterations” in 324 genes related to cancer and the information of “bTMB scores” as a comprehensive genomic profiling	October 2022
New to pipeline	SA237/Enspryng	MOGAD	P3(August 2022)
	SA237/Enspryng	AIE	P3(September 2022)
	RG7828/mosunetuzumab	r/r aNHL (in combinationn with Polivy)	P3(October 2022)
	RG6396/pralsetinib	Solid tumors	P2(October 2022)
	DONQ52	Celiac disease	P1(September 2022)
	RG6330/KRAS G12C inhibitor	Solid tumors	P1(September 2022)
	RG6433/SHP2 inhibitor	Solid tumors	P1(September 2022)
Medical conference	DONQ52	Non-clinical study results including MOA and results of clinical research：ICDS2022	October 2022
Others	**Introduction of PRIME technology**	A license agreement for Noile-Immune’s PRIME CAR-T technology	August 2022
	NXT007	Out-licensing agreement with Roche	August 2022
Development discontinued	RG7446/Tecentriq	RCC (adjuvant) (IMmotion010 study)	

* Out-licensed to Maruho in Japan　** PER/HER fixed-dose subcutaneous combination

DONQ52 (Celiac Disease)

Anti-HLA-DQ2.5/gluten peptides bispecific antibody for celiac disease. P1 study initiated.

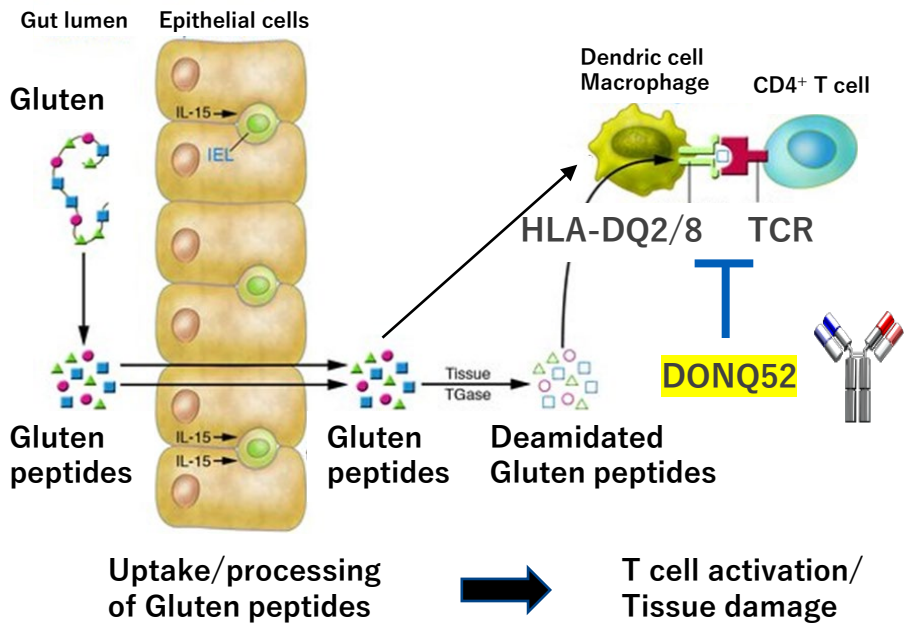
Celiac disease (CeD): Autoimmune disease caused by gluten. Abnormal immune reaction to gluten damages small intestine.

- ~1% of global population is affected by CeD.
- >90% of patients have HLA-DQ2.5 allele.
- Gluten Free Diet (GFD) is the only treatment and there are no available medicines.

DONQ52: Bispecific antibody against complex of HLA-DQ2.5/gluten peptides.

- DONQ52 directly inhibits gluten dependent T cell activation by neutralizing interaction of T cell receptor (TCR) and complex of HLA-DQ2.5/gluten peptides.
- DONQ52 covers >25 gluten derived peptides including all immunodominant gluten peptides for CeD.
- Gluten-specific blockade enables long-acting (subcutaneous injection) and high safety profile.

Gluten-specific T cell activation by HLA-DQ2.5/gluten peptides is key molecular pathogenesis of celiac disease



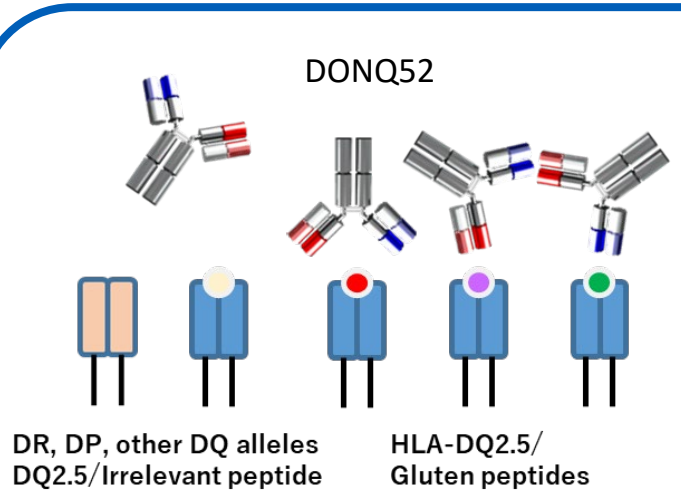
Adapted from Kagnoff MF. J Clin Invest. 2007;117(1):41-9.

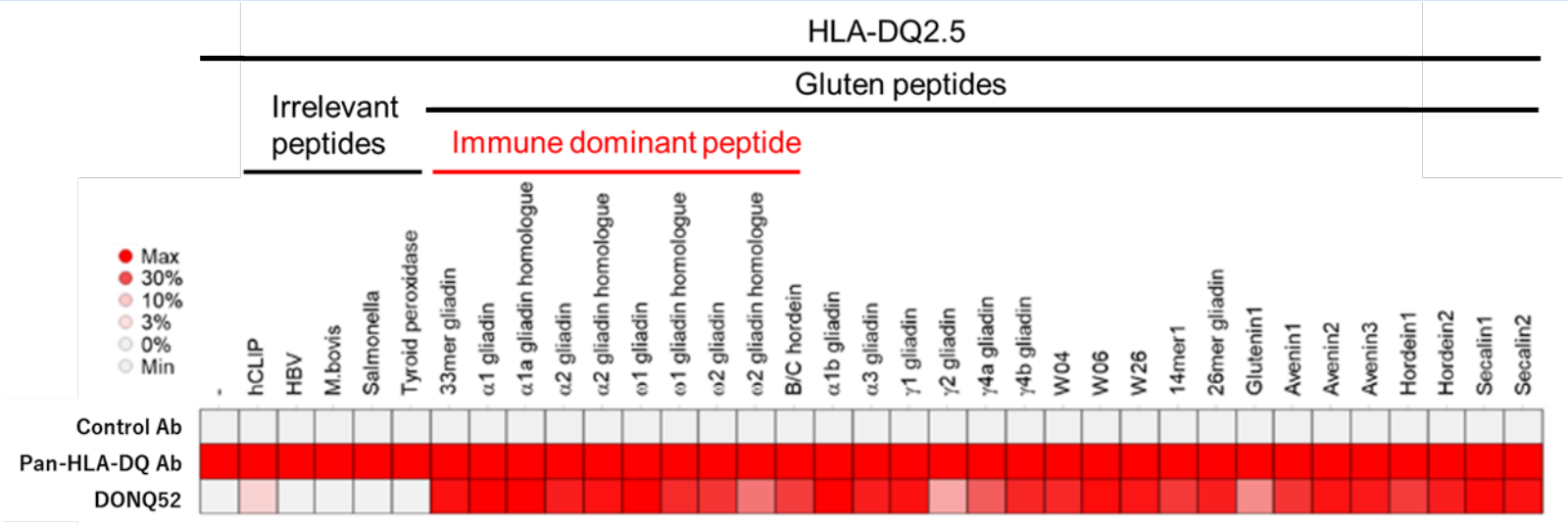
DONQ52 : Preclinical Study Results

DONQ52 binds to more than 25 types of gluten peptides that cause celiac disease

Binding property of DONQ52

- Specific binding to complex of HLA-DQ2.5/gluten peptides.
- No binding to HLA molecule itself or complex of HLA-DQ2.5/irrelevant peptides.
- Bispecific technology enables binding to more than 25 gluten peptides, including all dominant peptides responsible for celiac disease





Source: International Celiac Disease Symposium 2022

Overview of Development Pipeline

Accelerate Multiple Simultaneous Development to Maximize the Value of In-house Developed Late-stage Products

Global simultaneous developments of multiple diseases are ongoing for 6 products by Roche and 3rd party licensees

To be initiated

Roche-managed

GYM329

- Spinal muscular atrophy (P2/3)
- Facioscapulohumeral muscular dystrophy (P2)

2 indications

Enspryng**

- Generalized myasthenia gravis (P3)
- Myelin oligodendrocyte glycoprotein antibody–associated disease(MOGAD) (P3)
- Autoimmune encephalitis (AIE) (P3)

** Already launched for NMOSD

3 indications

Crovalimab

- Paroxysmal nocturnal hemoglobinuria (P3) → Filed (China)
- Atypical hemolytic uremic syndrome (P3)
- Guillain-Barré syndrome (P3)
- Sickle cell disease (P2)
- Lupus Nephritis (P1)

5 indications

3rd party-managed*

CKI27

- Ovarian cancer (P2)
- Non-small cell lung cancer (P2)

2 indications

OWL833

- Type 2 diabetes (P2)
- Obesity (P2)

2 indications

Nemolizumab

- Atopic dermatitis (P3) → Approved (Japan)
- Prurigo nodularis (P3)
- Chronic kidney disease associated pruritus (P2/3)

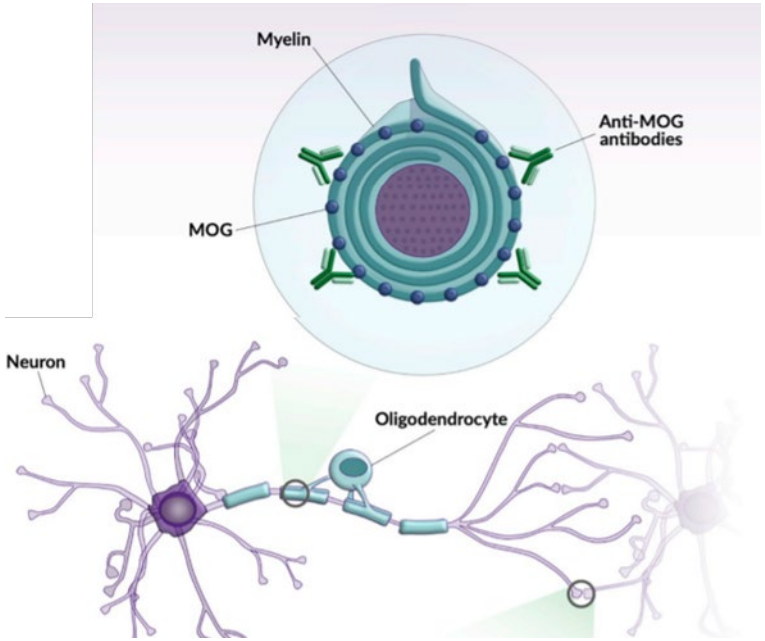
3 indications

* CKI27: Developed by Verastem, OWL833: Developed by Eli Lilly, Nemolizumab: Developed by Galderma (overseas) and Maruho (Japan)

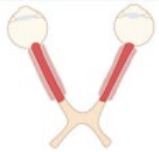
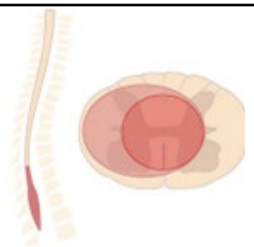
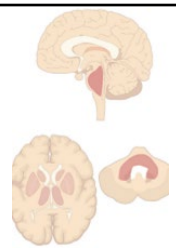
Enspryng: Myelin Oligodendrocyte Glycoprotein Antibody-associated Disease (MOGAD)

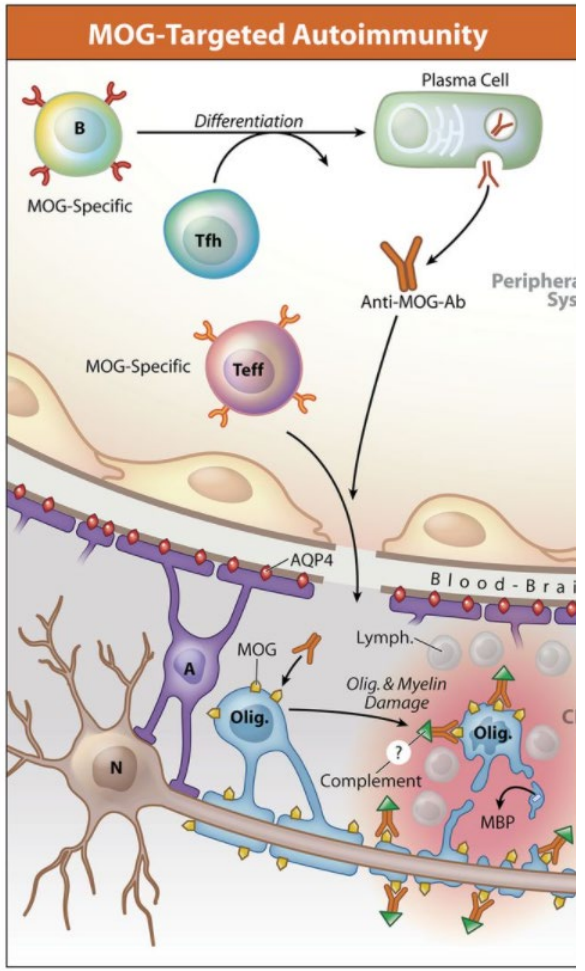
Blockade of IL-6 signalling may lead to reduced pathogenic autoantibody production and anti-inflammatory effects. Global Phase 3 study initiated.

- MOGAD is a demyelinating disorder in which a pathogenic autoantibody “anti-MOG antibody” binds to MOG, which is expressed on the surface of myelin sheath in CNS. Symptoms include optic neuritis, myelitis, and encephalitis.[1)]
- Currently, there are no approved therapies for MOGAD, and repeated recurrence are reported in some cases on available therapies. High UMN remains for efficacy and/or safety.[1,2,3)]
- The number of patients in Japan is estimated to be 2,000. The first epidemiological survey has been conducted since 2021.[4)]



Main pathological features in MOGAD[5)]

Optic nerve	Spinal Cord	Brain
		



A: Astrocyte, AQP4: aquaporin-4, Lymph.: lymphocyte, MBP: Myelin basic protein, MOG: Myelin oligodendrocyte glycoprotein, N: Neuron, Olig. : Oligodendrocyte

1) Ichiro N：Brain and Nerve. 69(11):1331-1336,2017
2) Ichiro N：Neurotherapy 36(3):220-224,2019
3) Zamvil SS, et al. Neurol Neuroimmunol Neuroinflamm. 2(1):e62, 2015
4) Specified non-profit corporation MS CABIN https://www.mscabin.org/archives/13551
5) Bruba GD, et al. RadioGraphics 2018; 38:169–193

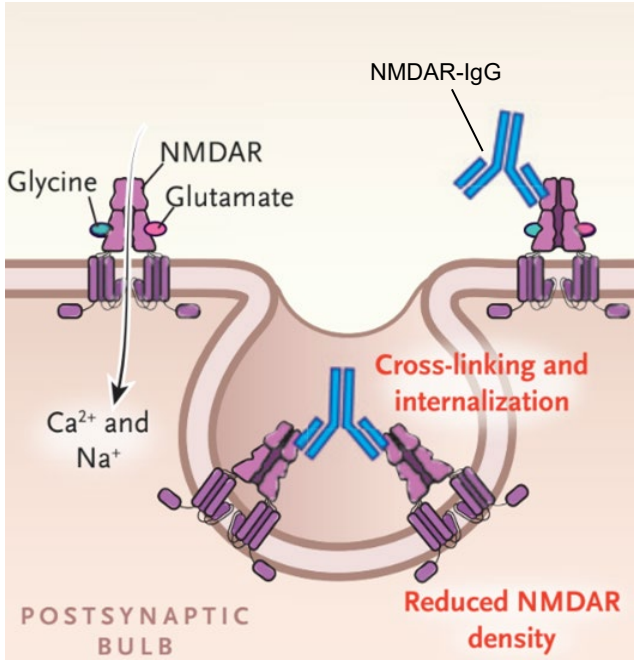
UMN: unmet medical need

Enspryng: Autoimmune Encephalitis (AIE)

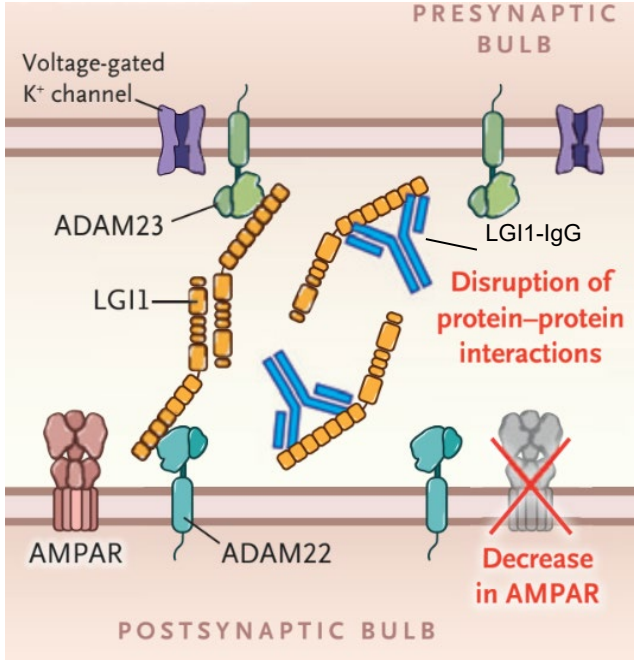
Blockade of IL-6 signalling may lead to a decrease in the production of pathogenic autoantibodies and normalization of BBB.[5)] Global Phase 3 study initiated.

- Autoimmune encephalitis is a pathological condition presenting with various psychiatric and neurological symptoms due to autoimmune responses to various antigens.[1,2)] Typical examples are anti-NMDA receptor encephalitis and anti-LGI1 antibody encephalitis.[3)]
- In addition to consciousness disturbance and memory disorder, convulsion-like seizure may be observed as clinical symptoms.[3)]
- There are no approved therapies for AIE. Since current therapies do not show sufficient efficacy and safety, UMN remains high.[1,2,3).]
- In Japan, estimated number of AIE patient is approximately 1,000 -2,000.[4)]

NMDAR-IgG[a]



LGI1-IgG[b]

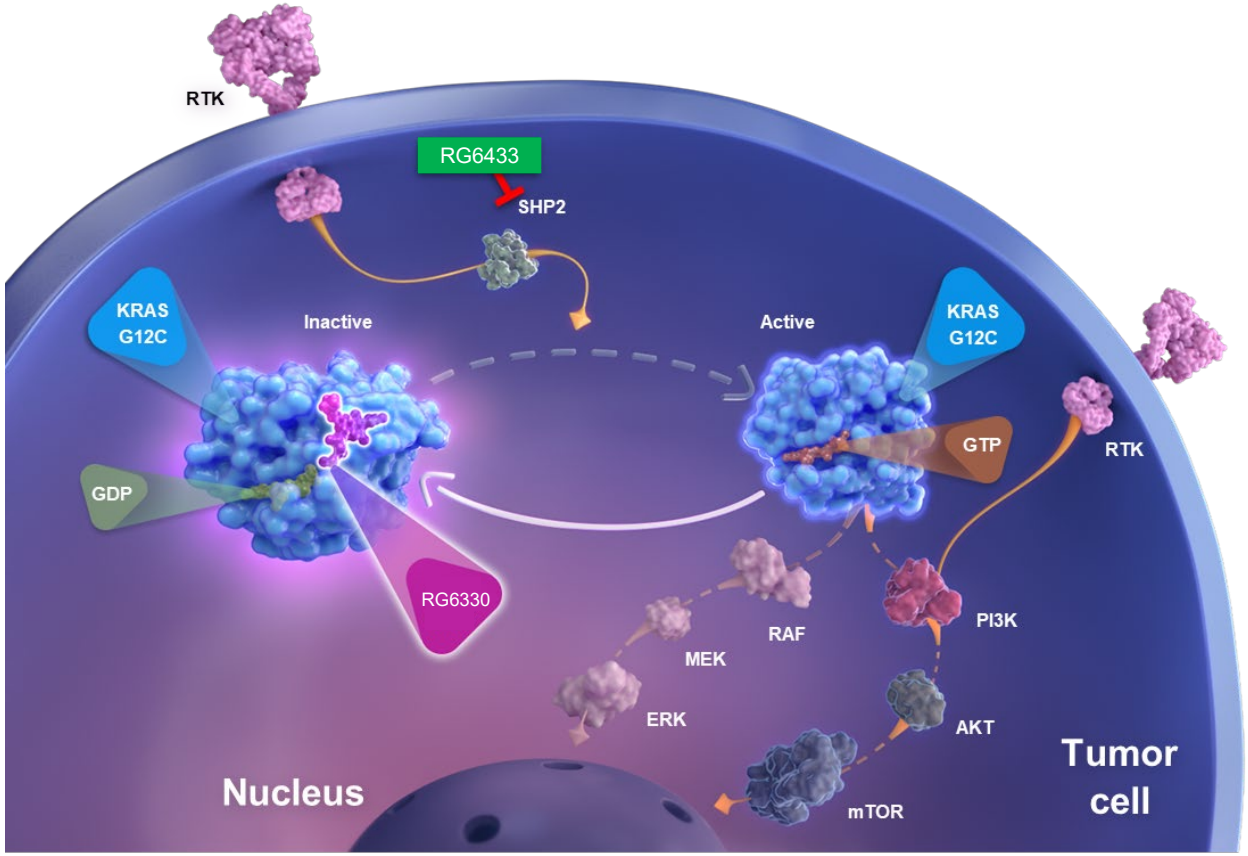


BBB: blood–brain barrier, LGI1: leucine-rich glioma-inactivated protein 1, NMDAR: N-methyl-D-aspartate receptor

1) Satoshi Yoneda: Journal of the Japanese Society of Internal Medicine 102 (8): 2060 -2064, 2013
2) Takashi Inuzuka, Masaru Kuriyama, Takashi Kanda: Brain and Nerve 68 (9): 989 -999, 2016
3) Yukitoshi Takahashi: Clinical Neurology 52 (11): 836 -839, 2012
4) Mariko Oishi, et al.: The 60th Annual Meeting of the Japanese Society of Neurology Pj-051, 2019
5) Takeshita Y, et al. Neurol Neuroimmunol Neuroinflamm. 2021 Oct 19;8(6):e1076
a IgG1 is the predominant antibody subclass in anti-NMDAR encephalitis.
b IgG4 is the predominant antibody subclass in anti-LGI1 encephalitis.

RG6330(KRAS G12C inhibitor)/ RG6433(SHP2 inhibitor)

The combination of RG6330 with RG6433 will be expected synergistic anti-tumor activity.
Local Phase 1 study initiated.



【RG6330 (KRAS G12C inhibitor)】

- GTP-bound KRAS activates multiple downstream signalling pathways involved in cell proliferation, migration, and survival, including MAPK and PI3K pathways. KRAS G12C is in constantly active state, and increases downstream oncogenic signalling, resulting in uncontrollable cancer cell growth and tumor formation.
- RG6330 is designed as an orally available small molecule, and preclinical models showed potent and selective inhibition of the KRAS G12C protein.

【RG6433 (SHP2 inhibitor)】

- Non-receptor protein tyrosine phosphatase SHP2 (PTPN11) plays an important role in the regulation of RAS/MAPK signal transduction, which is downstream of growth factor receptor activation.[1]
- RG6433 is a potent, selective, and orally bioavailable small-molecule SHP2 inhibitor that stabilizes SHP2 in a closed, auto-inhibited conformation.[1]

1. Bret Williams et al. AACR 2022

Overview of Development Pipeline

2022: Key R&D Milestones

	Product	Indication/Study name	Progress
Projects to be approved	Actemra	COVID-19 pneumonia (Japan)	✓
	Mitchga	Atopic dermatitis (Japan)	✓
	Hemlibra	Acquired hemophilia A (Japan)	✓
	Herceptin/Perjeta	HER2 positive colorectal cancer	✓
	Vabysmo	Neovascular age-related macular degeneration (nAMD)	✓
	Vabysmo	Diabetic macular edema (DME)	✓
	Tecentriq	Non-small cell lung cancer (NSCLC) [adjuvant]	✓
	Polivy	**Previously untreated diffuse large B-cell lymphoma (DLBCL)**	✓
P3/Pivotal readouts	Alecensa	ALINA Study: NSCLC [adjuvant]	2023
	crovalimab	COMMODORE 3 study (China): PNH	✓
	nemolizumab	OLYMPIA 2 study: Prurigo nodularis	✓
	gantenerumab	GRADUATE 1/2 study: Alzheimer's disease	
	Vabysmo	**BALATON/COMINO study: RVO**	
	Tecentriq	**IMpower030 study: NSCLC [neoadjuvant]**	2023
	Tecentriq	IMmotion010 study: RCC [adjuvant]	✕
	Tecentriq	IMvoke010 study: HNC [adjuvant]	Continuous assessment
	Tecentriq + Avastin	**IMbrave050 study: HCC [adjuvant]**	2023
	Tecentriq + tiragolumab	SKYSCRAPER-01 study: NSCLC [1st line]	Continuous assessment
	Tecentriq + tiragolumab	SKYSCRAPER-02 study: SCLC	✕

Letters in orange：in-house projects (development in global) Letters in blue：in-licensed from Roche (development and distribution in Japan)

*Underlined are new progress since July 21, 2022

Overview of Development Pipeline

Projected Submissions (Post PoC NMEs and Products)

as of October 24, 2022

NME **Line extension**

in-house

in-licensed (Roche)

Filed

- RG6264 (FDC, sc) BC/CRC
- GAZYVA (RG7159) CLL
- ACTEMRA (MRA/RG1569) COVID-19 pneumonia (US)
- ACTEMRA (MRA/RG1569) SSc-ILD (EU) ★
- HEMLIBRA (ACE910/RG6013) mild-moderate hemophilia A (EU)
- crovalimab (SKY59/RG6107) PNH (China)

2023

- TECENTRIQ (RG7446) 2L NSCLC + cabozantinib
- VABYSMO (RG7716) RVO
- TECENTRIQ (RG7446) NSCLC (neoadjuvant)
- AVASTIN (RG435) 1L SCLC + TECENTRIQ
- gantenerumab (RG1450) Alzheimer's Disease
- TECENTRIQ (RG7446) HNC (adjuvant)
- tiragolumab (RG6058) 1L NSCLC + TECENTRIQ
- TECENTRIQ+AVASTIN (RG7446＋RG435) HCC (adjuvant)
- ALECENSA (AF802/RG7853) NSCLC (adjuvant)
- TECENTRIQ (RG7446) 2L RCC + cabozantinib
- crovalimab (SKY59/RG6107) PNH
- TECENTRIQ (RG7446) 1L Urothelial Carcinoma

2024

- TECENTRIQ (RG7446) eBC (neoadjuvant) ★
- pralsetinib (RG6396) 2L NSCLC
- TECENTRIQ (RG7446) eBC (adjuvant) ★
- mosunetuzumab (RG7828) 3L FL
- TECENTRIQ (RG7446) MIBC (adjuvant)
- tiragolumab + TECENTRIQ (RG6058 + RG7446) NSCLC (Stage III)
- mosunetuzumab+Polivy (RG7828+RG7596) r/r aNHL ★
- ENSPRYNG (SA237/RG6168) gMG
- ranibizumab(PDS) (RG6321) nAMD/DME
- crovalimab (SKY59/RG6107) aHUS
- SRP-9001 (RG6356) DMD

2025 and beyond

- pralsetinib (RG6396) 1L NSCLC
- ENSPRYNG (SA237/RG6168) AIE ★
- mosunetuzumab (RG7828) 2L FL
- ENSPRYNG (SA237/RG6168) MOGAD ★
- giredestrant (RG6171) 1L BC
- GAZYVA (RG7159) LN
- giredestrant (RG6171) BC (adjuvant)
- TECENTRIQ (RG7446) 2L HCC
- crovalimab (SKY59/RG6107) SCD* (US/EU)
- TECENTRIQ+AVASTIN (RG7446＋RG435) HCC(intermediate stage)
- GYM329/RG6237 + Evrisdi SMA*
- tiragolumab + TECENTRIQ (RG6058 + RG7446) Esophageal cancer ☆

★ : new entry ★ : changes in submission year *Before obtaining PoC

Overview of Development Pipeline

Projects under Development (1/2)

As of October 24, 2022

	Phase I	Phase II	Phase III	Filed
Cancer	**LUNA18** - solid tumors **GC33 / codrituzumab** - HCC **ERY974** - solid tumors **STA551** - solid tumors **SOF10 (RG6440)** - solid tumors **SPYK04** - solid tumors **RG7828 / mosunetuzumab** - follicular lymphoma (3L) **RG7421 / cobimetinib** - solid tumors **RG7802 / cibisatamab** - solid tumors **RG6026 / glofitamab** - hematologic tumors **RG6194 / HER2-TDB** - solid tumors **RG6330 / KRAS G12C inhibitor** - solid tumors ★ **RG6433 / SHP2 inhibitor** - solid tumors ★	**RG6396 / pralsetinib** - NSCLC (2L) - solid tumors ★	**AF802 (RG7853) / Alecensa** - NSCLC (adjuvant) **RG7446 / Tecentriq** - NSCLC (neoadjuvant) - NSCLC (2L) - urothelial carcinoma (1L) - MIBC (adjuvant) - RCC (2L) - early BC (adjuvant) - early BC (neoadjuvant) - HCC (2L) - HNC (adjuvant) - prostate cancer (2L) **RG7446 / Tecentriq + RG435 / Avastin** - SCLC (1L) - HCC (adjuvant) - HCC (intermediate stage) **RG7440 / ipatasertib** - prostate cancer (1L) **RG6058 / tiragolumab + RG7446 / Tecentriq** - NSCLC (1L) - NSCLC(stage III) - esophageal cancer **RG6171 / giredestrant** - BC (1L) - BC (adjuvant) **RG7828 / mosunetuzumab** - follicular lymphoma (2L) **RG7828 / mosunetuzumab + RG7596 / Polivy** - r/r aNHL ★ **RG6396 / pralsetinib** - NSCLC (1L)	**RG7159 / Gazyva** - CLL **RG6264 (PER/HER)*** - BC/CRC ★

Letters in orange：in-house projects (development in global)　**Letters in blue**：in-licensed from Roche (development and distribution in Japan)

In principle, completion of first dose is regarded as the start of clinical studies in each phase.　★: Projects with advances in stages since July 21, 2022

* PER/HER fixed-dose subcutaneous combination

Overview of Development Pipeline

Projects under Development (2/2)

As of October 24, 2022

	Phase I	Phase II	Phase III	Filed
Immunology	**DONQ52** - Celiac disease ★		**RG7159 / Gazyva** - lupus nephritis	**MRA (RG1569) / Actemra (US)** COVID-19 pneumonia **MRA (RG1569) / Actemra (EU)** - SSc-ILD ★
Neurology	**GYM329 (RG6237)** - neuromuscular disease **RG7935 / prasinezumab** - Parkinson's disease **RG6100 / semorinemab** - Alzheimer's disease **RG6102 (BS-Gante)** - Alzheimer's disease	**GYM329 (RG6237) + RG7916/ Evrysdi** - SMA (PII/III) **RG7906 / ralmitaront** - schizophrenia	**SA237 (RG6168) / Enspryng** - generalized myasthenia gravis (gMG) - MOGAD ★ - AIE ★ **RG1450 / gantenerumab** - Alzheimer's disease **RG6042 / tominersen** - Huntington's disease **SRP-9001(RG6356) / delandistrogene moxeparvovec** -DMD *	
Hematology	**NXT007 (RG6512)** - hemophilia A (PI/II)	**SKY59 (RG6107) / crovalimab (US/EU)** - sickle cell disease (SCD)	**SKY59 (RG6107) / crovalimab** - PNH - Atypical hemolytic uremic syndrome (aHUS)	**ACE910 (RG6013) / Hemlibra (EU)** - mild-moderate hemophilia A **SKY59 (RG6107) / crovalimab (China)** - PNH ★
Ophthalmology	**RG6321 / PDS** - DME (PI/II) - nAMD (PI/II)		**RG7716 / Vabysmo** - retinal vein occlusion	
Other	**AMY109** - endometriosis			

Letters in orange：in-house projects (development in global) **Letters in blue**：in-licensed from Roche (development and distribution in Japan) * Sarepta manages the global study, including Japan

In principle, completion of first dose is regarded as the start of clinical studies in each phase. ★: Projects with advances in stages since July 21, 2022

Overview of Development Pipeline

Advances in Major Chugai Originated Projects Licensed Out to the 3rd Party

★: changes since July 21, 2022　　As of October 24, 2022

Development code	Mode of Action	Licensee	Granted rights to licensee	Indication	Stage	Progress
CKI27 (VS-6766)	RAF/MEK inhibitor	Verastem Oncology	exclusive global license for the manufacturing, development and marketing	Ovarian cancer	global: P2	• US FDA BTD（recurrent LGSOC in combination with defactinib）
				NSCLC	global: P2	—
					global: P1/2	• RAMP 203 trial (in combination with KRAS G12C inhibitor sotorasib) initiated • RAMP 204 trial (in combination with KRAS G12C inhibitor, adagrasib) initiated ★
CIM331/ nemolizumab	Anti-IL-31 receptor A humanized monoclonal antibody	Global (Galderma) Japan (Maruho)	Galderma exclusive global license for the development and marketing excluding Japan and Taiwan Maruho rights for development and marketing in the skin disease area for the Japanese market	Atopic dermatitis	global: P3	—
					Japan: launched ★	Granted regulatory approval for itch associated with atopic dermatitis
				Prurigo nodularis	global: P3	• US FDA BTD • Primary endpoint was met in the one of two P3 studies
					Japan: P2/3	—
				CKDaP	global: P2/3	—
OWL833 (LY3502970)	Oral non-peptidic GLP-1 receptor agonist	Eli Lilly and Company	worldwide development and commercialization rights	Type 2 diabetes	global: P2	• Conduct a 12-week proof of concept study in type 2 diabetes (P1b) ✓ Highest dose group of OWL833 shows 4.71 kg weight loss and 1.77% lowering of HbA1c
				Obesity	global: P2	• PK data in healthy volunteers were presented in June 2022

Overview of Development Pipeline

FoundationOne CDx Cancer Genomic Profile -Companion diagnostic indications-

As of October 24, 2022

Alterations	Cancer type	Relevant drugs
Activated *EGFR* gene alterations	Non-small cell lung cancer (NSCLC)	afatinib dimaleate, erlotinib hydrochloride, gefitinib, osimertinib mesylate, dacomitinib hydrate
EGFR exon 20 T790M alterations		osimertinib mesylate
ALK fusion genes		alectinib hydrochloride, crizotinib, ceritinib, brigatinib
ROS1 fusion genes		entrectinib
MET exon 14 skipping alterations		capmatinib hydrochloride hydrate
BRAF V600E and V600K alterations	Malignant melanoma	dabrafenib mesylate, trametinib dimethyl sulfoxide, vemurafenib, encorafenib, binimetinib
ERBB2 copy number alterations (HER2 gene amplification positive)	Breast cancer	trastuzumab (genetical recombination)
KRAS/NRAS wild-type	Colorectal cancer	cetuximab (genetical recombination), panitumumab (genetical recombination)
Microsatellite Instability-High		nivolumab (genetical recombination)
Microsatellite Instability-High	Solid tumors	pembrolizumab (genetical recombination)
Tumor Mutational Burden-High		pembrolizumab (genetical recombination)
NTRK1/2/3 fusion gene		entrectinib, larotrectinib sulfate
BRCA1/2 alterations	Ovarian cancer	olaparib
BRCA1/2 alterations	Prostate cancer	olaparib
FGFR2 fusion genes	Biliary tract cancer	pemigatinib

FoundationOne Liquid CDx Cancer Genomic Profile

Companion diagnostic indications

As of October 24, 2022

Alterations	Cancer type	Relevant drugs
Activated *EGFR* gene alterations	Non-small cell lung cancer (NSCLC)	afatinib dimaleate, erlotinib hydrochloride, gefitinib, osimertinib mesylate
EGFR exon 20 T790M alterations		osimertinib mesylate
ALK fusion genes		alectinib hydrochloride, crizotinib, ceritinib
ROS1 fusion genes		entrectinib
NTRK1/2/3 fusion gene	Solid tumors	entrectinib
BRCA1/2 alterations	Prostate cancer	olaparib

Public Clinical Trial Information regarding Chugai Originated Products to be Initiated

NOTE: No additional data other than public information are disclosed prior to initiation of trials

Development Code	Indication	Phase	CT information
AF802 / Alecensa	NSCLC (stage III) Platform study	P3	NCT05170204
SKY59 / crovalimab	GBS	P3	NCT05494619
	LN	P1	ISRCTN12809537
GYM329	FSHD	P2	2021-006255-34
RAY121	Immunology diseases	P1	https://jrct.niph.go.jp/latest-detail/jRCT2071220036

Abbreviations

ACT	Actemra
aHUS	atypical hemolytic uremic syndrome
AIE	autoimmune encephalitis
aNHL	aggressive B-cell non-Hodgkin lymphoma
BC	breast cancer
bTMB	blood tumor mutation burden
CKDaP	chronic kidney disease associated pruritus
CLL	chronic lymphocytic leukemia
DLBCL	diffuse large B-cell lymphoma
DMD	Duchenne muscular dystrophy
DME	diabetic macular edema
eBC	early breast cancer
FDC	fixed-dose combination
FL	follicular lymphoma
FSHD	facioscapulohumeral muscular dystrophy
GBS	Guillain-Barré syndrome
gMG	generalized myasthenia gravis
HCC	hepatocellular carcinoma
HEM	Hemlibra
HNC	head and neck carcinoma
ICDS	international celiac disease symposium
ILD	Interstitial lung disease
LGSOC	low-grade serous ovarian cancer
LN	lupus nephritis
MIBC	muscle-invasive bladder cancer
MOA	mode of action
MOGAD	myelin oligodendrocyte glycoprotein antibody–associated disease
nAMD	neovascular age-related macular degeneration
NSCLC	non-small cell lung cancer
PDS	port delivery system with ranibizumab
PNH	paroxysmal nocturnal hematuria
PS	profit share
r/r	relapsed or refractory
RCC	renal cell carcinoma
RON	Ronapreve
ROY	royalty
RVO	retinal vein occlusion
SCD	sickle cell disease
SCLC	small cell lung cancer
SSc	systemic sclerosis
TDB	T cell-dependent bispecific antibody

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