



Roche Roche Group

TOP INNOVATOR  
**TOPi 2030**

# Conference on FY2021.12 Financial Results

## CHUGAI PHARMACEUTICAL CO., LTD.

3 February 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 and are consistent with the Core concept disclosed by Roche. 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, including the return to shareholders.

Note:

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

# Agenda



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**Dr. Osamu Okuda**

President & CEO

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**Toshiaki Itagaki**

Executive Vice President & CFO

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**Tetsuya Yamaguchi**

Executive Vice President, Head of Project & Lifecycle Management Unit

# FY2021 Overview and FY2022 Forecast

**Dr. Osamu Okuda**

President & CEO

# 2021 Financial Performance

- Significant YoY increase in revenues and profits, exceeding the revised forecast for 2021
- Achieved record-high revenues, operating income, and net income for five consecutive fiscal years

Core (billions of JPY)	2020 Jan - Dec actual	2021 Jan - Dec actual	Growth (year on year)		Revised Forecast	
					Jan - Dec	Vs. 2021 actual
<b>Revenues</b>	<b>786.9</b>	<b>999.8</b>	<b>+212.9</b>	<b>+27.1%</b>	<b>970.0</b>	<b>103.1%</b>
Domestic sales	409.1	518.9	+109.8	+26.8%	513.0	101.2%
Overseas sales	224.2	283.9	+59.7	+26.6%	268.5	105.7%
ROOI	153.6	196.9	+43.3	+28.2%	188.5	104.5%
<b>Operating profit</b>	<b>307.9</b>	<b>434.1</b>	<b>+126.2</b>	<b>+41.0%</b>	<b>400.0</b>	<b>108.5%</b>
Operating margin	39.1%	43.4%	+4.3%pts	-	41.2%	-
<b>Net income</b>	<b>219.4</b>	<b>311.5</b>	<b>+92.1</b>	<b>+42.0%</b>	<b>293.0</b>	<b>106.3%</b>
<b>EPS (yen)*</b>	<b>133.39</b>	<b>189.35</b>	<b>+55.96</b>	<b>+42.0%</b>	<b>178.00</b>	<b>106.4%</b>

- Domestic sales significantly increased due to the growth of Tecentriq, Hemlibra, Kadcyra, Actemra, and steady market penetration of new products such as Ronapreve (supply to the government), Enspryng, Polivy, Evrysdi, and F1LCDx, despite the effect of drug price revisions and generics.
- Overseas sales increased as Hemlibra far exceeded expectations, although Actemra's export to Roche decreased as expected
- ROOI increased mainly due to an increase in royalty and profit-sharing income based on the growth in overseas' local sales of Hemlibra
- Achieved the full-year forecast, which was revised upward on October 22.

ROOI: Royalties and other operating income

\* Effective July 1, 2020, Chugai has implemented a three-for-one stock split of its common stock. EPS is calculated based on the assumption that the stock split was implemented at the beginning of fiscal year 2020.

# Review of Strategic Policies for 2021 (1/2)

## Continuous creation of R&D output

With the contribution of projects not anticipated at the beginning of the fiscal year, regulatory filings, approvals, and launches exceeded the plan

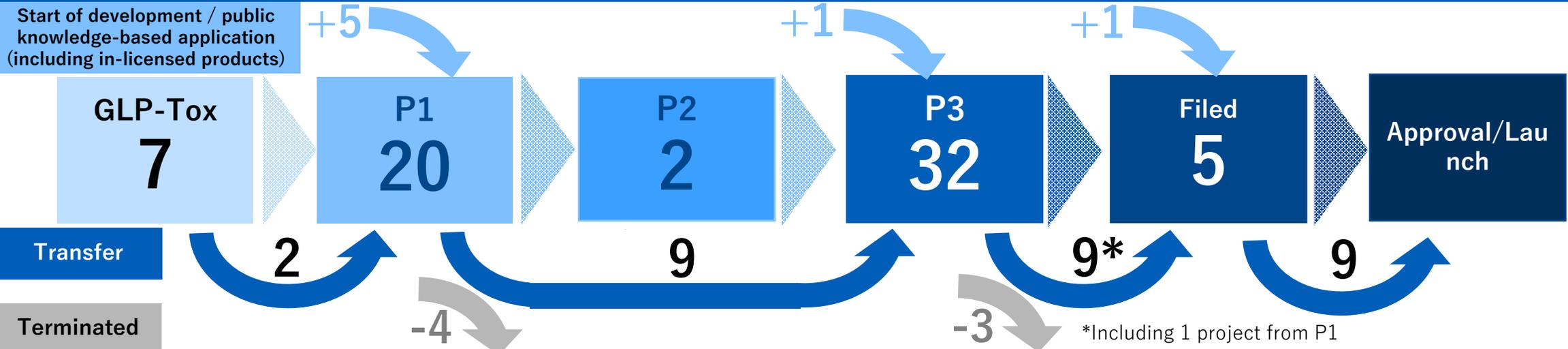
- Approval/Launch (9): Polivy (r/r DLBCL), Evrysdi (SMA), F1LCDx, Ronapreve/Actemra (COVID-19), Cellcept (GVHD), etc.
- Filed (10): Faricimab (DME, nAMD), Tecentriq (NSCLC Adjuvant), etc.

Acquired PoC in 2 projects, steady progress in early and late-stage development projects

- P3: Started GP3 for 10 projects including Roche projects and in-house projects
- PoC: Obtained PoC by the licensee for in-house developed projects CKI27 and OWL833
- P1: Started P1 of in-house proprietary technology projects for mid-size molecule LUNA18 and antibody SOF10

### Changes in the number of R&D projects

※ As of February 3, 2022



# Review of Strategic Policies for 2021 (2/2)

## Maximizing value of growth drivers

- Tecentriq: Market penetration accelerated by additional indication for hepatocellular carcinoma
- Enspryng: Approved in a total of 62 countries (as of December 2021). Domestic sales grew more than expected
- Polivy, Evrydsi: Market penetration exceeded expectations as a new product
- Hemlibra: The delay in global market penetration due to COVID-19 has gradually resolved and is now on a sustainable growth trend
- Actemra: Increase global demand and strengthen/expand supply system with COVID-19
- Distribution policy: Implemented an efficient distribution policy

## Acceleration of DX

- Established antibody design technology (LI/LO\*) utilizing AI technology
- Improved efficiency of clinical trial operations
- Evolution of a new customer engagement model
- Started building a production system by utilizing robotics
- Selected as a DX brand for the second consecutive year

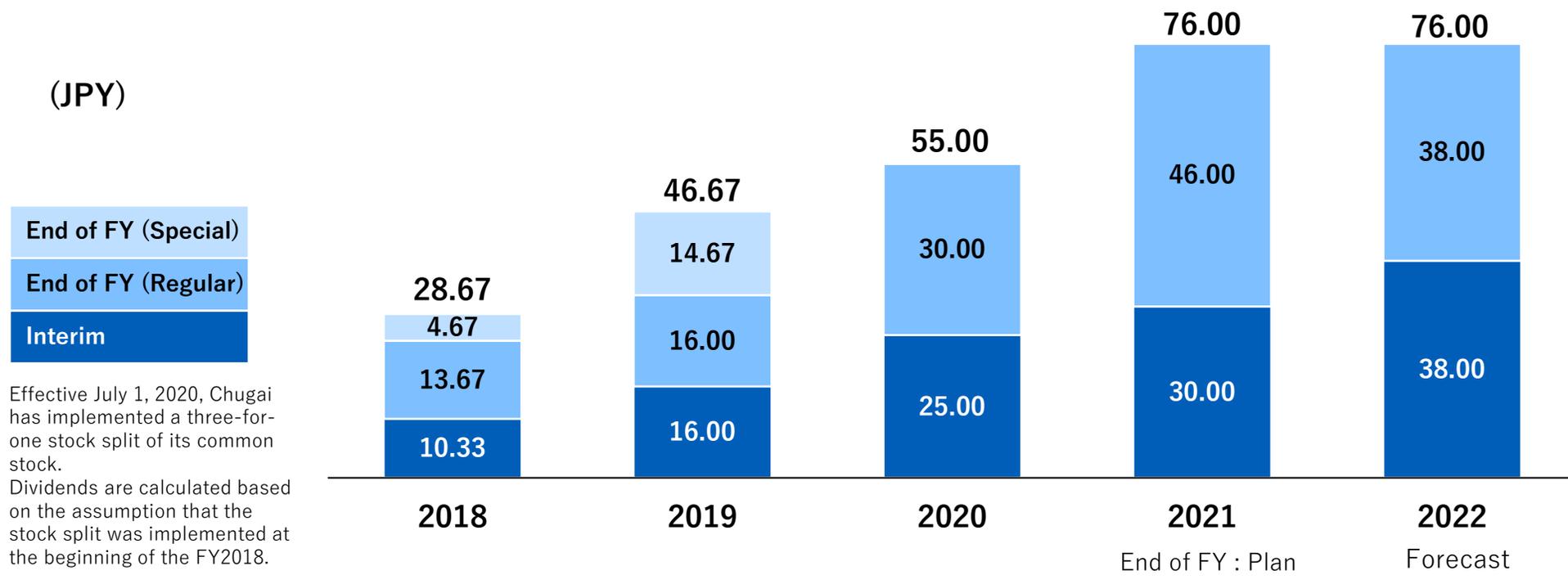
## Strengthen business foundation

- Promoted proper operation of the new personnel system (revised the position profile based on the new growth strategy)
- Achieved single-year environmental targets (waste recycling ratio, final disposal ratio, WET tests conducting ratio, chemical substances in wastewater)
- Continued selection to major ESG indices (DJSI, FTSE4Good, MSCI ESG Leaders)
- Established and built an internal system for the execution of insight business
- Prepared company-wide risk map/risk appetite statement

# Contribution to shareholders

## ■ Basic profit distribution principles

- ✓ Taking into account strategic funding needs and earnings prospects, Chugai sets a target for a consolidated dividend payout ratio of 45% on average in comparison with Core EPS, with an aim to continuously provide a stable allocation of profit to all shareholders.



Effective July 1, 2020, Chugai has implemented a three-for-one stock split of its common stock. Dividends are calculated based on the assumption that the stock split was implemented at the beginning of the FY2018.

Dividend payout ratio	5-year average	2018	2019	2020	2021	2022
	Single FY	48.6%	48.7%	45.8%	41.2%	40.1%

# 2022 Forecast

- Revenues and profits are expected to increase due to the growth in mainstay/new products and an increase in COVID-19-related revenues
- Aiming to achieve record high financial results for six consecutive years, with over 1 trillion JPY revenues for the first time since founded

Core (billions of JPY)	2021 Jan - Dec actual	2022 Jan - Dec forecast	Growth (year on year)	
<b>Revenues</b>	<b>999.8</b>	<b>1150.0</b>	<b>+150.2</b>	<b>+15.0%</b>
Domestic sales	518.9	646.3	<b>+127.4</b>	<b>+24.6%</b>
Overseas sales	283.9	385.2	<b>+101.3</b>	<b>+35.7%</b>
ROOI	196.9	118.5	<b>-78.4</b>	<b>-39.8%</b>
<b>Operating profit</b>	<b>434.1</b>	<b>440.0</b>	<b>+5.9</b>	<b>+1.4%</b>
Operating margin	43.4%	38.3%	-5.1%pts	-
<b>Net income</b>	<b>311.5</b>	<b>312.5</b>	<b>+1.0</b>	<b>+0.3%</b>
<b>EPS (yen)*</b>	<b>189.35</b>	<b>190.00</b>	<b>+0.65</b>	<b>+0.3%</b>

- In domestic sales, in addition to the significant increase in Ronapreve, new products such as Hemlibra, Polivy, Enspryng, and Evrysdi will steadily penetrate the market.
- Overseas sales are expected to increase significantly due to Actemra and Hemlibra
- Regarding ROOI, royalty income related to the initial shipment of Hemlibra will decrease, but this will be covered by the increase in export sales and royalty income related to intellectual property rights
- Revenues, operating profit, and net income will reach record-highs

\* Effective July 1, 2020, Chugai has implemented a three-for-one stock split of its common stock. EPS is calculated based on the assumption that the stock split was implemented at the beginning of fiscal year 2020.

# Strategic Policies for 2022

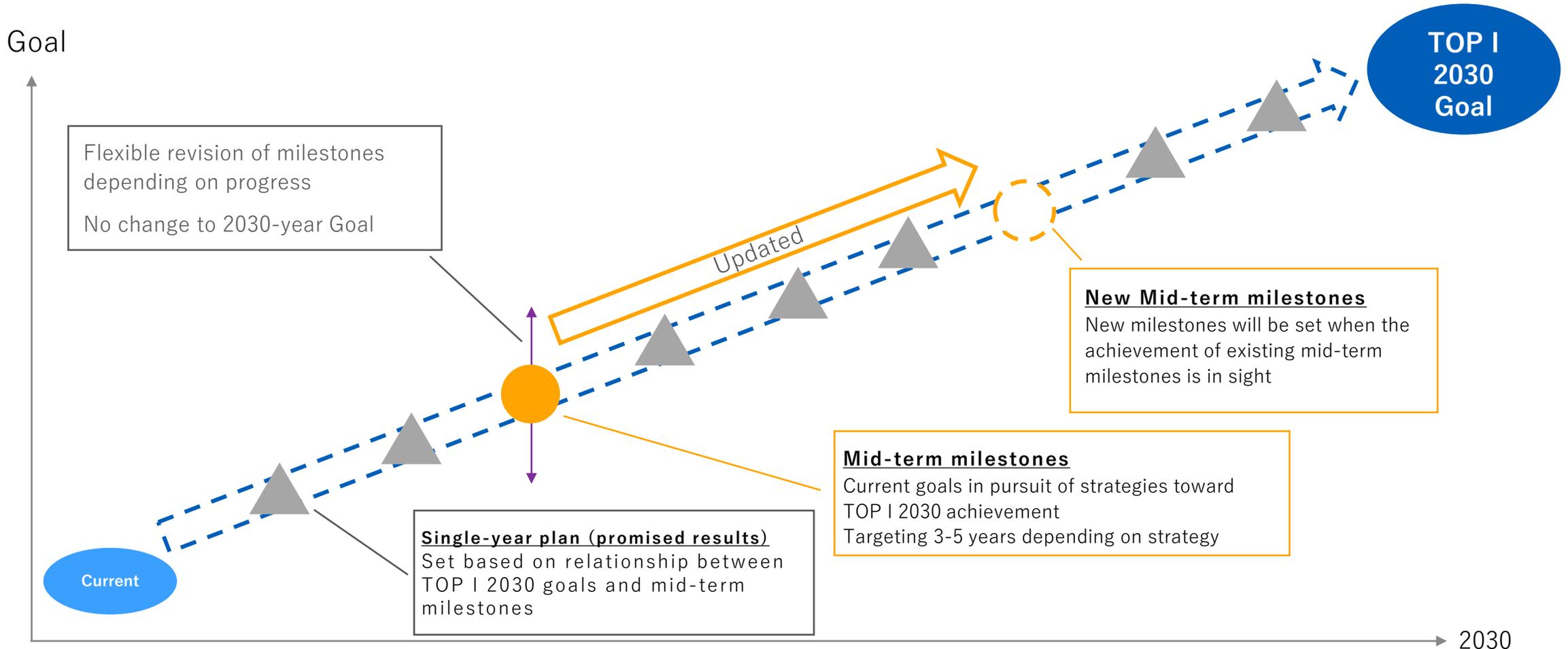
<p><b>Continuous creation of R&amp;D output</b></p>	<ul style="list-style-type: none"> <li>• Expansion and steady progress in mid-size molecule projects (progress of LUNA18 and subsequent projects, construction of manufacturing system)</li> <li>• Continuous creation of in-house new projects (accelerating drug discovery with new antibody technology and exploring new modalities)</li> <li>• Proof of the value of in-house Pre-PoC projects (PoC acquisition and P1 study progress)</li> <li>• Maximize project value of growth drivers for in-house projects (acceleration of development including expansion of indication for crovalimab, Enspryng, and Alecensa)</li> <li>• Steady achievement of approval/application plan: Application for Tecentriq (4 cancer types), tiragolumab (SCLC), HER/PER fixed-dose combination drug (BC), etc.</li> </ul>
<p><b>Maximize the value of growth drivers</b></p>	<ul style="list-style-type: none"> <li>• Successful introduction of new products to the market (faricimab (DME/nAMD)、Tecentriq (NSCLC adjuvant)、Polivy (1L DLBCL), etc.)</li> <li>• Accelerating market penetration of growth drivers in Japan and overseas (Hemlibra, Tecentriq, Polivy, Enspryng, Evrysdi, etc.)</li> <li>• Establishment of the new distribution system (further penetration of product value)</li> </ul>
<p><b>Strengthen business foundation</b></p>	<ul style="list-style-type: none"> <li>• Streamlining and strengthening the entire value chain (production, development, global regulatory, etc.)</li> <li>• Further strengthening of the ESG foundation (environmental investment, governance)</li> <li>• Development of foundations for creating innovation (human resources strategy, digital utilization)</li> </ul>



\* Research and Early Development

# Positioning of Mid-term milestones

- We will stop developing company-wide 3-year mid-term business plans to review and update strategies/plans in an agile manner
- Confirm validity of TOP I 2030 goals, Mid-term milestones, and Single-year plan



# Mid-term Milestones (1/5)

Milestones <Target year>		Progress
Drug Discovery	Acquisition of ePoC for LUNA18 <2024>	● On Schedule
	Continuous Creation of Drug Discovery Projects Utilizing Mid-size Molecule Technology <2023-2025> (Quantitative target for PC transition exists)	PC transition: zero* (2021)
	Establishment of New Technologies that Enhance Competitive Advantage (Acquisition of new MOA) <2023-2025>	● On Schedule
	Developing Next-Generation Antibody Technologies to Solve Drug-Wants • PC transition of new antibody engineering technologies that work selectively with tissue and cells following Switch-Ig <2023>	● On Schedule
	Establishment of a Technology Platform and New Modality Research Platform Comprising of Multiple Modalities with Competitive Advantages • PoC of new technologies through combination of protein engineering technology and new modalities <2023> • Project creation and PC transition by combining antibody engineering technologies and new modalities <2025>	● On Schedule ● On Schedule
	Strengthening the Drug Discovery Process by Utilizing Digital Technology • Antibodies: Efficiency of the discovery process through machine learning technology <2023> • Implementation of lab automation at Yokohama site <2024> • Improve drug discovery productivity by establishing a digital infrastructure (Quantitative target exists for FTE reduction) <2024>	● On Schedule ● On Schedule ● On Schedule
	Creation and Promotion of Innovative Drug Discovery Projects by Strengthening Biology • Development of a system for utilizing human clinical samples to improve the accuracy of non-clinical research <2024> • Creation of a platform for drug discovery approaches that target continuous innovation from a biological perspective <2024>	● On Schedule ● On Schedule
	Capturing External Innovation • Incorporation of new modalities, technologies, numerators (Quantitative target exists for the number of projects implemented) <2024>	In-licensed: 2 projects (2021)

\* PC transition in antibody / small molecule projects: total 3

# Mid-term Milestones (2/5)

Milestones <Target year>		Progress
Development	<b>Strengthen the Clinical Predictability Platform and Implement Model &amp; Simulation (M&amp;S) Projects</b> <ul style="list-style-type: none"> <li>Improving clinical predictability through M&amp;S and implementing clinical trials based on M&amp;S &lt;2025&gt;                             <ul style="list-style-type: none"> <li>Utilize M&amp;S for molecular design, product candidate selection, safety range forecast, FIH dosing, etc. from the early stages of trials (Quantitative target exists for the percentage of applicable themes)</li> </ul> </li> <li>Implementation of patient segmentation based on pathological biomarkers &lt;2025&gt;</li> </ul>	<p>● On Schedule</p> <p>● On Schedule</p>
	<b>Accelerate value expansion of in-house developed products through simultaneous development of multiple diseases</b> <ul style="list-style-type: none"> <li>Multiple projects for simultaneous development of multiple diseases based on science and commerciality &lt;2023&gt;</li> </ul>	<p>● On Schedule</p>
	<b>Proof of value of in-house projects</b> <ul style="list-style-type: none"> <li>Establishing general-purpose indicators that lead to true endpoint assessment of patients &lt;2025&gt;</li> </ul>	<p>● On Schedule</p>
	<b>Evolution of Late-Stage Development Operations (Quantitative target exists)</b> <ul style="list-style-type: none"> <li>Increase workforce productivity &lt;2023&gt;</li> <li>Implementation of clinical/regulatory applications utilizing RWDs, control group data, disease registry data, etc. &lt;2023&gt;</li> </ul>	<p>● On Schedule</p> <p>● On Schedule</p>

# Mid-term Milestones (3/5)

Milestones <Target year>		Progress
PT	<b>Establishment of Manufacturing System and Process for Mid-size Molecules</b> <ul style="list-style-type: none"> <li>Establishment of mid-size molecule CMC technologies and production bases for API and formulations &lt;2024&gt;                             <ul style="list-style-type: none"> <li>✓ Start operation of FJ2 and manufacturing of investigational drugs</li> <li>✓ Operation of high-difficulty formulation building and start of manufacturing for investigational drugs</li> <li>✓ Establishment of initial commercial manufacturing system (FJ3)</li> </ul> </li> <li>Shortening the time to PoC in collaboration with non-clinical functions &lt;2024&gt;</li> </ul>	<p>● On Schedule</p> <p>● On Schedule</p>
	<b>Establishment of Biopharmaceutical API Manufacturing System in Response to Doubling of R&amp;D output</b> <ul style="list-style-type: none"> <li>Establish a manufacturing system through facilities dedicated to APIs (FIHs) (UK4) &lt;2024&gt;</li> <li>Establish cost reduction technologies for in-house production &lt;2024&gt;</li> <li>Develop antibody pharmaceutical technologies to become the world's forerunner &lt;2027&gt;</li> <li>Shortening the time to IND in collaboration with non-clinical functions &lt;2024&gt;</li> </ul>	<p>● On Schedule</p> <p>● On Schedule</p> <p>● On Schedule</p> <p>● On Schedule</p>
	<b>Establishment of an Efficient Manufacturing System for CPMC</b> <ul style="list-style-type: none"> <li>Strengthen core manufacturing technologies, establish a cost-competitive CPMC system, and firmly establish operations &lt;2023&gt;</li> <li>Establish a CMO management system for future product portfolio &lt;2023&gt;</li> <li>Launch a new operational model at other sites through the development of digital and IT infrastructure &lt;2023&gt;</li> <li>Reflecting the use of robotics in the design of new facilities &lt;2025&gt;</li> </ul>	<p>● On Schedule</p> <p>● On Schedule</p> <p>● On Schedule</p> <p>● On Schedule</p>

PT: Pharmaceutical Technology

# Mid-term Milestones (4/5)

Milestones <Target year>		Progress
VD	<b>Building an Engagement Model to Meet Diversifying Customer Needs</b> <ul style="list-style-type: none"> <li>Implement a precise individual strategy that combines in-person, remote, and digital channels &lt;2023&gt;                             <ul style="list-style-type: none"> <li>✓ Customer satisfaction (cancer): No. 1 in obtaining information other than MRs</li> <li>✓ Customer satisfaction (MA Priority Activity Disease Area Assessment): Top 3 in all areas</li> </ul> </li> <li>✓ Customer satisfaction (providing safety information): No. 1</li> </ul>	No.2/No.1 * Top 2 ** (In all disease areas where products are sold) No.1***
	<b>Creation of Unique Evidence Contributing to Personalized Medicine</b> <ul style="list-style-type: none"> <li>Realization of integrated use of internal and external data for predicting effectiveness and safety &lt;2024&gt;                             <ul style="list-style-type: none"> <li>✓ Provide to healthcare professional research papers about biomarker evidence leading to Personalized Medical &amp; Safety Care</li> <li>✓ Start research to provide solutions utilizing personalized evidence</li> </ul> </li> </ul>	● On Schedule
	<b>Functional Reforms Through Resource Shifts and Digital Use, etc.</b> <ul style="list-style-type: none"> <li>Systematically withdraw from mature areas and invest resources in new areas (Quantitative targets exist) &lt;2023&gt;</li> <li>Establishment of a business execution system that does not interfere with remote work, and the realization of assignments of employees with specialized knowledge from all over the country, regardless of their location &lt;2025&gt;</li> </ul>	● On Schedule  ● On Schedule
	<b>Contribute to Further Advancement of PHC by Expanding New Portfolio (monitoring the efficacy of therapies) &lt;2024&gt;</b>	● On Schedule

VD: Value Delivery

\* Source: MCI survey results <Owned media ranking (2nd), Medical portal site ranking (1st)>

\*\* Source: INTAGE Healthcare Inc., survey results

\*\*\* Source: The total results of all respondents of "INTAGE Healthcare Inc., 2021 questionnaire about safety information needs"

# Mid-term Milestones (5/5)

Milestones <Target year>		Progress
Foundation (People & Organization)	<b>Increase in active employees based on awareness survey results</b> <ul style="list-style-type: none"> <li>Percentage of active employees: Achieved the same level as companies with strong global performance &lt;2024&gt;</li> </ul>	(No survey conducted in 2021)
	<b>Acceleration and penetration of D&amp;I</b> <ul style="list-style-type: none"> <li>Positive response rate for employee awareness survey innovation questions (Quantitative target exists) &lt;2024&gt;</li> <li>Ratio of female managers/Ratio of female managers with subordinates: 17%/17% achieved &lt;2023&gt;</li> </ul>	(No survey conducted in 2021) 15.9%/15.0%
Foundation (Digital)	<b>Improve Efficiency of All Value Chains</b> <ul style="list-style-type: none"> <li>Improve productivity of targeted operations based on the impact of digital investment projects (Quantitative target exists) &lt;2025&gt;</li> </ul>	● On Schedule
Foundation (Environment)	<b>Strengthen the Foundation for Sustainability at the Global Level</b> <ul style="list-style-type: none"> <li>Continued selection for Dow Jones Sustainable Index World &lt;2025&gt;</li> <li>Scope 1 + 2 CO<sub>2</sub> emissions: Achieved 40% reduction (compared to 2019) &lt;2025&gt;</li> <li>Use of CFCs: Achieve 25% reduction (compared to 2020) &lt;2025&gt;</li> </ul>	DJSI World Selected ● On Schedule ● On Schedule
Foundation (Quality)	<b>Next-Generation Quality Management that Balances Quality and Efficiency with an Eye Toward New Modalities and New Business Processes</b> <ul style="list-style-type: none"> <li>Productivity improvement: Personnel and costs per product and development projects (Quantitative target exists) &lt;2024&gt;</li> <li>Establishment of a Chugai Quality System for Total Assurance of Products in New Domains &lt;2024&gt;</li> </ul>	● On Schedule ● On Schedule
Foundation (Overseas)	<b>Strengthen Overseas Business Foundation to Drive Growth and Maximize Chugai products Global Value</b> <ul style="list-style-type: none"> <li>Launch 6 in-house products globally (ACT, ALC, HEM, ENS, SKY59, CIM331) &lt;2025&gt;</li> <li>Establishment of early development and regulatory systems at U.S. and European subsidiaries in response to an increase in early-stage projects &lt;2025&gt;</li> </ul>	4 products ● On Schedule
Foundation (Insight Business)	<b>Search for commercialization of insight business</b> <ul style="list-style-type: none"> <li>Establishment of an Insight Business promotion system (infrastructure development, capabilities, and information aggregation as a hub) &lt;2024&gt;</li> <li>Start using data assets aggregated through in-house projects or Use Case related to the FMU business &lt;2025&gt;</li> </ul>	● On Schedule ● On Schedule

# Mid- to Long-term Revenue Outlook (Excluding Ronapreve)

- **Short-Mid-term:** Expect a growth trend in the short-mid term by making up for the decline in sales of Actemra and Avastin, both major products, through further market penetration of several major products developed in-house and the launch of new Roche products
- **Long-term:** Increased revenues and sustainable growth are expected both in Japan and overseas due to sales growth of in-house created products, launch of in-house early development products using new antibody technologies and mid-size molecules, and domestic growth and launch of Roche products

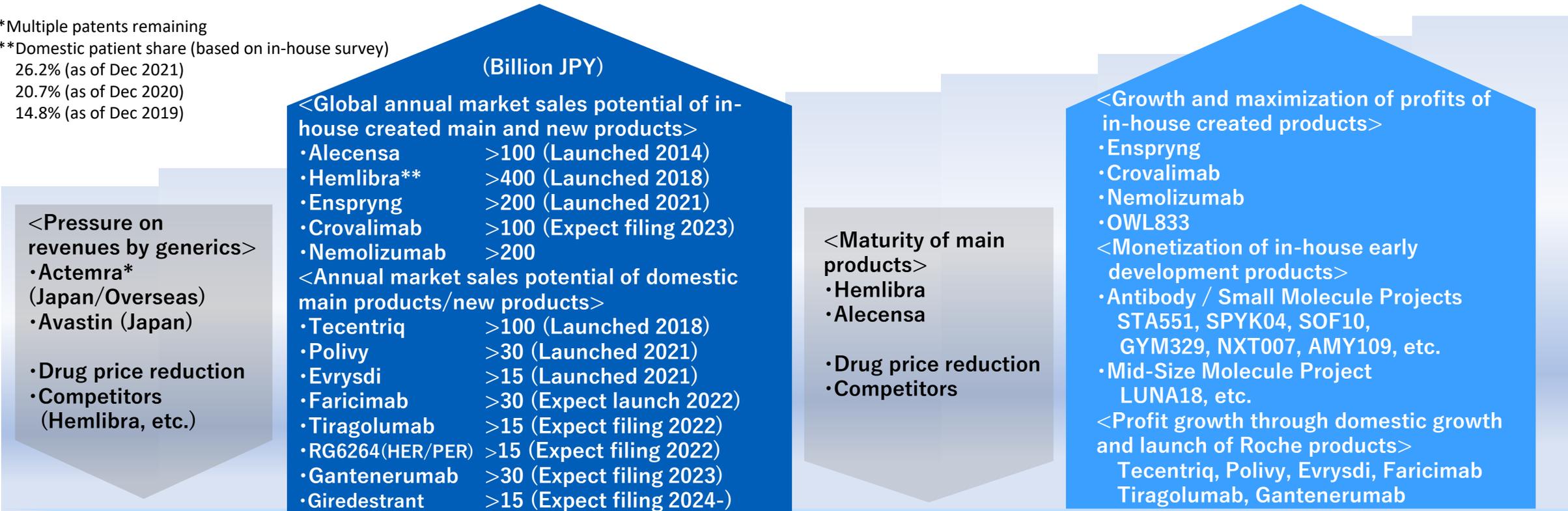
\*Multiple patents remaining

\*\*Domestic patient share (based on in-house survey)

26.2% (as of Dec 2021)

20.7% (as of Dec 2020)

14.8% (as of Dec 2019)



Mid-term (- 2025)

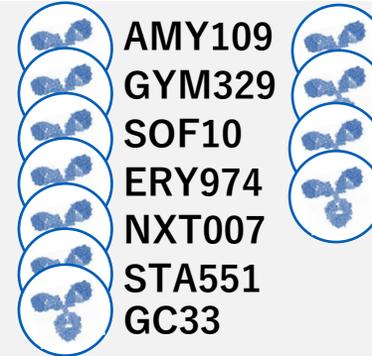
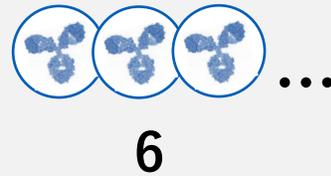
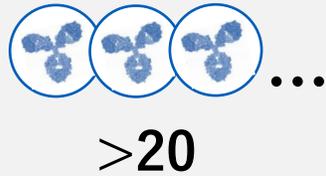
Long-term (- 2030)

# Research Portfolio of Each Modality

as of February 3, 2022



## Antibody drugs



AMY109  
GYM329  
SOF10  
ERY974  
NXT007  
STA551  
GC33

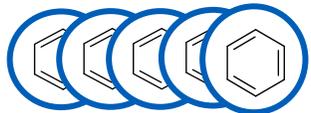


**nemolizumab**  
crovalimab  
Enspryng (gMG)  
Hemlibra (AHA)

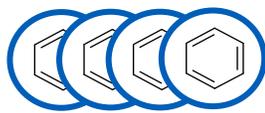


Enspryng  
Hemlibra  
Actemra

## Small molecule drugs



Hit Identification  
5



Lead Optimization  
4

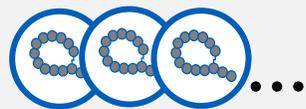


SPYK04  
**EOS789**  
**OWL833**  
**CKI27**  
Alecensa (NSCLC adjuvant)

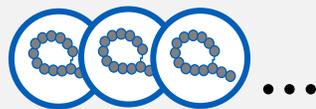


Alecensa  
Edirol  
Oxarol  
**Deberza**

## Mid-size molecule drugs



Lead Identification  
16



Lead Optimization  
10



LUNA18

Orange: Outsourced to a third party other than Roche

# New Management Structure

Underline: new position/role

Name	Rank	Supervisory responsibility
Osamu Okuda	Representative Director, President CEO	<u>Chairman of the Board of Directors (role)</u> <u>Corporate Planning, Partnering, External Affairs and Audit</u>
Hisafumi Yamada	<u>Director</u> , Executive Vice President	Project & Lifecycle Management (R&D), Research, Translational Research, <u>Clinical Development and Pharmaceutical Technology</u>
Toshiaki Itagaki	<u>Director</u> , Executive Vice President CFO	Finance & Accounting, Corporate Communication and Purchasing

- Hisafumi Yamada and Toshiaki Itagaki are scheduled to be appointed as directors upon approval at the 111th Ordinary General Meeting of Shareholders to be held on March 29, 2022
- Tatsuro Kosaka, Chairman and Representative Director, and Motoo Ueno, Representative Director, Deputy Chairman, will retire on March 29, 2022, and will be appointed as Senior Advisors at the Board of Directors meeting held on the same day.

# Summary

- In 2021, revenues and profits increased for the fifth consecutive year, achieving record-high. In 2022, we expect revenue and profit increase for the sixth consecutive year, exceeding 1 trillion yen for the first time since the company's foundation
- As the first year of TOP I 2030, strategic policies were achieved almost as planned
- With abundant pipelines and steady progress in R&D, including mid-size molecules, we expect sustainable growth over the mid to long term towards the realization of TOP I 2030
- By disclosing the progress of development pipelines consisting of various modalities and the mid-term milestones, we will continue to clarify the path of growth
- Under the new management structure, we aim to become a "top innovator in the global healthcare industry"

# FY2021 Consolidated Financial Overview (Core)

**Toshiaki Itagaki**

Executive Vice President & CFO

# P/L Jan - Dec (Year on Year)

(Billions of JPY)	2020	2021	Growth	
<b>Revenues</b>	<b>786.9</b>	<b>999.8</b>	+ 212.9	+ 27.1%
Sales	633.3	802.8	+ 169.5	+ 26.8%
Domestic	409.1	518.9	+ 109.8	+ 26.8%
Overseas	224.2	283.9	+ 59.7	+ 26.6%
Royalties and other operating income	153.6	196.9	+ 43.3	+ 28.2%
Royalty and profit-sharing income	129.6	187.2	+ 57.6	+ 44.4%
Other operating income	24.1	9.8	- 14.3	- 59.3%
<b>Cost of sales</b>	<b>-272.3</b>	<b>-335.5</b>	- 63.2	+ 23.2%
(cost to sales ratio)	43.0%	41.8%	-1.2%pts	-
<b>Operating expenses</b>	<b>-206.7</b>	<b>-230.2</b>	- 23.5	+ 11.4%
M&D and G&A <sup>*1</sup>	-93.2	-100.4	- 7.2	+ 7.7%
Research and development	-113.5	-129.8	- 16.3	+ 14.4%
<b>Operating profit</b>	<b>307.9</b>	<b>434.1</b>	+ 126.2	+ 41.0%
(operating margin)	39.1%	43.4%	+4.3%pts	-
Financial account balance	-3.0	-2.5	+ 0.5	- 16.7%
Income taxes	-85.5	-120.1	- 34.6	+ 40.5%
<b>Net income</b>	<b>219.4</b>	<b>311.5</b>	+ 92.1	+ 42.0%
<b>EPS (JPY) <sup>*2</sup></b>	<b>133.39</b>	<b>189.35</b>	+55.96	+ 42.0%

## Domestic sales

Significant increase due to sales growth of new products as well as mainstay products

## Overseas sales

Decrease in sales of Actemra, but significant increase in export of Hemlibra

## Royalty and profit-sharing income

Significant increase in income for Hemlibra

## Other operating income

Decrease in one-time income

## Cost of sales

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

## Operating expenses

Increase of M&D and G&A expenses due to business tax and promotion of digital marketing  
Increase of research and development expenses due to progress of projects, etc.

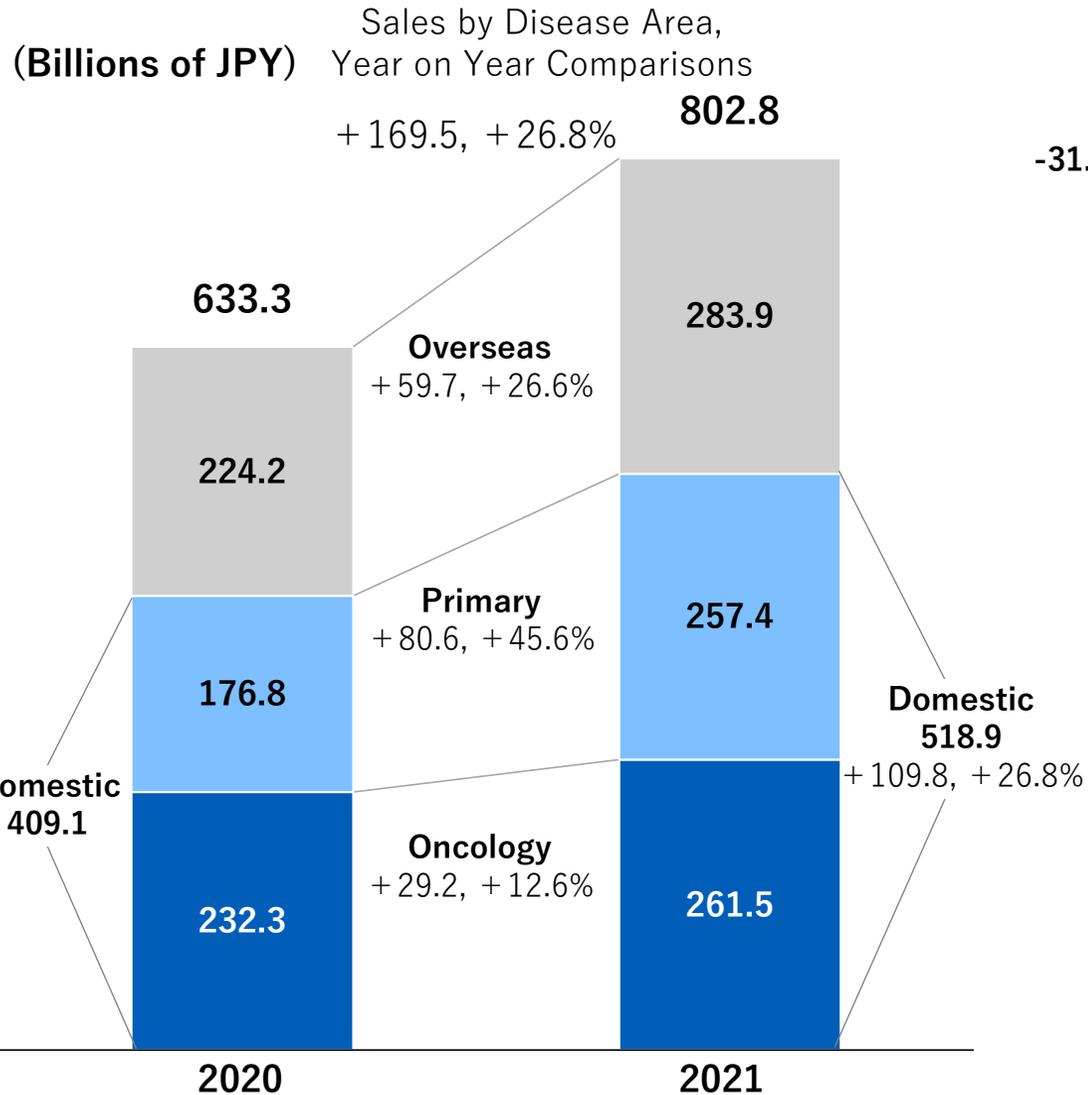
## Operating profit

Increased due to higher royalty and profit-sharing income as well as increase in sales

<sup>\*1</sup> M&D: Marketing and distribution, G&A: General and administration

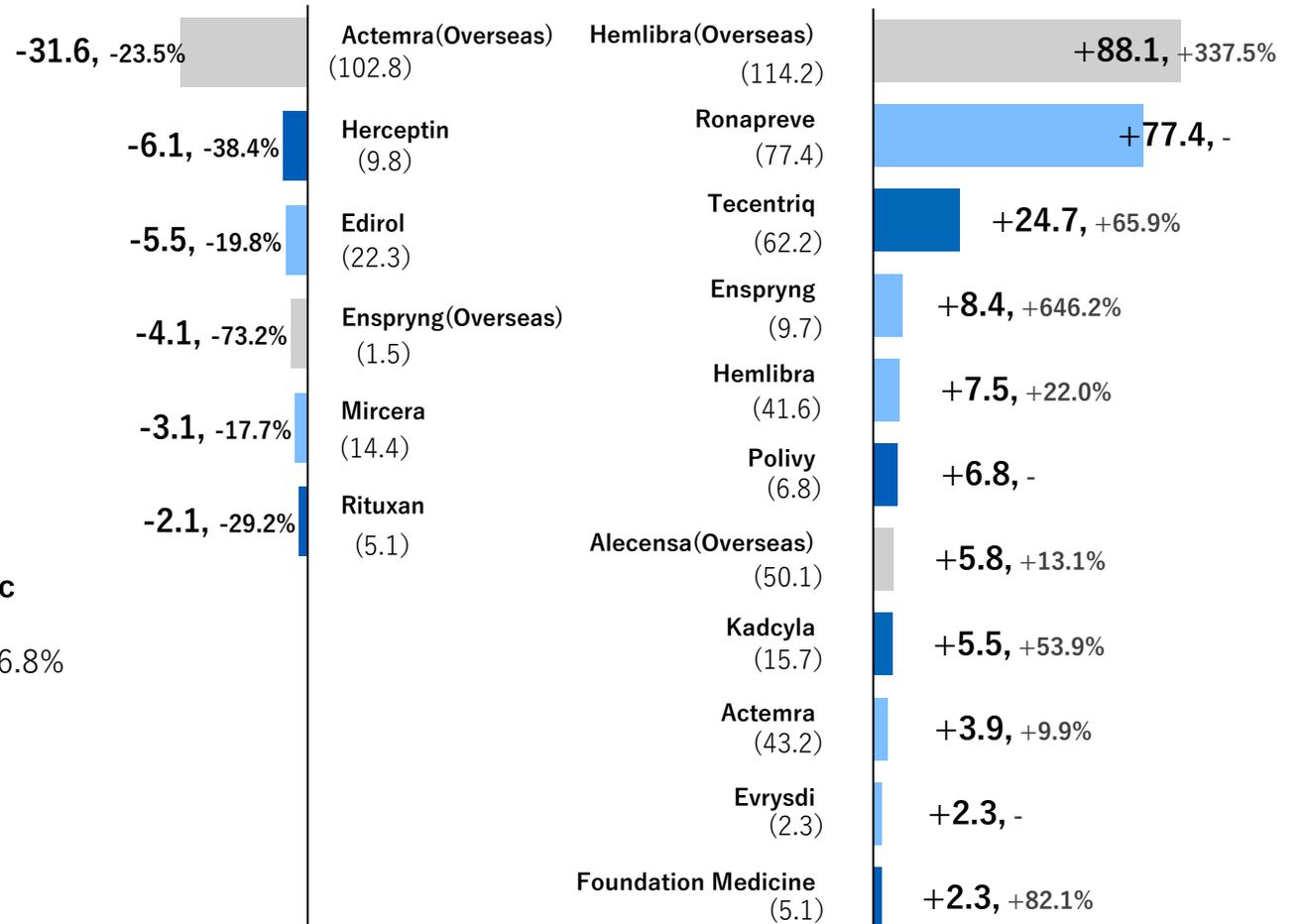
<sup>\*2</sup> Effective July 1, 2020, Chugai implemented a three-for-one stock split of its common stock. EPS are calculated based on the assumption that the stock split was implemented at the beginning of the previous fiscal year.

# Sales Jan - Dec (Year on Year)



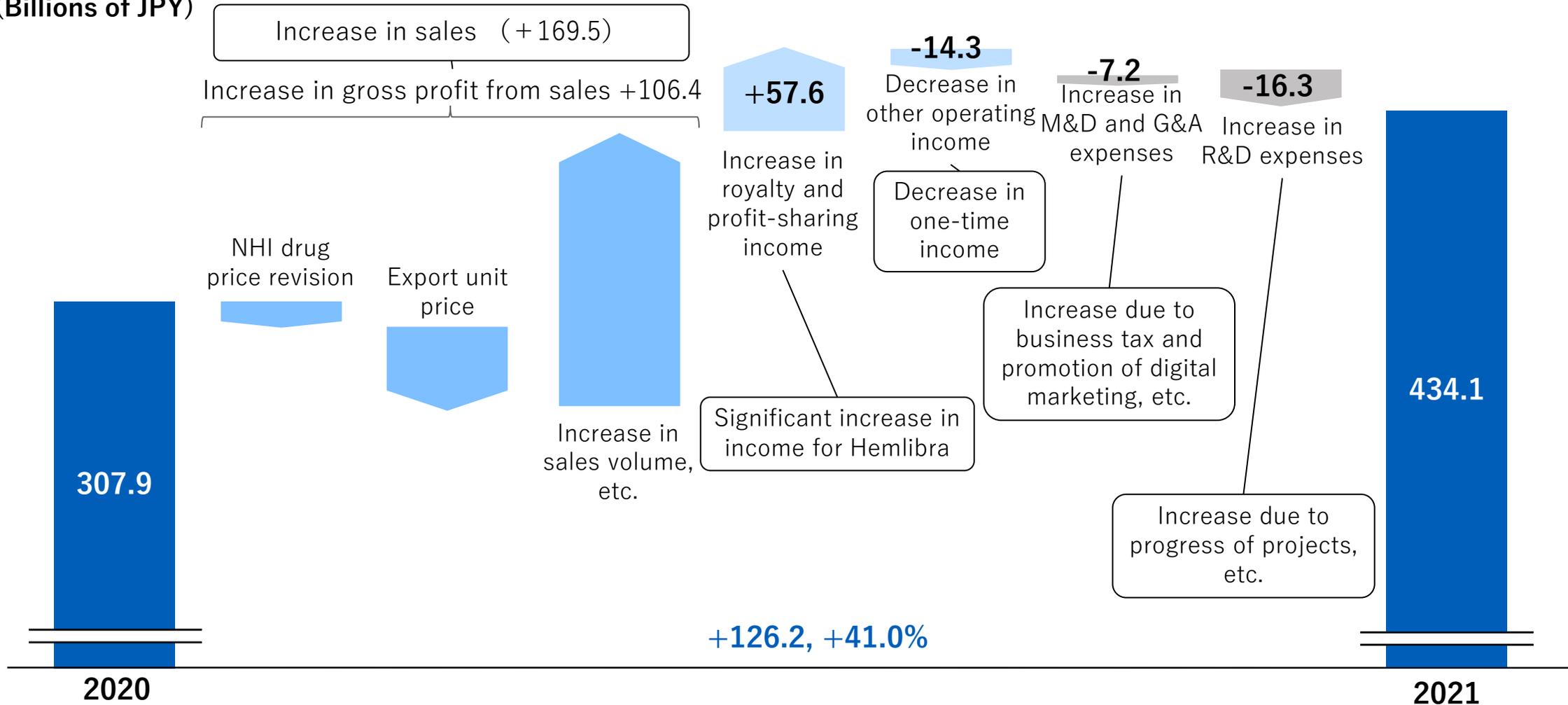
Sales by Products, Year on Year Changes

( ): Actual sales in FY2021  
%: Year-on-year percentage change



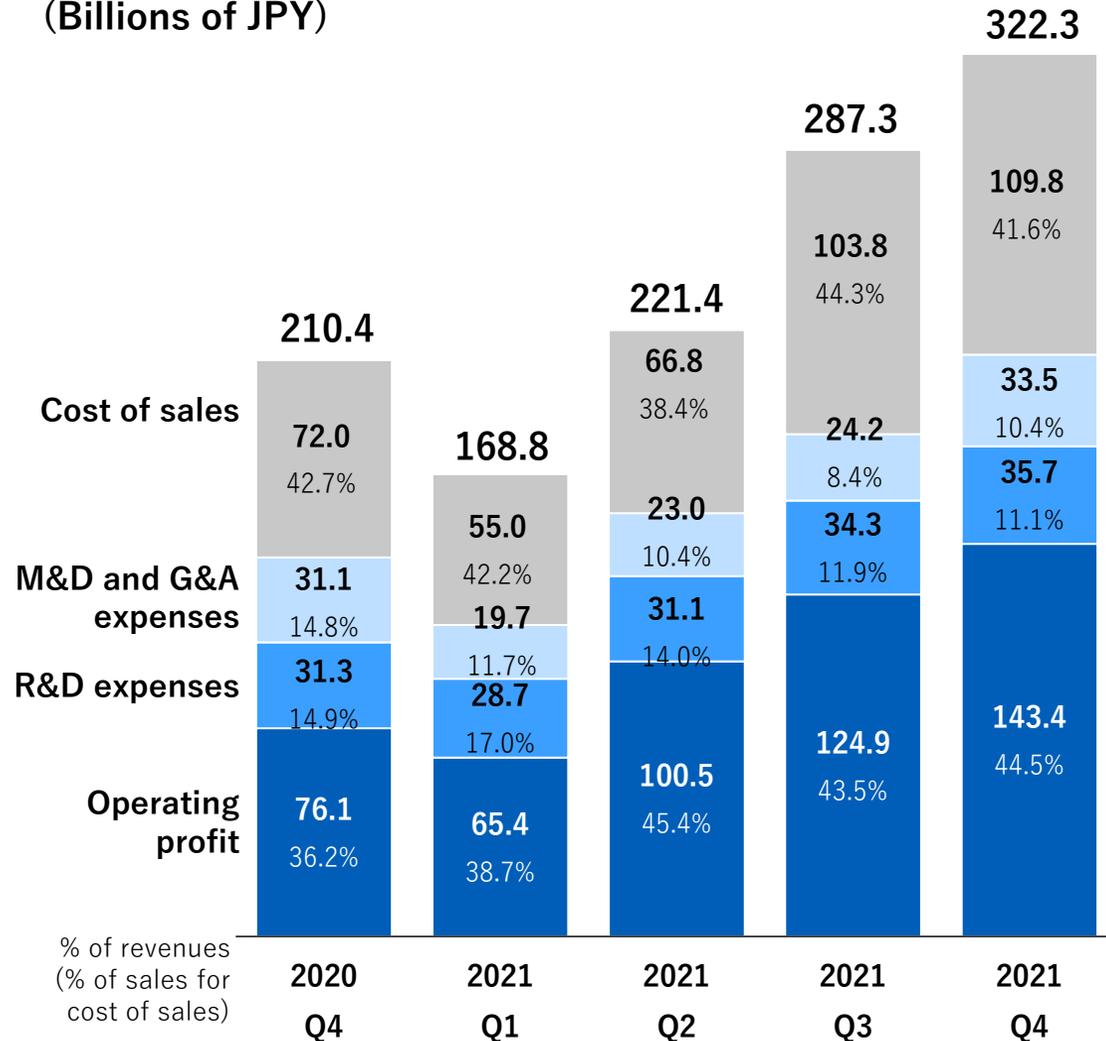
# Operating Profit Jan - Dec (Year on Year)

(Billions of JPY)



# Structure of Costs and Profit by Quarter

(Billions of JPY)



## vs. Year on Year (2020 Q4)

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

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

Operating profit: increase of +67.3 (+88.4%)

## vs. Previous Quarter (2021 Q3)

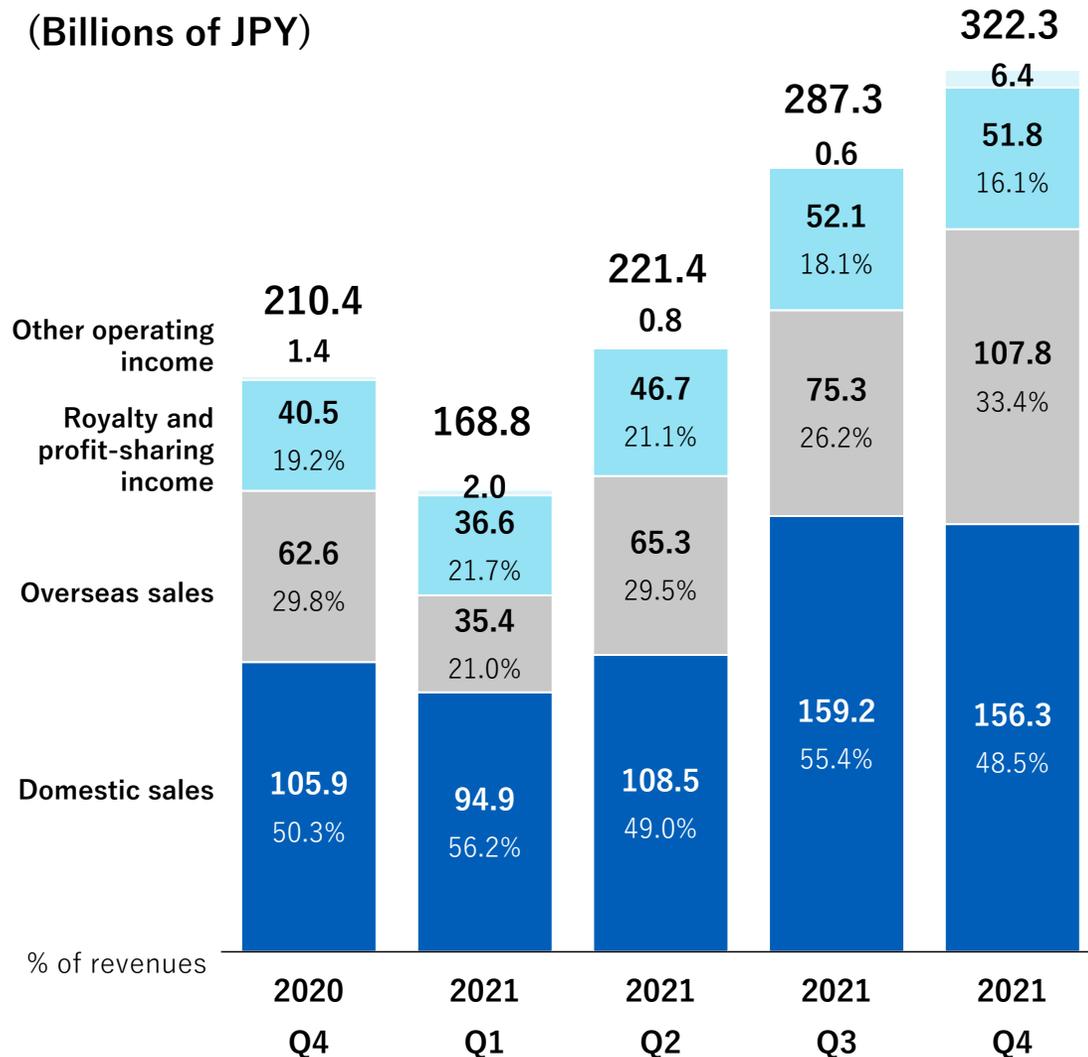
Cost of sales ratio: improved due to a change in product mix, etc.

M&D and G&A expenses: increase due to the trend of costs incurred in previous years

Operating profit: increase of +18.5 (+14.8%)

# Structure of Revenues by Quarter

(Billions of JPY)



## vs. Year on Year (2020 Q4)

Domestic sales: steady increase due to sales of new products and mainstay products grew despite impact of generic drugs

Overseas sales: significant increase in export of Hemlibra

Royalty and profit-sharing income: increase in income for Hemlibra and Actemra

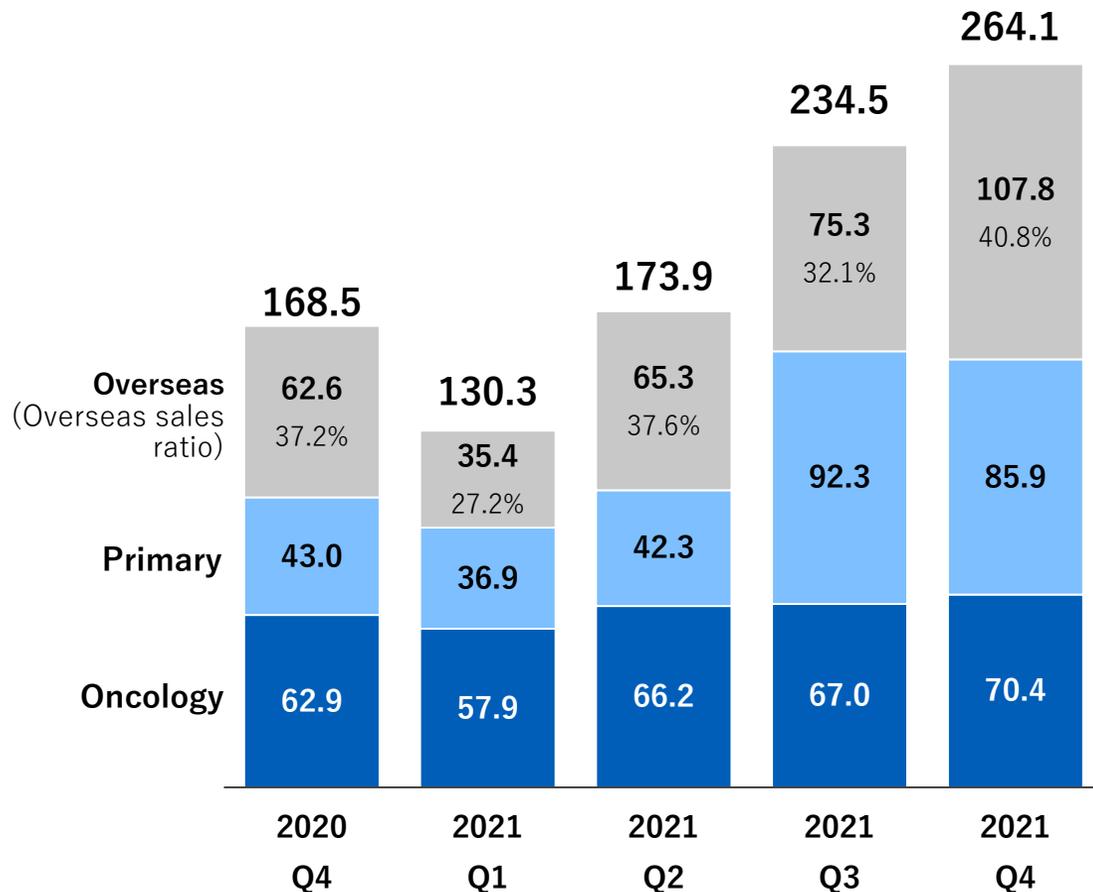
## vs. Previous Quarter (2021 Q3)

Domestic sales: slight decrease (See next slide)

Overseas sales: significant increase in export of Hemlibra and Actemra

# Structure of Sales by Quarter

(Billions of JPY)



vs. Year on Year (2020 Q4)

<b>Oncology</b>	Tecentriq:	+4.1	Polivy:	+3.3
	Kadcyla:	+1.3	Herceptin:	-1.3
<b>Primary</b>	Ronapreve:	+34.6	Hemlibra:	+2.8
	Enspryng:	+2.5		
<b>Overseas</b>	Hemlibra:	+48.0	Actemra:	+2.5
	Enspryng:	-3.7		

vs. Previous Quarter (2021 Q3)

<b>Oncology</b>	Polivy:	+0.7	Tecentriq:	+0.6
<b>Primary</b>	Ronapreve:	-8.2	Edirol:	-5.0
	Tamiflu*:	+1.9	Hemlibra:	+1.7
	Evrysdi:	+1.5		
<b>Overseas</b>	Hemlibra:	+24.0	Actemra:	+13.7
	Alecensa:	-5.4		

\* Govt. stockpiles, etc.

# P/L Jan - Dec (vs. Forecast)

(Billions of JPY)	2021		+/-	Achiev.
	Forecast*	Actual		
<b>Revenues</b>	<b>970.0</b>	<b>999.8</b>	<b>+ 29.8</b>	<b>103.1%</b>
Sales	781.5	802.8	+ 21.3	102.7%
Domestic	513.0	518.9	+ 5.9	101.2%
Overseas	268.5	283.9	+ 15.4	105.7%
Royalties and other operating income	188.5	196.9	+ 8.4	104.5%
Royalty and profit-sharing income	179.5	187.2	+ 7.7	104.3%
Other operating income	9.0	9.8	+ 0.8	108.9%
<b>Cost of sales</b>	<b>- 339.0</b>	<b>- 335.5</b>	<b>+ 3.5</b>	<b>99.0%</b>
(cost to sales ratio)	43.4%	41.8%	-1.6%pts	-
<b>Operating expenses</b>	<b>- 231.0</b>	<b>- 230.2</b>	<b>+ 0.8</b>	<b>99.7%</b>
M&D and G&A	- 99.5	- 100.4	- 0.9	100.9%
Research and development	- 131.5	- 129.8	+ 1.7	98.7%
<b>Operating profit</b>	<b>400.0</b>	<b>434.1</b>	<b>+ 34.1</b>	<b>108.5%</b>
(operating margin)	41.2%	43.4%	+2.2%pts	-
<b>Net income</b>	<b>293.0</b>	<b>311.5</b>	<b>+ 18.5</b>	<b>106.3%</b>
<b>EPS (JPY)</b>	<b>178.00</b>	<b>189.35</b>	<b>+ 11.35</b>	<b>106.4%</b>

\*Revised Forecast(Announced on October 22, 2021)

## Domestic Sales

Various products outperformed the forecast  
(see next slide)

## Overseas sales

Exports of Hemlibra exceeded the forecast

## Royalty and profit-sharing income

Income for Actemra and Hemlibra exceeded the forecast

## Cost of Sales

Cost to sales ratio improved due to a change in product mix from the forecast, etc.

## Operating expenses

Progress almost as expected

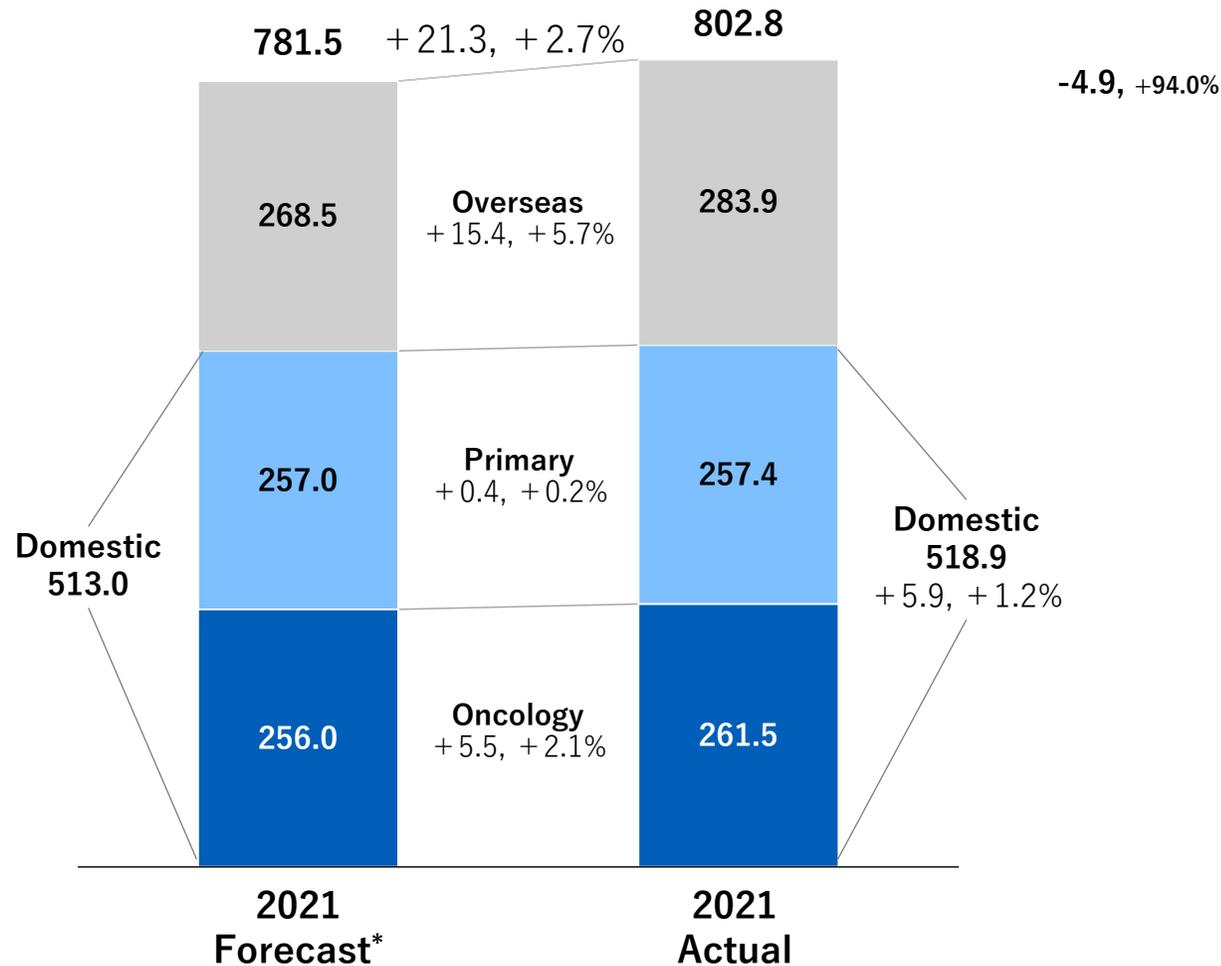
## Operating profit

Actual profit exceeded forecast by +34.1 (+8.5%) due to higher sales, royalty and profit-sharing income

# Sales Jan - Dec (vs. Forecast)

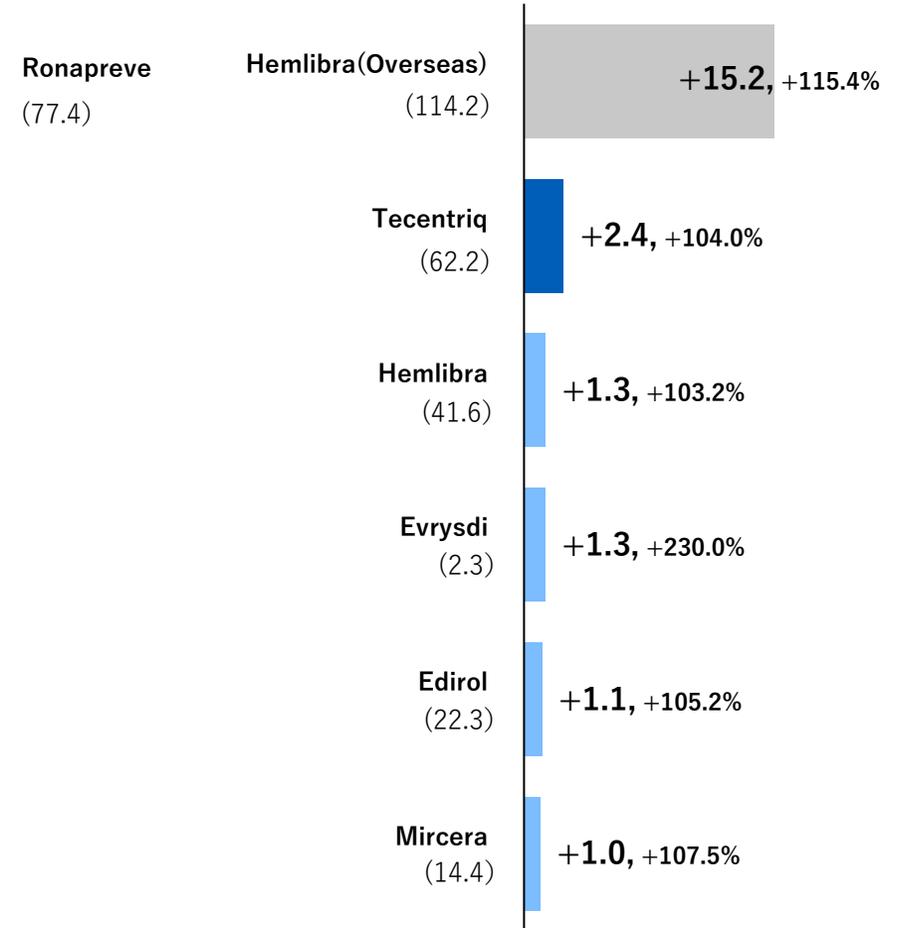
(Billions of JPY)

Sales by Disease Area,  
Year on Year Comparisons



Sales by Products,  
Actual vs Forecast Comparisons

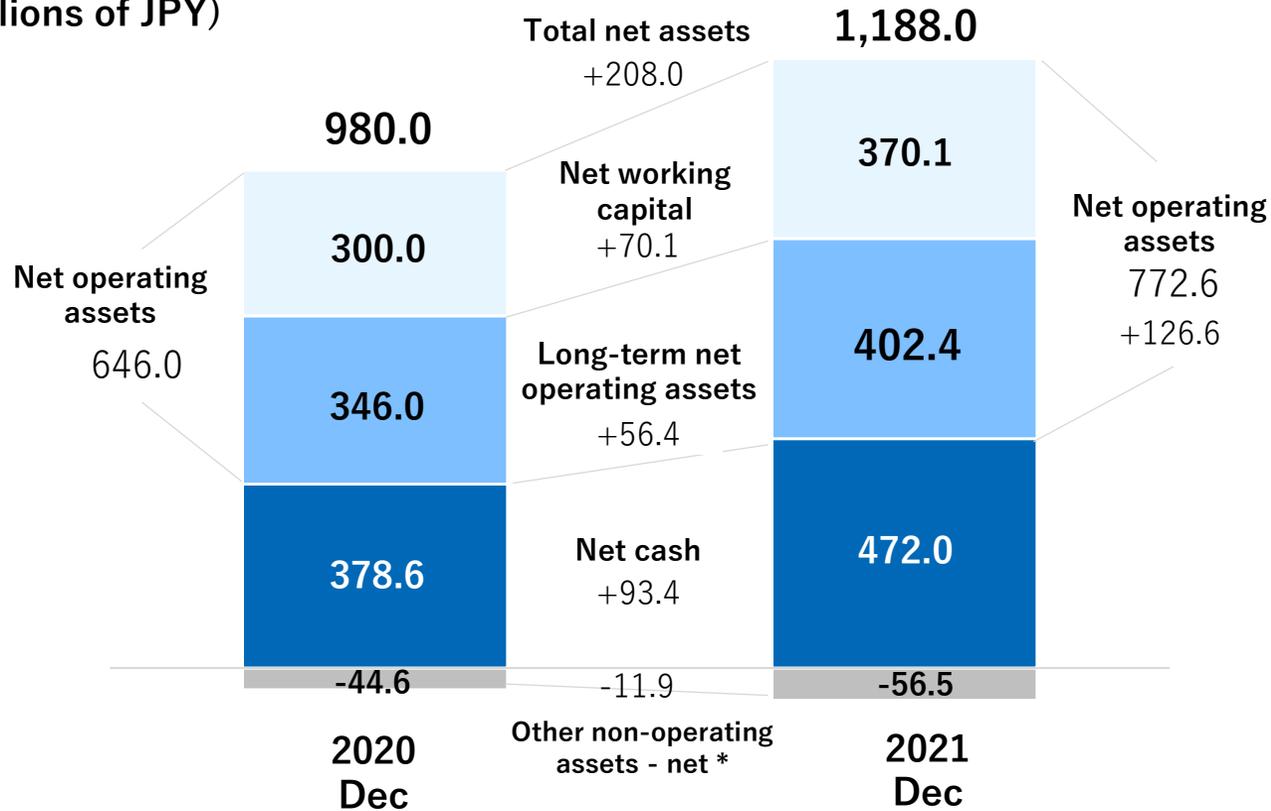
( ): Actual sales in FY2021  
%: Achievement



\*Revised Forecast(Announced on October 22, 2021)

# Financial Position (vs. 2020 Year End)

(Billions of JPY)



## Increase in net working capital

Increase mainly in trade accounts receivable

## Increase in long-term net operating assets

Increase mainly in property, plant and equipment

## Increase in net cash

(See next slide)

## Decrease in other non-operating assets – net

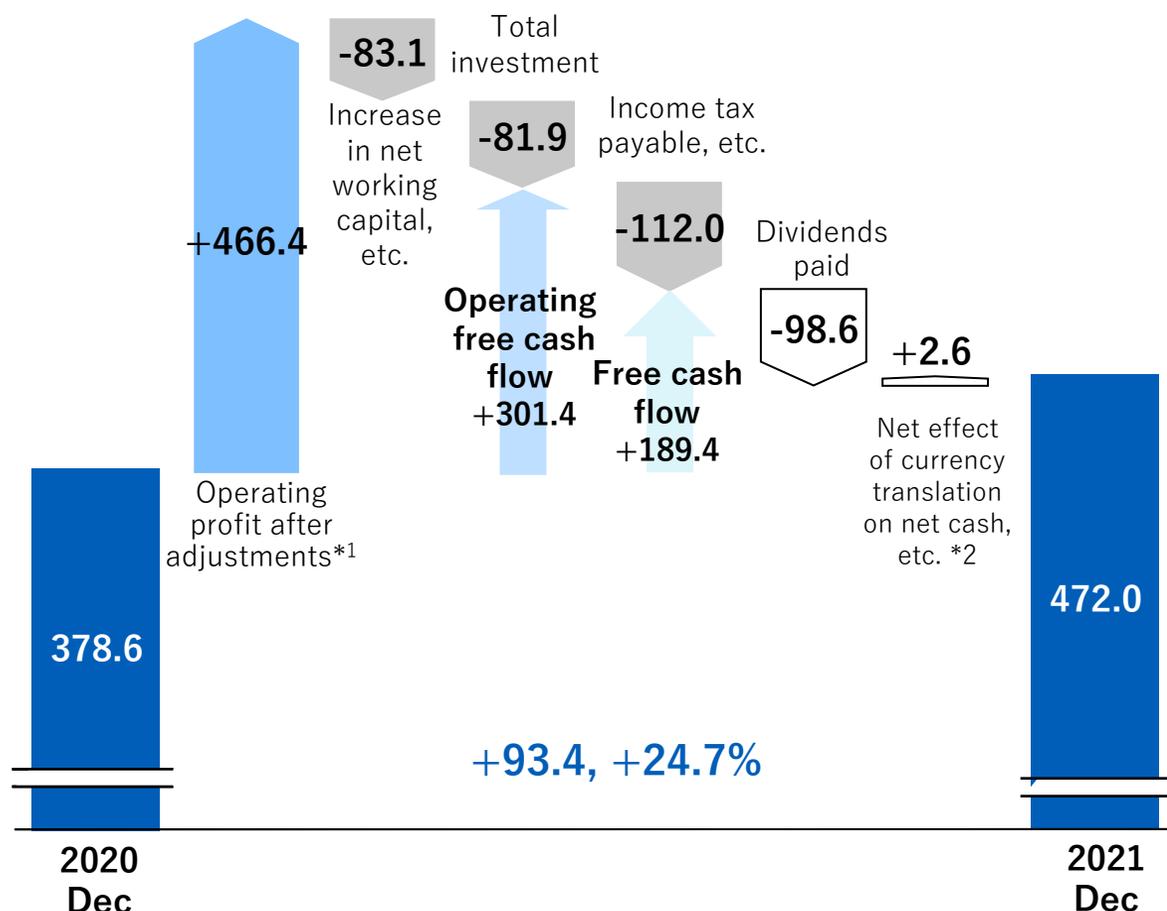
Increase mainly in accrued corporate tax

\* E.g., deferred income tax assets, accrued corporate tax, etc.

Total assets	1,235.5	+303.2	1,538.7
Total liabilities	-255.5	-95.2	-350.7
<b>Total net assets</b>	<b>980.0</b>	<b>+208.0</b>	<b>1,188.0</b>
Ratio of equity attributable to Chugai shareholders	79.3%	-2.1%pts	77.2%

# Net Cash (vs. 2020 Year End)

(Billions of JPY)



<b>Operating profit after adjustment *1</b>	<b>+466.4</b>
Operating profit *1	+421.9
Depreciation, amortization and impairment *1	+37.2
<b>Increase in net working capital, etc.</b>	<b>-83.1</b>
<b>Total investment</b>	<b>-81.9</b>
Property, plant and equipment	-66.0
Payment for lease liabilities	-9.0
Intangible assets	-6.9
<b>Operating free cash flow</b>	<b>+301.4</b>
<b>Income tax payable, etc.</b>	<b>-112.0</b>
Income tax payable	-104.1
<b>Free cash flow</b>	<b>+189.4</b>
<b>Dividends paid</b>	<b>-98.6</b>
<b>Net effect of currency transaction on net cash, etc. *2</b>	<b>+2.6</b>

\*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



**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



**Ukima Branch:** Construction of antibody API manufacturing building for early-stage clinical development



Research and development

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



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



Comprehensive collaboration in research activity with **IFReC**



# P/L 2022 Forecast

(Billions of JPY)	2021 Actual	2022 Forecast	Growth	
<b>Revenues</b>	<b>999.8</b>	<b>1150.0</b>	+ 150.2	+ 15.0%
Sales	802.8	1031.5	+ 228.7	+ 28.5%
Domestic	518.9	646.3	+ 127.4	+ 24.6%
Overseas	283.9	385.2	+ 101.3	+ 35.7%
Royalties and other operating income	196.9	118.5	- 78.4	- 39.8%
Royalty and profit-sharing income	187.2	114.0	- 73.2	- 39.1%
Other operating income	9.8	4.5	- 5.3	- 54.1%
<b>Cost of sales</b>	<b>- 335.5</b>	<b>- 460.0</b>	<b>- 124.5</b>	<b>+ 37.1%</b>
(cost to sales ratio)	41.8%	44.6%	+2.8%pts	-
<b>Operating expenses</b>	<b>- 230.2</b>	<b>- 250.0</b>	<b>- 19.8</b>	<b>+ 8.6%</b>
M&D and G&A	- 100.4	- 100.5	- 0.1	+ 0.1%
Research and development	- 129.8	- 149.5	- 19.7	+ 15.2%
<b>Operating profit</b>	<b>434.1</b>	<b>440.0</b>	<b>+ 5.9</b>	<b>+ 1.4%</b>
(operating margin)	43.4%	38.3%	-5.1%pts	-
<b>Net income</b>	<b>311.5</b>	<b>312.5</b>	<b>+ 1.0</b>	<b>+ 0.3%</b>
<b>EPS (JPY)</b>	<b>189.35</b>	<b>190.00</b>	<b>+ 0.65</b>	<b>+ 0.3%</b>

## Domestic sales

Despite impact from NHI drug price revision and launch of generic drugs, increase due to sales growth of new products as well as mainstay products, including Ronapreve

## Overseas sales

Increase in income for Hemlibra and Actemra

## Royalty and profit-sharing income

Decrease in royalty income for Hemlibra regarding initial shipping inventory

## Other operating income

Decrease in one-time income

## Cost of sales

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

## Operating expenses

Increase of research and development expenses due to progress of projects, etc.

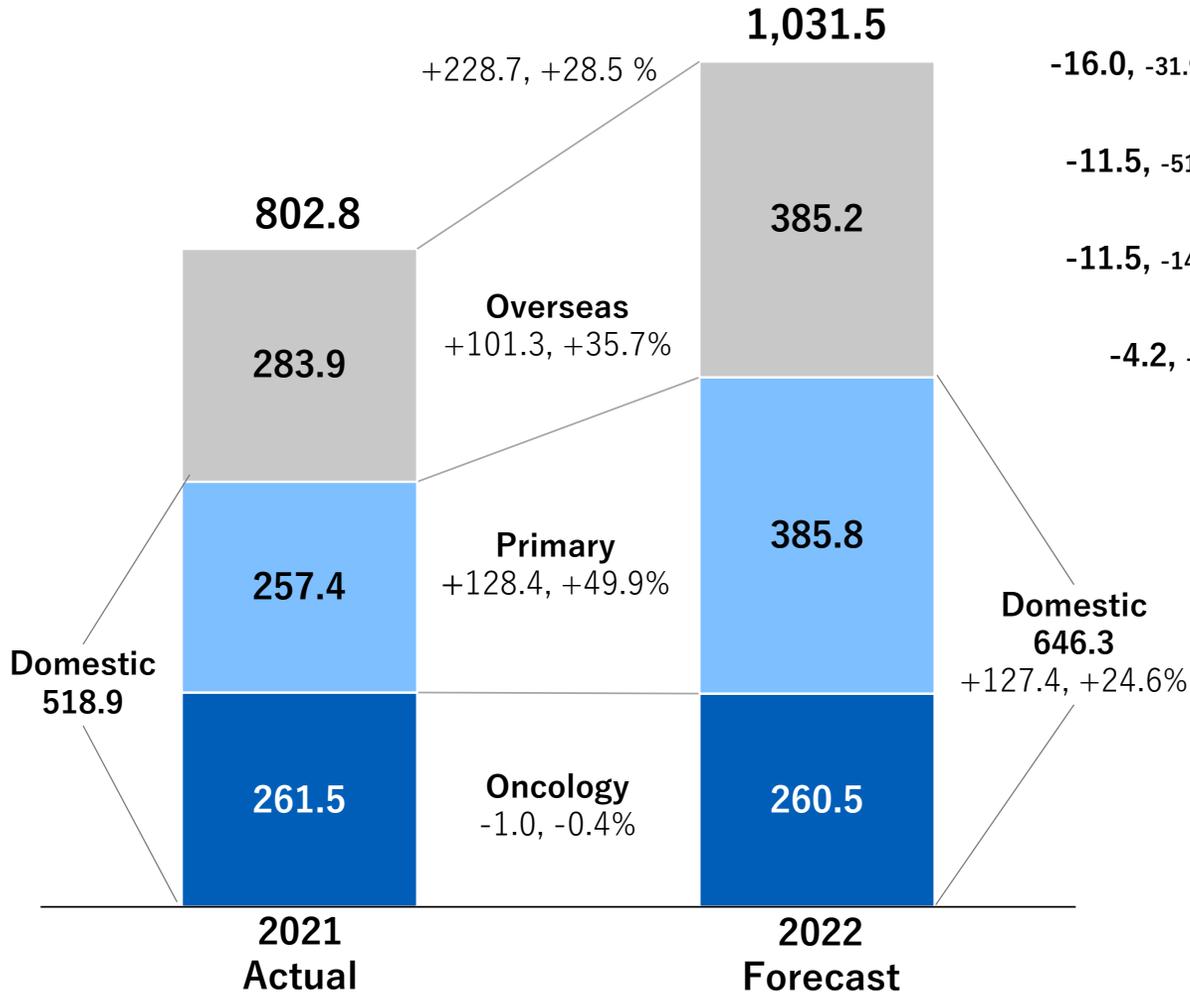
## Operating profit

The increase in sales will offset the decline in royalties and other operating income and the rise in operating expenses.

# Sales 2022 Forecast

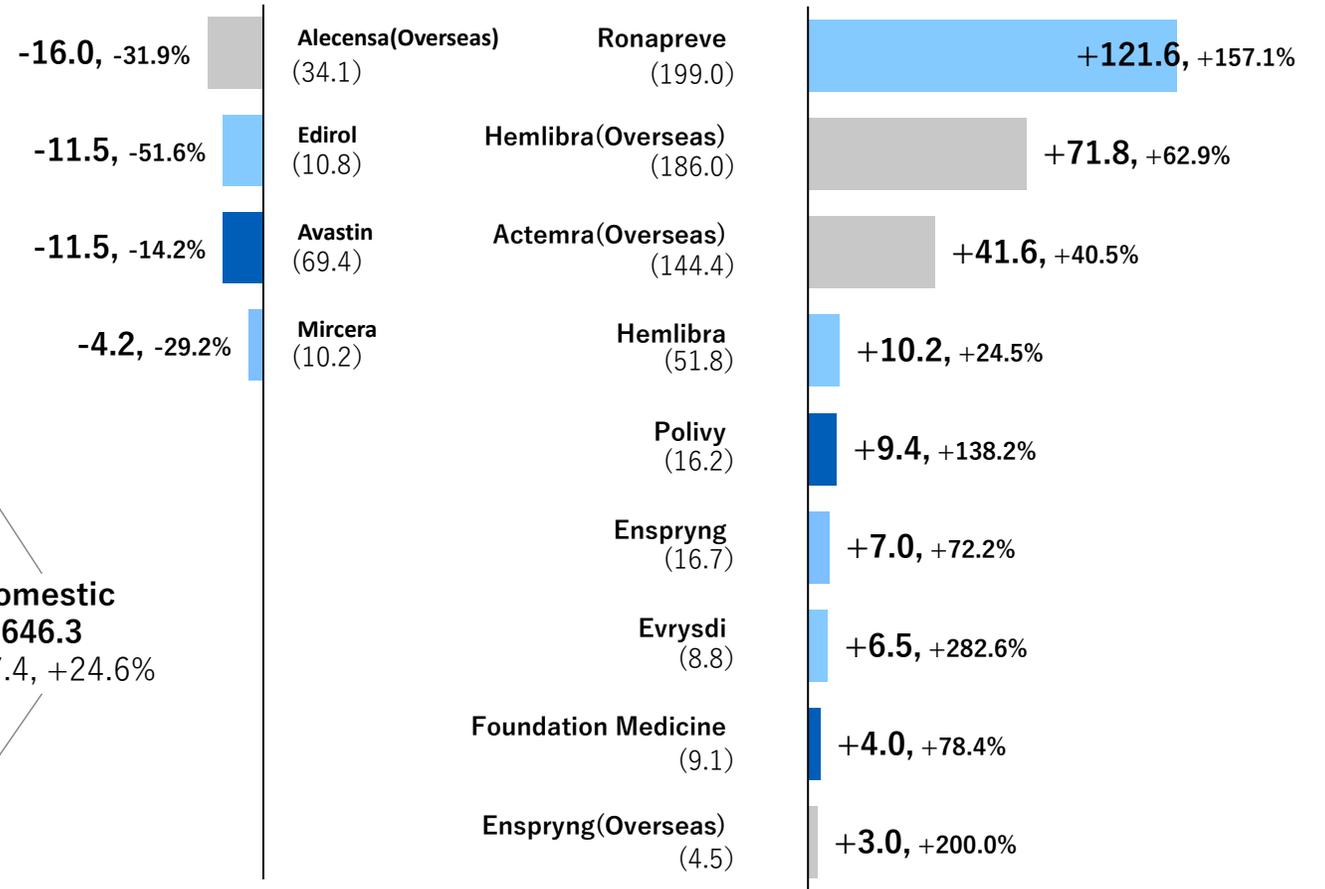
(Billions of JPY)

Sales by Disease Area,  
Year on Year Comparisons



Sales by Products,  
Year on Year Changes

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



# Export of Actemra to Roche

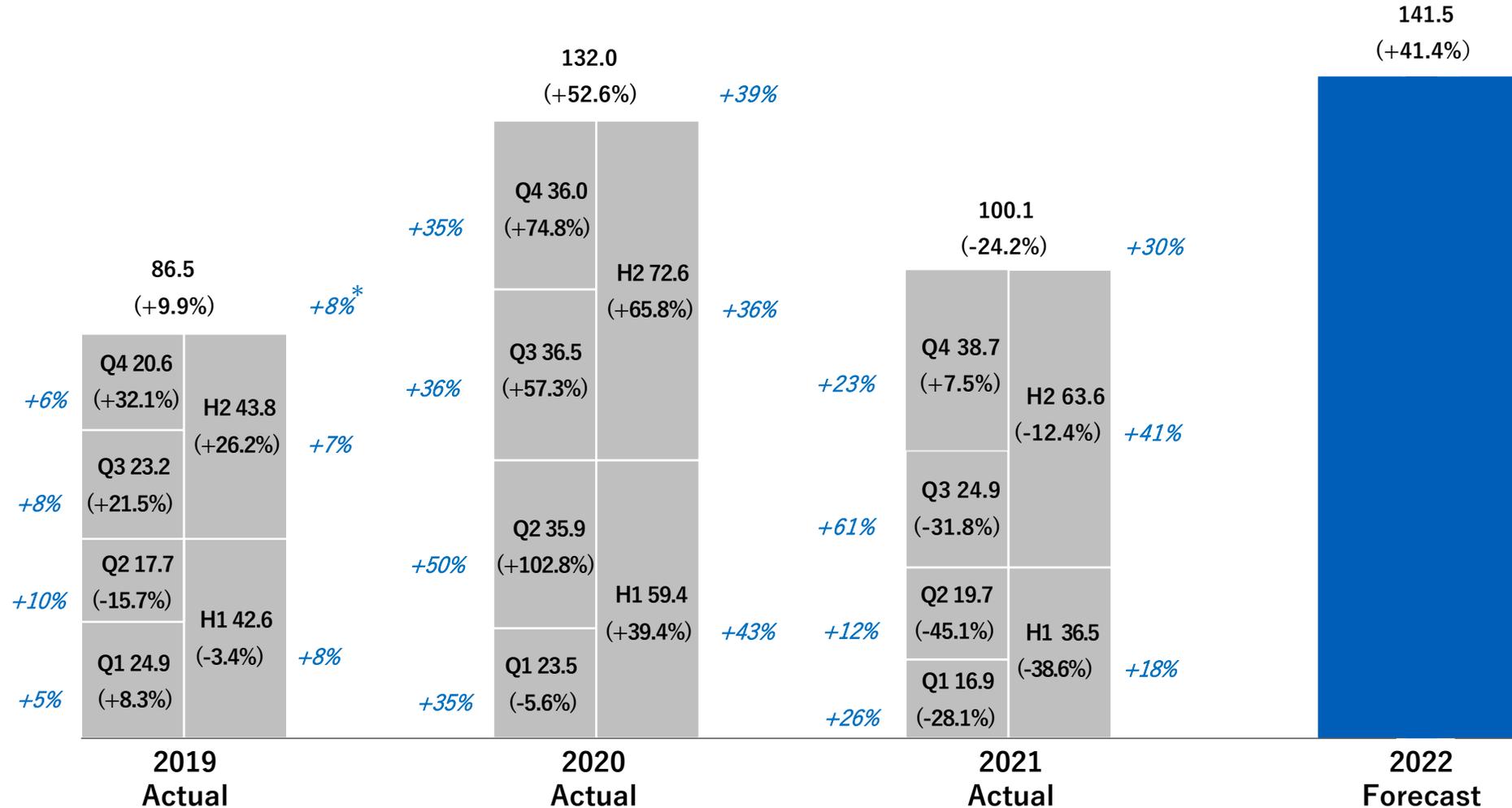
(Billions of JPY)

=: year on year growth

black: Chugai sales to Roche

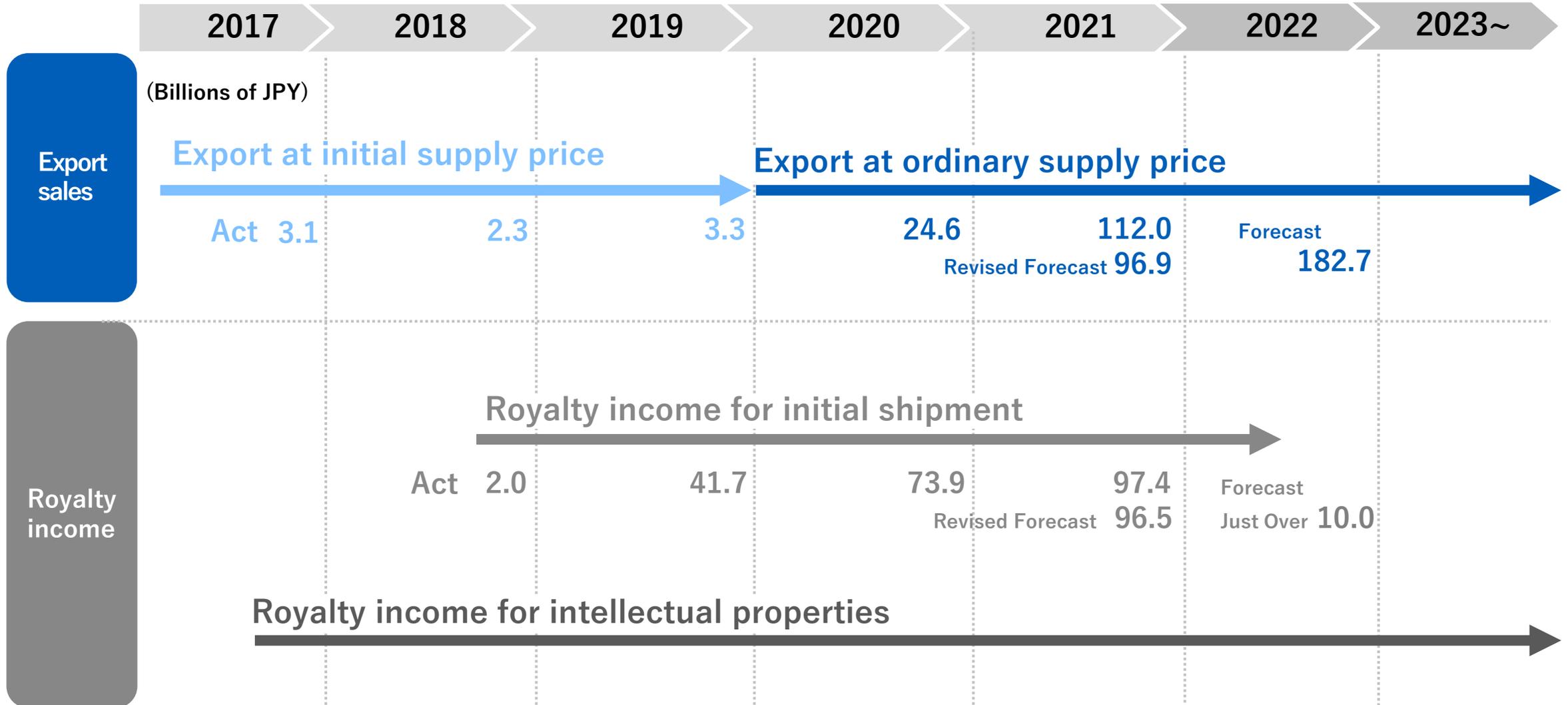
blue\*: Roche sales excluding Japan (for reference)

\*Growth rates in blue are calculated with the effects of exchange rate fluctuations eliminated.



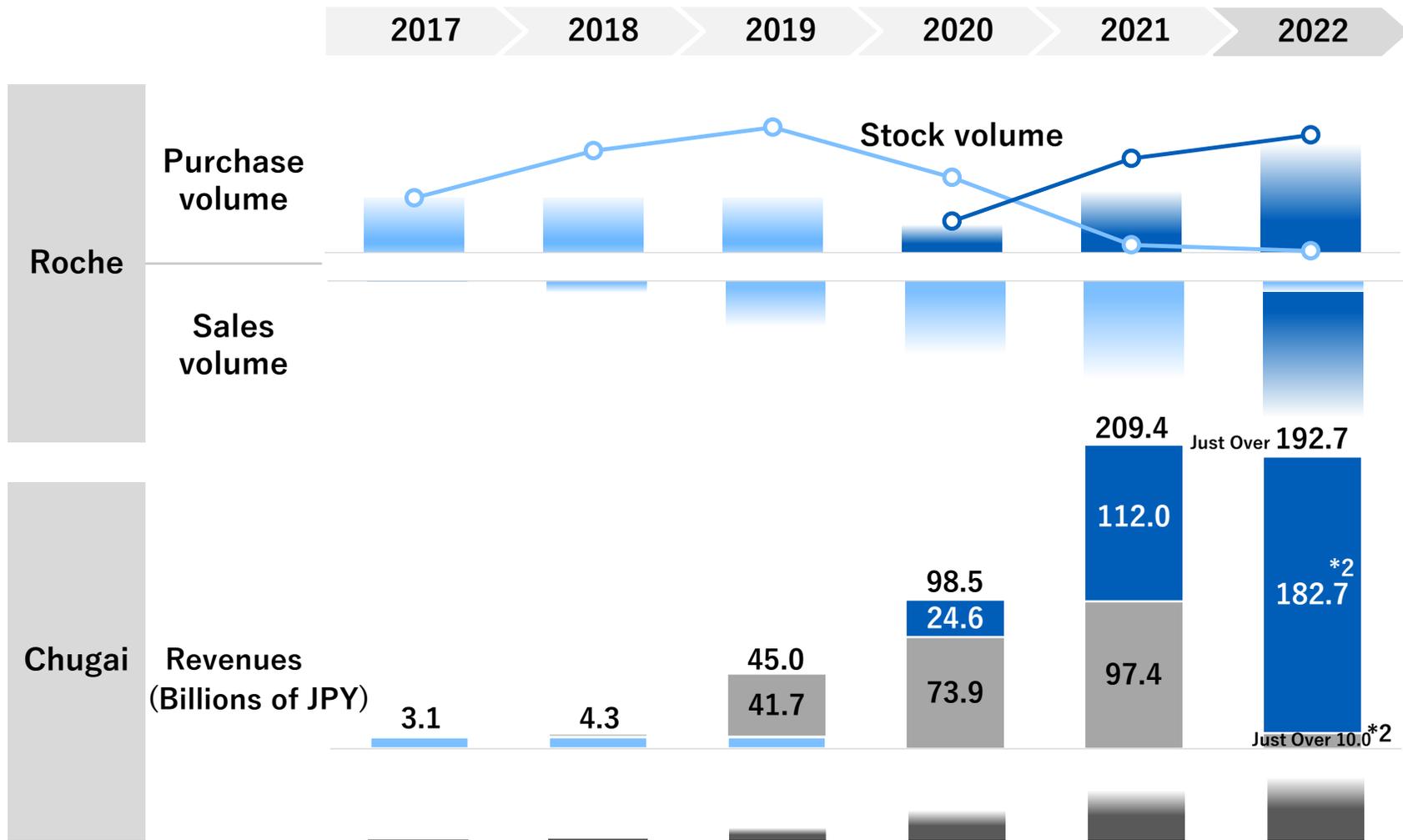
# Outline of Hemlibra Sales to Roche

(Excluding profit-sharing income and expenses in co-promotion countries)



# Outline of Hemlibra Sales to Roche

Image for Timing of Export Sales and Royalty Income\*1



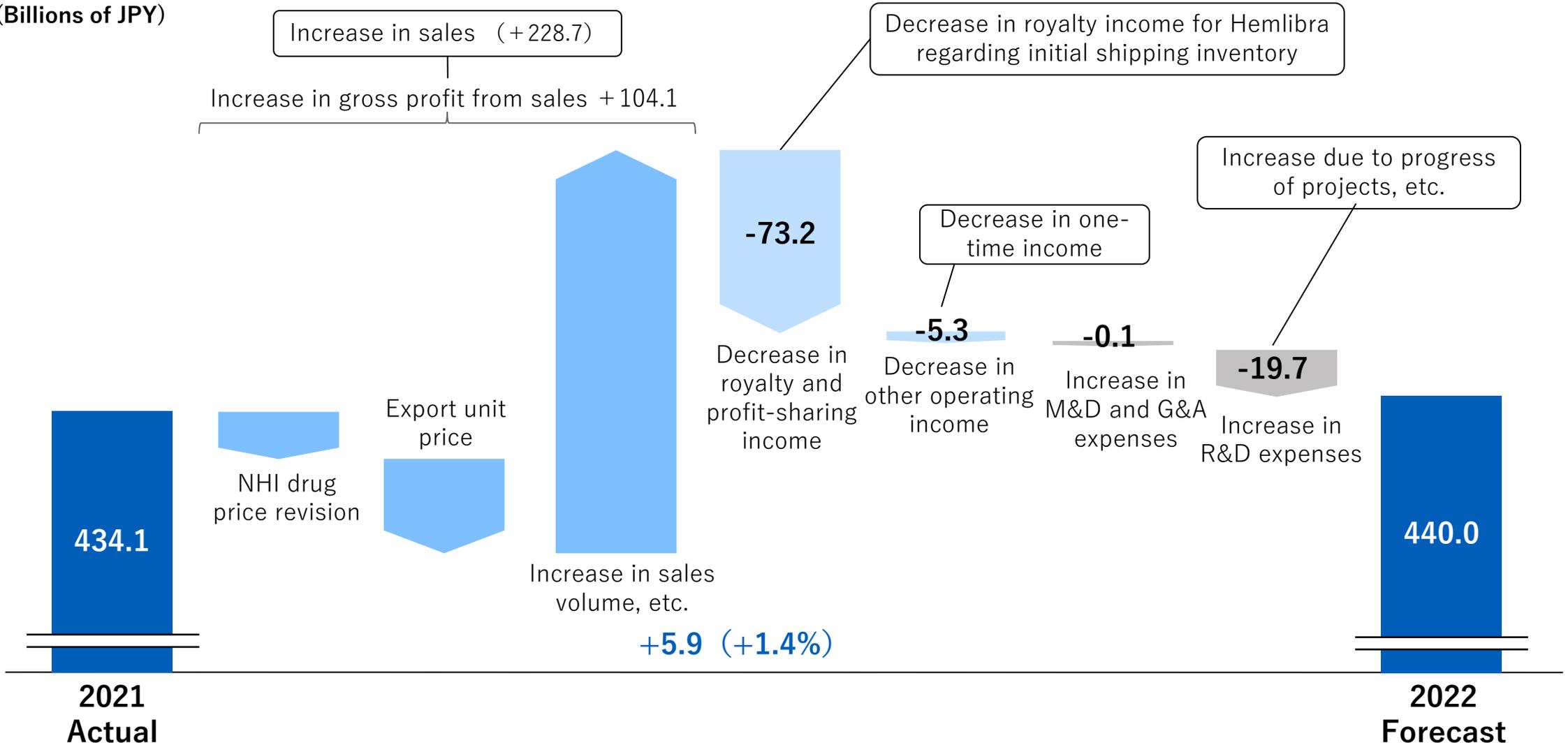
\*1 This is a conceptual image and may differ from actual amount and volume.

- Ordinary supply
- Initial supply (sales amount is based on first-in first-out method)
- Stock volume of ordinary supply (Year End)
- Stock volume of initial supply (Year End)

- \*2 Forecast
- Export sales at ordinary supply price
  - Export sales at initial supply price
  - Royalty income for initial shipment
  - Royalty income for intellectual properties

# Operating Profit 2022 Forecast

(Billions of JPY)



# Appendix

# IFRS and Core Results Jan – Dec

(Billions of JPY)	IFRS results	Non-core items		Core results
		Intangible assets	Others	
<b>Revenues</b>	<b>999.8</b>			<b>999.8</b>
Sales	802.8			802.8
Royalties and other operating income	196.9			196.9
Cost of sales	-338.1	+2.7		-335.5
<b>Operating expenses</b>	<b>-239.7</b>	<b>+4.1</b>	<b>+5.5</b>	<b>-230.2</b>
M&D and G&A	-102.4		+2.0	-100.4
Research and development	-137.3	+4.1	+3.5	-129.8
<b>Operating profit</b>	<b>421.9</b>	<b>+6.7</b>	<b>+5.5</b>	<b>434.1</b>
Financial account balance	-2.5			-2.5
Income taxes	-116.4	-2.0	-1.6	-120.1
<b>Net income</b>	<b>303.0</b>	<b>+4.7</b>	<b>+3.8</b>	<b>311.5</b>
<b>EPS (JPY)</b>	<b>184.17</b>			<b>189.35</b>

## Non-Core items

(Billions of JPY)

### Intangible assets

Amortization	+2.2
Impairment	+4.5

### Others

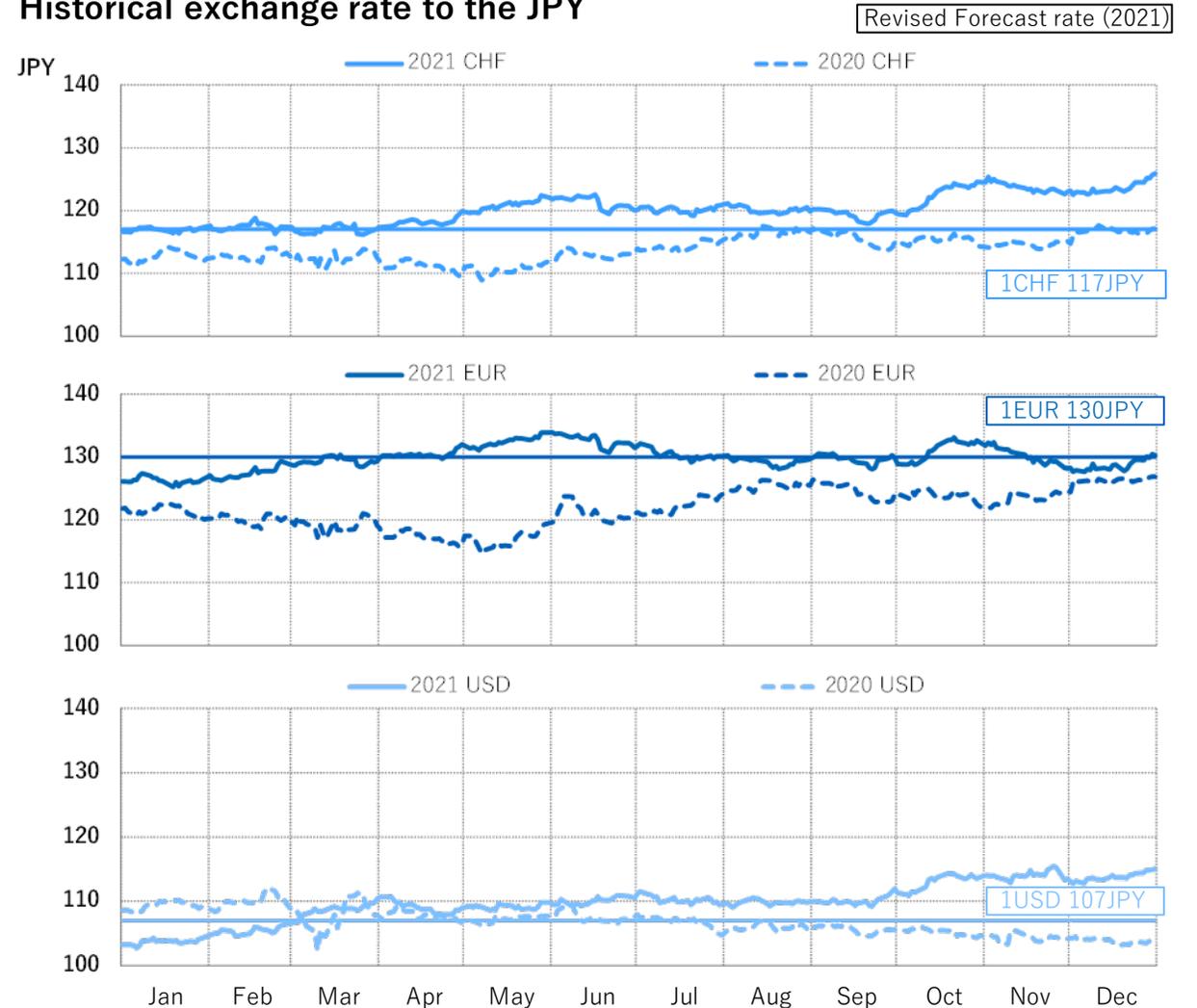
Restructuring expenses, etc.	+5.5
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# Impact from Foreign Exchange (vs. Revised Forecast)

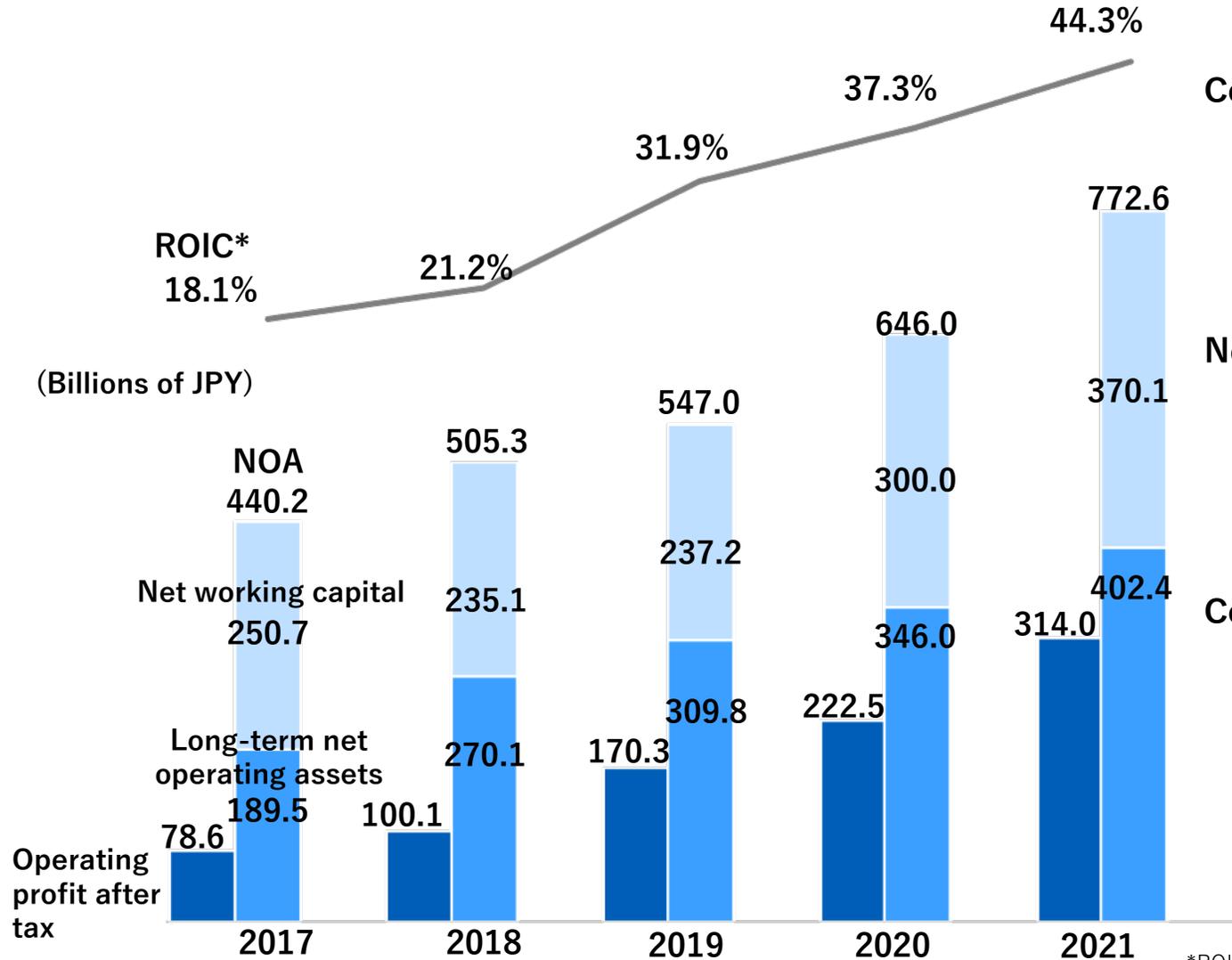
(billions of JPY)	FX impact 2021 (FX impact vs. Assumption)	
<b>Revenues</b>	Sales	-0.3
	Royalties and other operating income	+1.7
<b>Cost of sales &amp; Operating expenses</b>	Cost of sales	-1.4
	Operating expenses	-0.7
<b>Operating profit</b>	<b>-0.6</b>	

Market average exchange rate(JPY)	2020 Actual	2021 Assumption	2021 Actual
1CHF	113.72	117.00	120.10
1EUR	121.69	130.00	129.83
1USD	106.80	107.00	109.75

Historical exchange rate to the JPY



# ROIC



## Core operating profit after tax

Steady increase due to sales growth of new products as well as mainstay products, export of Hemlibra and royalty income.

## Net operating assets (NOA)

Increase mainly in long-term net operating assets, due to aggressive capital investment such as Chugai Life Science Park Yokohama.

## Core ROIC

As a result of the growth rate of core operating profit after tax exceeding the increase rate of net operating assets (NOA), core ROIC has risen continuously.

\*ROIC = core operating profit after tax / the average of opening and ending NOA balances  
Opening balance as of FY2019 was adjusted by the adoption of IFRS16 Leases.

# Overview of Development Pipeline

**Tetsuya Yamaguchi**

Executive Vice President, Head of Project & Lifecycle Management Unit

# Q4 Topics (1/2)



As of February 3, 2022

Approved	Ronapreve	Prevention of symptomatic COVID-19, Subcutaneous administration	November 2021
	Herceptin	Advanced or recurrent HER2-positive salivary gland cancer not amenable to curative resection	November 2021
	FoundationOne CDx	pembrolizumab* : advanced or recurrent solid tumors with Tumor mutational burden-high	November 2021
	Rituxan	Refractory pemphigus vulgaris and pemphigus foliaceus	December 2021
	Actemra	COVID-19 pneumonia (EU)	December 2021
	Actemra	COVID-19 pneumonia (JP)	January 2022
Filed	Hemlibra	Acquired Hemophilia A	November 2021
	Polivy	Previously untreated diffuse large B-cell lymphoma (DLBCL)	December 2021
	FoundationOne CDx	- dacomitinib hydrate: NSCLC (Activated <i>EGFR</i> gene alterations)	December 2021
		- brigatinib: NSCLC ( <i>ALK</i> fusion genes)	
	- dabrafenib mesilate, trametinib dimethyl sulfoxide: NSCLC ( <i>BRAF</i> V600E alterations)		
	- encorafenib, binimetinib: Malignant melanoma ( <i>BRAF</i> V600E and V600K alterations)		
Phase transition	RG7828/ mosunetuzumab	Follicular lymphoma	P3 study (October 2021)
	RG6396/pralsetinib	Non-small cell lung cancer (NSCLC)	P3 study (November 2021)

Letters in orange : in-house projects    Letters in blue : in-licensed (Roche)

\* Application under review and not yet approved for the drug indication

# Q4 Topics (2/2)



As of February 3, 2022

<b>Pipeline entry</b>	<b>SKY59/crovalimab</b>	Atypical hemolytic uremic syndrome (aHUS)	P3 study (October 2021)
<b>Development discontinued</b>	<b>PCO371</b>	Hypoparathyroidism	
	<b>RG6422 (AT-527)</b>	COVID-19	
	<b>Suvenil</b>	Knee osteoarthritis/Shoulder periartthritis (China)	
	<b>AMY109</b>	Solid tumors	
<b>Medical conference</b>	<b>Hemlibra</b>	HAVEN 6 study: interim data	ASH (December 2021)
	<b>Polivy</b>	POLARIX study: previously untreated DLBCL	ASH (December 2021)
<b>Others</b>	<b>Edirol</b>	Osteoporosis	Launch of authorized generic version of Edirol by Towa Pharmaceutical (December 2021)
	<b>OWL833</b>	Type 2 diabetes: advanced to Phase 2**	September 2021
	<b>OWL833</b>	Obesity: initiation of Phase 2 study**	September 2021
	<b>SRP-9001/RG6356*</b>	Duchenne muscular dystrophy (DMD)	License-in agreement (December 2021)
	<b>faricimab</b>	DME: P3 studies (YOSEMITE / RHINE)	Published in Lancet
	<b>faricimab</b>	nAMD: P3 studies (TENAYA / LUCERNE)	Published in Lancet

Letters in orange : in-house projects    Letters in blue : in-licensed (Roche)

DME: diabetic macular edema    nAMD: neovascular age-related macular degeneration

\* Global P3 study for DMD is managed by Sarepta Therapeutics including Japan, while Chugai will be responsible for the regulatory filing and marketing in Japan.

\*\* Conducted by licensee, Eli Lilly and Company

# Advances in Chugai Originated Projects Licensed Out to the 3<sup>rd</sup> Party

★: changes since July 26, 2021

As of February 3, 2022

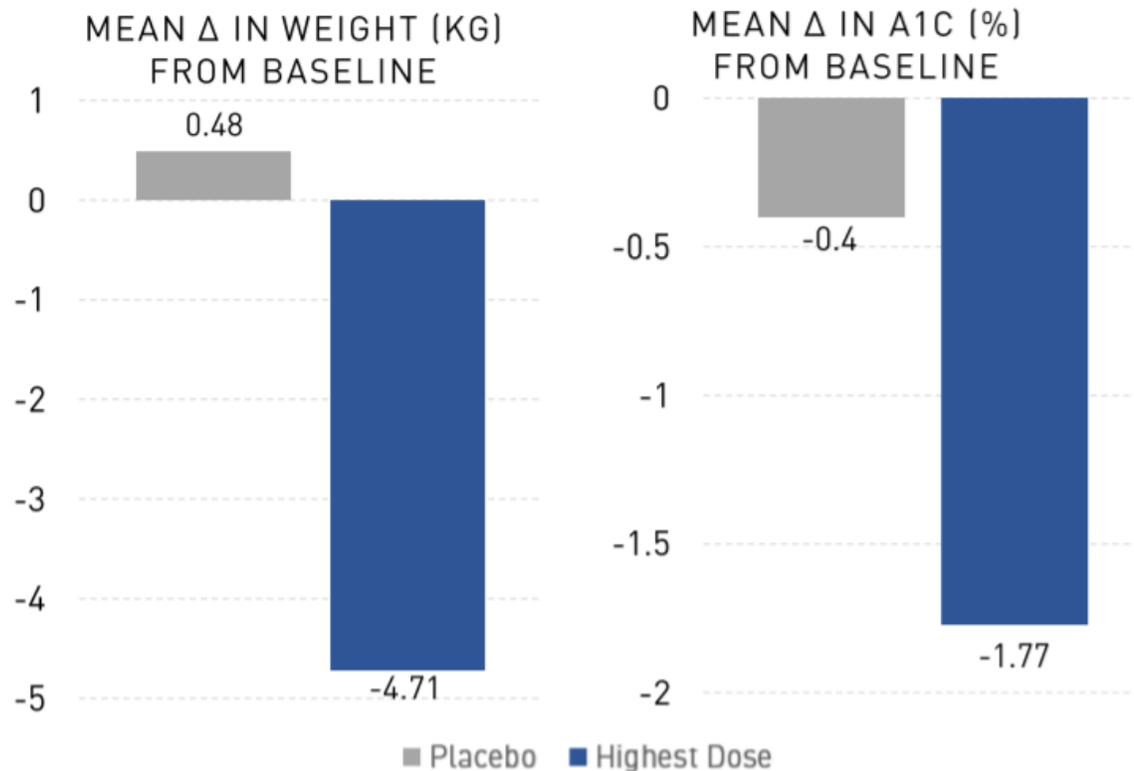
Development code Chugai/generic name (partner code)	Licensee	Indication	Stage	Mode of Action	Progress
<b>CKI27</b> (VS-6766)	Verastem Oncology	Ovarian cancer	global: P2	RAF/MEK inhibitor	<ul style="list-style-type: none"> <li>US FDA BTD (recurrent LGSOC* in combination with defactinib)</li> <li>RAMP 203 trial (in combination with KRAS G12C inhibitor sotorasib) to be initiated in Q1 2022 ★</li> <li>RAMP 204 trial (in combination with KRAS G12C inhibitor, adagrasib) to be initiated in Q2 2022 ★</li> </ul>
		NSCLC	global: P2		
			global: P1/2★		
<b>CIM331/ nemolizumab</b>	Global (Galderma)	Atopic dermatitis	global: P3	Anti-IL-31 receptor A humanized monoclonal antibody	<ul style="list-style-type: none"> <li>US FDA BTD</li> </ul>
			Japan: Filed		
	Japan (Maruho)	Prurigo nodularis	global: P3		
			Japan: P2/3		
<b>OWL833</b> (LY3502970)	Eli Lilly and Company	Type 2 diabetes	global: P2★	Oral non-peptidic GLP-1 receptor agonist	<ul style="list-style-type: none"> <li>Conduct a 12-week proof of concept study in type 2 diabetes (P1b)</li> <li>✓ Highest dose group of OWL833 shows 4.71 kg weight loss and 1.77% lowering of HbA1c ★</li> <li>Initiated P2 study in September 2021 ★</li> </ul>
		Obesity** ★	global: P2		

\*LGSOC: low-grade serous ovarian cancer \*\*In 2016, more than 1.9 billion adults, 18 years and older, were overweight. Of these, over 650 million were obese. Worldwide, obesity has nearly tripled since 1975. (Source: WHO Obesity and overweight Fact sheet <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>)

# OWL833: Favorable Efficacy and Safety in T2D

## ■ Potential contribution to T2D patients as a more convenient treatment option

### 12-WEEK PROOF OF CONCEPT IN T2D



- **A 12-week proof of concept study in T2D (P1b)**
  - ✓ Suggests possible equivalence to subcutaneous GLP-1 receptor agonists
    - Weight loss 4.71kg
    - HbA1c lowering up to 1.77% points
    - Safety and tolerability consistent with other GLP-1 receptor agonists
- **Expected features of a small molecule, OWL833**
  - ✓ Better bioavailability
  - ✓ Better manufacturing cost structure
  - ✓ Easier administration with no requirement to fast
  - ✓ Once daily oral administration

# Development Status of Treatments for COVID-19

Treatment	Development status
<p><b>Actemra</b> (Moderate II to Severe)</p>	<p>&lt;Japan&gt;</p> <ul style="list-style-type: none"> <li>● Additional indication for SARS-CoV-2 pneumonia (limited to patients requiring oxygen intervention) (Filed in December 2021, Approved in January 2022)</li> </ul> <p>&lt;Overseas&gt;</p> <ul style="list-style-type: none"> <li>● US: FDA Emergency Use Authorization granted (June 2021)</li> <li>● EU: Approved for severe COVID-19 treatment (December 2021)</li> <li>● WHO:                             <ul style="list-style-type: none"> <li>✓ recommended IL-6 receptor blockers including Actemra for treatment in severe COVID-19 patients receiving corticosteroids (July 2021)</li> <li>✓ announced that IL-6 receptor blockers are expected to remain effective for the management of patients with severe or critical Omicron-associated COVID-19 (November 2021)</li> </ul> </li> </ul>
<p><b>Ronapreve</b> (Asymptomatic to Moderate I )</p>	<ul style="list-style-type: none"> <li>● SARS-CoV-2 infection and prevention of symptomatic SARS-CoV-2 infection (First approval in July, additional indications in November 2021, respectively)</li> <li>● Neutralizing activity against Omicron variant (B.1.1.529/BA.1) was confirmed to be diminished, and revised the package insert based on the data (December 2021)</li> <li>● On the other hand, Ronapreve has shown to retain its efficacy against other variants of concern, including Delta. Efficacy against future emerging variants has not been denied.</li> </ul>
<p><b>AT-527</b></p>	<ul style="list-style-type: none"> <li>● Decision was made to discontinue development in December 2021</li> </ul>

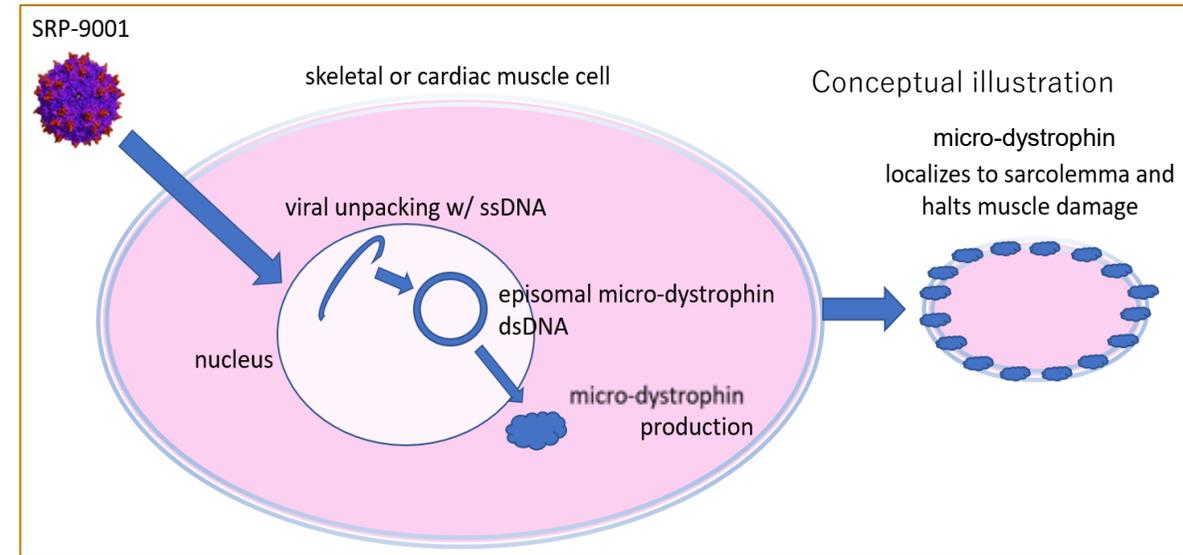
# Micro-dystrophin Gene Therapy SRP-9001/RG6356

## ■ Express a shortened, functional dystrophin protein inside the targeted muscle

- ✓ Delandistrogene moxeparvovec (SRP-9001/ RG6356) is an investigational gene transfer therapy developed for targeted muscle expression of micro-dystrophin, a shortened, functional dystrophin protein, that addresses the genetic cause of DMD.



- Aims to express **micro-dystrophin** – a smaller but still functional version of dystrophin, used because naturally-occurring dystrophin is too large to fit in an AAV vector<sup>1</sup>.
- Employs the **AAVrh74 vector**, which has a robust affinity for muscle cells, making it an ideal choice for delivering the micro-dystrophin transgene. AAVrh74 also has a relatively low level of pre-existing immunity<sup>1</sup>.
- The **MHCK7 promoter** drives the expression of the micro-dystrophin transgene selectively in skeletal and cardiac muscle, and contains an **α-MHC enhancer** that has been shown to drive high protein expression, particularly in cardiac muscle.<sup>1,2</sup>

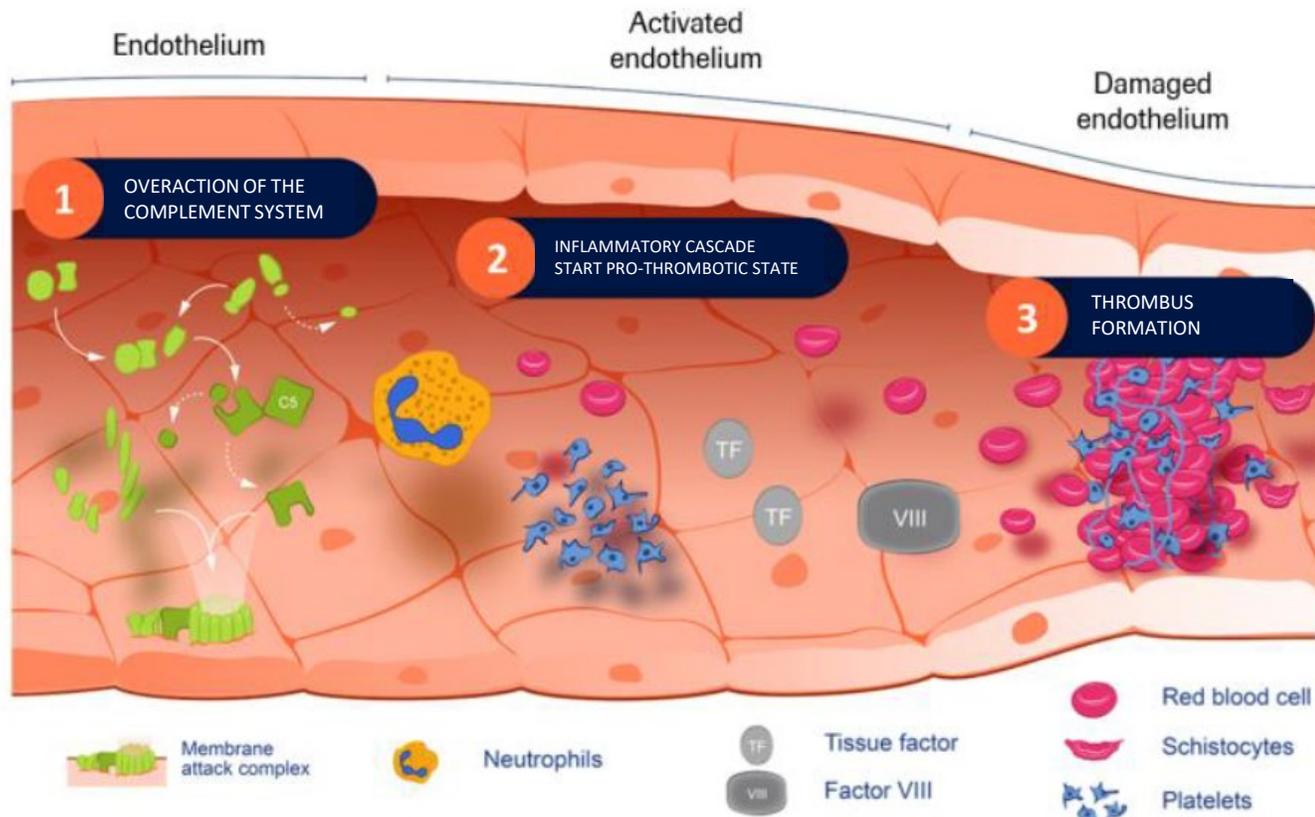


Source: Roche internal materials

1. Asher D, et al. Clinical development on the frontier: gene therapy for duchenne muscular dystrophy. Expert Opinion on Biological Therapy. 2020; 20:263-274;  
 2. Salva MZ, et al. Design of Tissue-specific Regulatory Cassettes for High-level rAAV-mediated Expression in Skeletal and Cardiac Muscle. Mol Ther. 2007; 15:320-9;

# Atypical Hemolytic Uremic Syndrome (aHUS)

- **Crovalimab: Binds to C5 and inhibits the cleavage of C5a and C5b, thereby blocking the activated terminal complement cascade completely**



- aHUS is caused by uncontrolled complement activation in the alternative pathway. A variety of genetic defects in complement-related factors or acquired autoantibodies to the complement regulators are associated with the onset.
- Ultra-rare disease characterized by severe and life-threatening acute kidney damage, decreased platelets, and MHA\*
- Many people with aHUS form the membrane attack complex (MAC) due to complement abnormalities, and cause endothelial disorders, activated platelets and thrombosis.
- Children with aHUS account for 40% of all cases
- About 200 patients are estimated in Japan (Source: aHUS registry cohort; Survey conducted by research team at the Ministry of Health, Labour and Welfare 2018)

\* MHA: microangiopathic hemolytic anemia

# Potential Market Sales of Post PoC Projects

[Expected year when each project will reach its peak-sales] **projects in black:** between 2022 to 2029; **projects in purple:** 2030 and beyond.

In-house projects

★★★★★ Global over 400 bn yen	★★★★ Global over 200 bn yen	★★★ Global over 100 bn yen	★ Global below 100 bn yen
<b>Hemlibra</b> (Hemophilia A, acquired hemophilia A)	<b>Enspryng</b> (NMOSD, gMG, etc.) <b>nemolizumab*</b> (Prurigo nodularis, atopic dermatitis)	<b>Alecensa</b> (NSCLC, NSCLC adjuvant, ALCL, etc.) <b>crovalimab</b> (PNH, aHUS, sickle cell disease, etc.)	

In-licensed (Roche)

★★★★★ Domestic over 60 bn yen	★★★★ Domestic over 30 bn yen	★★★ Domestic over 15 bn yen	★ Domestic below 15 bn yen
<b>Tecentriq</b> <b>[over 100 bn. yen]</b> (NSCLC, SCLC, urothelial carcinoma, RCC, prostate cancer, HCC, triple negative breast cancer, ovarian cancer, head and neck carcinoma, esophageal cancer, pancreatic adenocarcinoma, etc.)	<b>Polivy</b> (DLBCL) <b>faricimab</b> (nAMD, DME, RVO) <b>gantenerumab</b> (Alzheimer's disease)	<b>Evrysdi</b> (Spinal muscular atrophy) <b>HER/PER fixed-dose combination</b> (Early breast cancer, metastatic breast cancer) <b>tiragolumab</b> (NSCLC stage III, NSCLC (1L), SCLC (1L), esophageal cancer) <b>giredestrant</b> (Early breast cancer, metastatic breast cancer)	<b>Gazyva</b> (Follicular lymphoma, etc.)

\* Licensed out to Galderma (global) and Maruho (domestic), respectively. Based on the forecasts by Galderma and Maruho NOTE: expected indications based on peak-sales forecast are noted in brackets

NMOSD: neuromyelitis optica spectrum disorder, gMG: generalized myasthenia gravis, NSCLC: non-small cell lung cancer, ALCL: anaplastic large cell lymphoma, PNH: paroxysmal nocturnal hemoglobinuria, aHUS: atypical hemolytic uremic syndrome, RCC: renal cell carcinoma, HCC: hepatocellular carcinoma, DLBCL: diffuse large B-cell lymphoma, nAMD: neovascular age-related macular degeneration, DME: diabetic macular edema, RVO: retinal vein occlusion

# 2022: Key R&D Milestones

<p><b>Projects to be approved</b></p>	<p><b>Actemra</b>  <b>nemolizumab</b>  <b>Herceptin/Perjeta</b>  <b>faricimab</b>  <b>faricimab</b>  <b>Tecentriq</b>  <b>Hemlibra</b>  <b>Polivy</b></p>	<p>COVID-19 pneumonia                  Atopic dermatitis                  HER2 positive colorectal cancer                  Neovascular age-related macular degeneration (nAMD)                  Diabetic macular edema (DME)                  Non-small cell lung cancer (NSCLC) [adjuvant]                  Acquired hemophilia A                  Previously untreated diffuse large B-cell lymphoma (DLBCL)</p>	<p>✓</p>
<p><b>P3/Pivotal readouts</b></p>	<p><b>Alecensa</b>  <b>gantenerumab</b>  <b>Tecentriq</b>  <b>Tecentriq</b>  <b>Tecentriq</b>  <b>Tecentriq + Avastin</b>  <b>Tecentriq + tiragolumab</b>  <b>Tecentriq + tiragolumab</b></p>	<p>ALINA Study: NSCLC [adjuvant]                  GRADUATE1/2 Study: Alzheimer's disease                  IMpower030 Study: NSCLC [neoadjuvant]                  IMmotion010 Study: RCC [adjuvant]                  IMvoke010 Study: HNC [adjuvant]                  IMbrave050 Study: HCC [adjuvant]                  SKYSCRAPER-01 Study: NSCLC [1st line]                  SKYSCRAPER-02 Study: SCLC</p>	

Letters in orange : in-house projects, Letters in blue : in-licensed(Roche)

# Projected Submissions (Post PoC NMEs and Products)

		NME	Line extension			
<b>in-house</b>						
<b>in-licensed (Roche)</b>						
<b>Filed</b>						
		HEMLIBRA ★ (ACE910/RG6013) Acquired hemophilia A				
		crovalimab (SKY59/RG6107) PNH				
TECENTRIQ (RG7446) NSCLC (adjuvant)	faricimab (RG7716) nAMD	AVASTIN (RG435) SCLC	faricimab (RG7716) RVO	AVASTIN (RG435) HCC(intermediate stage)	giredestrant (RG6171) Breast Cancer (adjuvant)	SRP-9001 (RG6356) DMD ★
POLIVY ★ (RG7596) 1L DLBCL	faricimab (RG7716) Diabetic Macular Edema	AVASTIN (RG435) HCC (adjuvant)	gantenerumab (RG1450) Alzheimer's Disease	TECENTRIQ (RG7446) HCC(intermediate stage)	giredestrant (RG6171) Breast Cancer	crovalimab (SKY59/RG6107) aHUS ★
TECENTRIQ (RG7446) Ovarian Cancer	tiragolumab (RG6058) SCLC	TECENTRIQ (RG7446) HCC (adjuvant)	tiragolumab (RG6058) NSCLC	TECENTRIQ (RG7446) Early Breast Cancer	tiragolumab (RG6058) Esophageal Cancer	ENSPRYNG (SA237/RG6168) gMG
TECENTRIQ (RG7446) RCC (adjuvant)	RG6264 (FDC, sc) Breast Cancer	TECENTRIQ (RG7446) 2L RCC	ALECENSA (AF802/RG7853) NSCLC (adjuvant)	TECENTRIQ (RG7446) MIBC (adjuvant)	tiragolumab (RG6058) NSCLC (Stage III)	pralsetinib (RG6396) NSCLC ★
TECENTRIQ (RG7446) Urothelial Carcinoma	TECENTRIQ (RG7446) HNC (adjuvant)	TECENTRIQ (RG7446) NSCLC (neoadjuvant)	ipatasertib ★ (RG7440) Prostate Cancer	TECENTRIQ (RG7446) NSCLC (Stage III)	TECENTRIQ (RG7446) Esophageal Cancer	mosunetuzumab ★ (RG7828) Follicular lymphoma
<b>2022</b>		<b>2023</b>		<b>2024 and beyond</b>		

DLBCL: diffuse large B-cell lymphoma  
 FDC: fixed-dose combination  
 nAMD: neovascular age-related macular degeneration  
 HCC: hepatocellular carcinoma  
 PNH: paroxysmal nocturnal hemoglobinuria

RCC: renal cell carcinoma  
 NSCLC: non-small cell lung cancer  
 SCLC: small cell lung cancer  
 HNC: head and neck carcinoma  
 MIBC: muscle-invasive bladder cancer  
 gMG: generalized myasthenia gravis  
 RVO: retinal vein occlusion  
 DMD: duchenne muscular dystrophy  
 aHUS: atypical hemolytic uremic syndrome

as of February 3, 2022

# Projects under Development (1/2)

As of February 3, 2022

	Phase I	Phase II	Phase III	Filed	
Cancer	<b>GC33 / codrituzumab</b> - HCC	<b>RG6026 / glofitamab</b> - hematologic tumors	<b>OBP-301*</b> - esophageal cancer	<b>AF802 (RG7853) / Alecensa</b> - NSCLC (adjuvant)	<b>RG6396 / pralsetinib</b> - NSCLC ★
	<b>ERY974</b> - solid tumors	<b>RG7446 / Tecentriq (Actemra or tiragolumab combo)</b> - pancreatic adenocarcinoma		<b>RG7440 / ipatasertib</b> - prostate cancer	<b>RG435 / Avastin (Tecentriq combo)</b> - SCLC - HCC (adjuvant) - HCC (intermediate stage)
	<b>RG7421 / cobimetinib</b> - solid tumors	<b>RG6194 / HER2-TDB</b> - solid tumors		<b>RG6264 (Herceptin+Perjeta)</b> - breast cancer (Fixed-dose combination, subcutaneous injection)	<b>RG7446 / Tecentriq</b> - NSCLC (neoadjuvant) - NSCLC(stage III) - urothelial carcinoma - MIBC (adjuvant) - RCC (adjuvant) - RCC - early breast cancer - ovarian cancer - HCC (adjuvant) - HCC (intermediate stage) - HNC (adjuvant) - esophageal cancer
	<b>RG7802 / cibusatamab</b> - solid tumors	<b>OBP-301**</b> (Tecentriq/Avastin combo) - HCC		<b>RG6058 / tiragolumab (Tecentriq combo)</b> - SCLC - NSCLC - NSCLC(stage III) - esophageal cancer	
	<b>STA551</b> - solid tumors	<b>SOF10 (RG6440)</b> - solid tumors		<b>RG6171 / giredestrant</b> - breast cancer - breast cancer (adjuvant)	
	<b>SPYK04</b> - solid tumors	<b>LUNA18</b> - solid tumors		<b>RG7828 / mosunetuzumab</b> - Follicular lymphoma ★	
					<b>RG7446 / Tecentriq</b> - NSCLC (adjuvant)
					<b>RG7596 / Polivy</b> - DLBCL ★

In principle, completion of first dose is regarded as the start of clinical studies in each phase.

★: Projects with advances in stages since October 22, 2021

Letters in orange: in-house projects Letters in blue: in-licensed (Roche)

\* to be succeeded to Oncolys BioPharma Inc. by October 2022 \*\* to be discontinued by October 2022

DLBCL: diffuse large B-cell lymphoma  
HCC: hepatocellular carcinoma  
SCLC: small cell lung cancer  
RCC: renal cell carcinoma

NSCLC: non-small cell lung cancer  
HNC: head and neck carcinoma  
MIBC: muscle-invasive bladder cancer  
TDB: T cell-dependent bispecific

# Projects under Development (2/2)

As of February 3, 2022

	Phase I	Phase II	Phase III	Filed
<b>Autoimmune</b>	<b>RG7880 (IL-22 fusion protein)</b> - inflammatory bowel disease			
<b>Neurology</b>	<b>RG7935 / prasinezumab</b> - Parkinson's disease <b>GYM329 (RG6237)</b> - neuromuscular disease <b>RG6100 / semorinemab</b> - Alzheimer's disease <b>RG6102 (BS-Gante)</b> - Alzheimer's disease	<b>RG7906 / ralmitaront</b> - schizophrenia	<b>RG1450 / gantenerumab</b> - Alzheimer's disease <b>RG6042 / tominersen</b> - Huntington's disease	<b>SA237 (RG6168) / Enspryng</b> - generalized myasthenia gravis (gMG)
<b>Others</b>	<b>AMY109</b> - endometriosis <b>NXT007</b> - hemophilia A (PI/II) <b>RG7992 (anti-FGFR1/KLB)</b> - non-alcoholic steatohepatitis		<b>RG7716 / faricimab</b> - retinal vein occlusion	<b>RG7716 / faricimab</b> - DME - nAMD <b>ACE910 (RG6013) / Hemlibra (JPN)</b> - Acquired hemophilia A ★

In principle, completion of first dose is regarded as the start of clinical studies in each phase.

★: Projects with advances in stages since October 22, 2021

Letters in orange: in-house projects    Letters in blue: in-licensed (Roche)

gMG: generalized myasthenia gravis

PNH: paroxysmal nocturnal hemoglobinuria

nAMD: neovascular age-related macular degeneration

DME: diabetic macular edema

NOTE: As for RG6356/SRP-9001, global P3 study (EMBARK) for DMD is conducted by Sarepta Therapeutics in collaboration with Roche. Sarepta manages the global study, including Japan, while Chugai is responsible for the regulatory filing and marketing in Japan.

# FoundationOne CDx Cancer Genomic Profile -companion diagnostic indications-

As of February 3, 2022

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

\* Underlined are the companion diagnostic features and relevant drugs currently filed for regulatory approval

\*\* Application under review and not yet approved for the drug indication

# FoundationOne Liquid CDx Cancer Genomic Profile

## Companion diagnostic indications

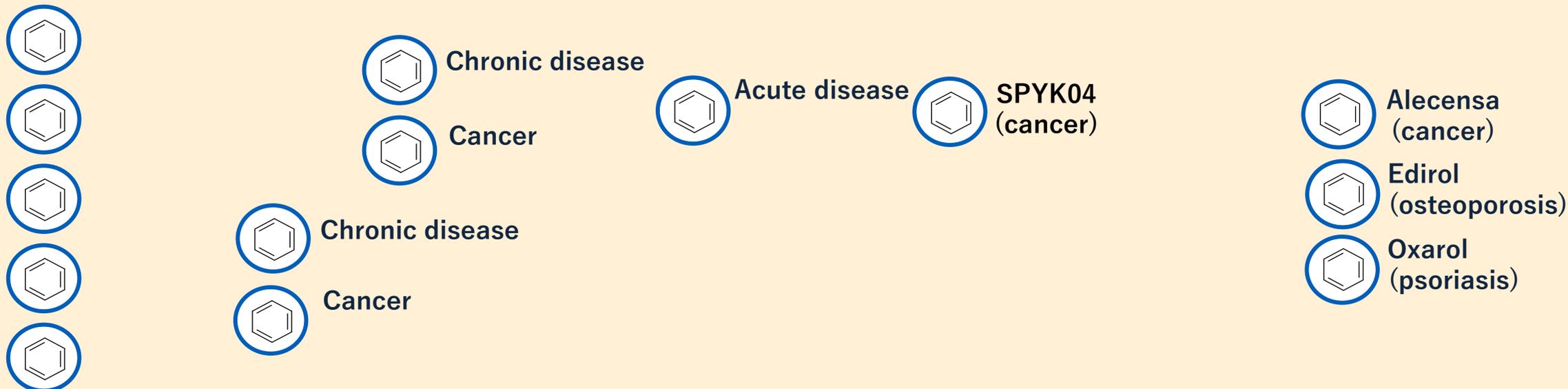
As of February 3, 2022

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

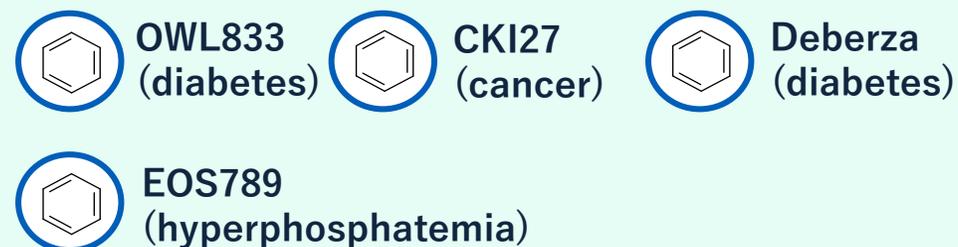
# Small molecule Drug Discovery: Research Portfolio

As of February 3, 2022

## In-house molecule

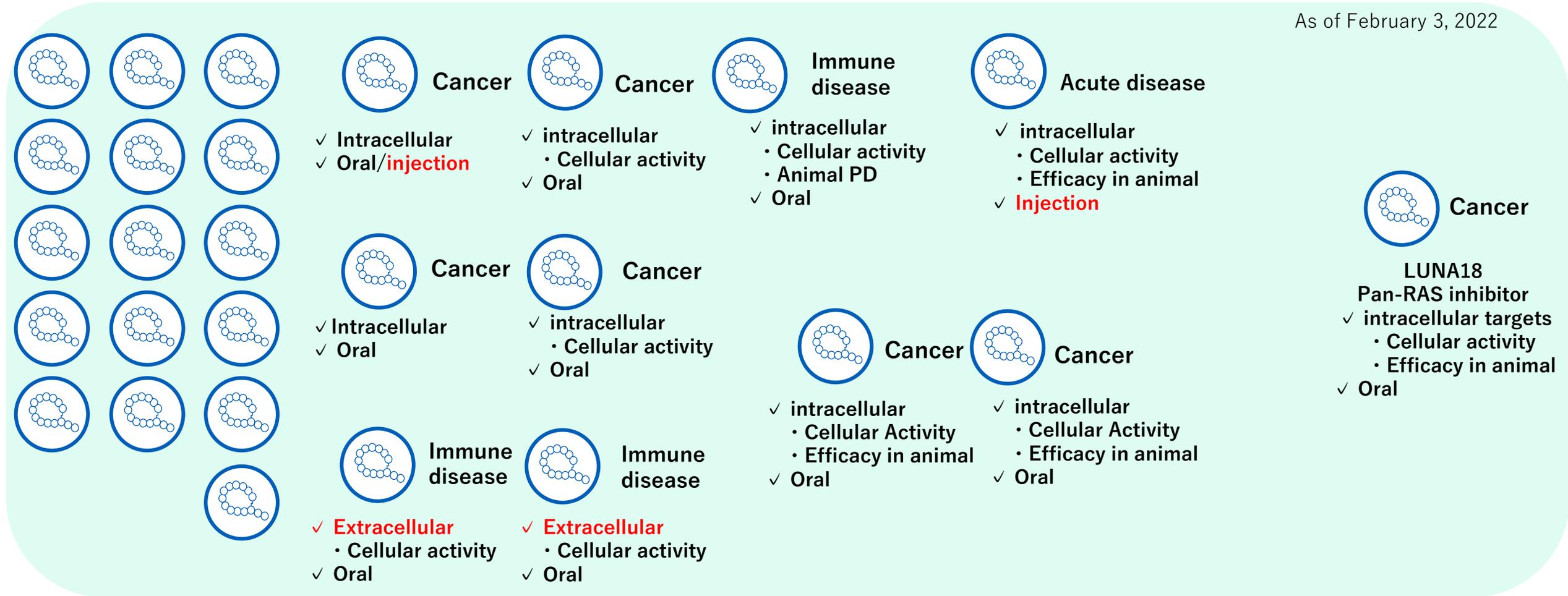


## Out-licensed molecule



# Mid-Size Molecule Drug Discovery: Research Portfolio

As of February 3, 2022



# Antibody Project Pipeline Utilizing Antibody Engineering Technologies

\* Projects that utilize multiple technologies are displayed in each technology. As of February 3, 2022

Recycling Antibody®  
Sweeping Antibody®  
etc.



SOF10 (cancer/P1)



Enspryng



AMY109  
(endometriosis/P1)



nemolizumab  
(atopic dermatitis/Filed)

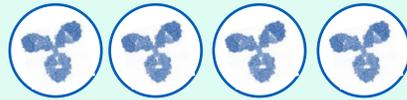


GYM329/RG6237  
(SMA/P1)



crovalimab (PNH/P3)  
PNH: Paroxysmal nocturnal hemoglobinuria

Bispecific antibody (Non-Oncology)



NXT007 (hemophilia A/P1)



Hemlibra

Bispecific antibody (Oncology, Dual-Ig® etc.)



ERY974 (cancer/P1)

Switch Antibody™



STA551 (cancer/P1)

PAC-Ig™, new technologies, etc.



*and more*



codrituzumab (cancer/P1)



Actemra

Discovery

GLP-tox

Clinical trial

Launched

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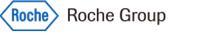
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INNOVATION BEYOND IMAGINATION