CHUGAI

Roche Group

Annual Report 2020

Fiscal year ended December 31, 2020

Activity Report

CHUGAI PHARMACEUTICAL CO., LTD.

Contents

Chugai in Action

Outline of Functions

	Roles/Features	Strengths (○)/Weaknesses (△)
Research	・Focusing on generating a steady stream of innovative new drugs with first-in-class[1] or best-in-class[2] potential to address unmet medical needs[3] ・Biopharmaceutical R&D track record of over 30 years. Currently developing antibody engineering technology and drug discovery and technology platform for multiple modalities such as small and mid-size molecules[4] ・Building powerful external networks with the Roche Group's world-leading research infrastructure, academia, etc. ・Contributing to global healthcare as a whole through presentation of research findings at scientific conferences, etc.	○ Unique drug discovery technology in biopharmaceuticals and mid-size molecules ○ Collaborative system for sharing of the Roche Group's research resources and infrastructure (large-scale, high-quality chemical library, genes and nucleic acids platforms, etc.) △ Infrastructure for recruiting highly specialized researchers is incomplete △ Insufficient drug discovery research resources
Development	・Establishment of a lifecycle management (LCM) system for integrated control of functions at the individual project level ・Conducting a wide range of clinical studies using scientific methods that combine speed with efficiency in collaboration with numerous medical institutions and clinical research centers ・Progressing with wide-ranging global development (global studies) and simultaneous development of drugs and companion diagnostics intended for personalized healthcare (PHC) through alliance with the Roche Group, resulting in advanced development projects and related approval applications ・Coordinating with medical professionals and patient groups from the clinical development stage to realize patient-centric healthcare	○ Extensive development track record across a wide range of diseases ○ Track record in development of new molecules using proprietary technology ○ High success rate in the in-house development of innovative products ○ System for global collaboration with Roche △ Constant and cross-functional operation of the process for proof of value △ Infrastructure development and acquisition of human resources for utilization of real world-data (RWD), data assets, and cutting-edge technologies
Pharmaceutical Technology and Production	・Putting in place a worldwide supply chain encompassing production bases and contract manufacturing organizations ・Evolving manufacturing functions based on Japan-leading bioproduction technologies, manufacturing facilities and inspection capabilities, and the advantage of Roche Group membership ・Building and patenting technology platforms aimed at commercial production of innovative medicines such as next-generation antibodies and mid-size molecules	○ Advanced therapeutic antibody production technology and state-of-the-art equipment ○ Proven track record of global inspections and applications (Hemlibra, Alecensa, and Enspryng) ○ Timely identification and response to requests from regulatory authorities that can be shared with the Roche Group △ Creation of an efficient production system utilizing external resources in accordance with rapid changes in demand
Marketing	・Contributing to the advancement of healthcare as a leader in the fields of therapeutic antibodies and oncology, including promoting standards of care and proper use of medicines ・Working for widespread introduction and advanced development of PHC as a pioneer in the field ・Conducting consulting activities including flexible provision of specialist information, liaison services for regional healthcare, and support to healthcare professionals	○ Leading presence in specialty areas, such as biopharmaceuticals and PHC ○ A system for providing advanced solutions based on regional and customer characteristics, multidisciplinary team care and drug safety activities utilizing a database of adverse events, etc. △ Increase in competing products and new market entrants

Outline of Functions

	Roles/Features	Strengths (○)/Weaknesses (△)
Medical Affairs	・Strengthening systems for healthcare compliance and governance of contract-based post-marketing studies, including by becoming one of the first companies to operate schemes ・Initiatives in evidence generation and scientific communication ・Expanding and upgrading global medical information functions	○ Extensive track record in generating evidence ○ Global collaboration with Roche and overseas subsidiaries △ Adaptability to conducting increasingly diverse clinical research
Drug Safety	・Building pharmacovigilance system to meet the world's strictest standards and most comprehensive global regulations ・Providing solutions to patients and healthcare professionals using drug safety information ・Formulating drug risk management plans (RMPs) and ensuring their full implementation	○ Industry-leading achievements (introduction of the database tool and establishment of Safety Experts, etc.) ○ Solid partnership with the Drug Safety Division of Roche Group ○ A track record of industry activities in areas utilizing epidemiological and medical data △ Response to the constant shortage of high-quality human resources
Quality and Regulatory Compliance	・Integrating healthcare compliance, good practice guidelines and regulations (GxP) compliance, and digital compliance in an organizational structure that treats regulatory activities, compliance, and quality as a three-in-one concept ・Protecting the rights of patients and clinical trial subjects and ensuring the reliability of data by pursuing product and service quality that resonates with all stakeholders under the slogan "Quality That Inspires"	○ Active utilization of digital technologies, including the establishment of an electronic signature system, digitalization of the quality assurance system, and introduction of artificial intelligence (AI) in the supervision of activities to provide marketing information ○ Quality assurance achieving successful maintenance and strengthening of world-class quality, including in the supply chain ○ Digital compliance system to speed up digital transformation (DX) △ Establishment of new Chugai quality adapted to new modalities and new processes
Intellectual Property	・Aggressively acquiring intellectual property (IP) rights focused on important R&D projects and actively securing rights outside Japan with a view to global co-development ・Strategically seeking to acquire lifecycle patents, as well as patents relating to the substance and use, when filing product patent applications ・Building a unique database in antibody engineering technology for use in formulating IP strategy	○ Expanded and upgraded portfolio of technological patent applications ○ Progress in securing rights for products △ Increase in IP disputes related to global development products △ Difficult environment for securing of technological patent rights in Europe and the United States due to more stringent patent registration criteria

1. An original drug that is highly novel and useful, and will significantly change the therapeutic system
2. A drug that offers clear advantages over other existing drugs in the same category, such as those with the same molecular target
3. Medical need that is not adequately met due to a lack of effective treatments
4. Molecules with a molecular weight between 500 and 2,000. Mid-size molecules are expected to be capable of inhibiting protein–protein interaction (PPI) in intercellular molecules, which is difficult to achieve with antibodies and small molecules.

Response to the COVID-19 Pandemic

As a business operating in the healthcare industry, our response to the worldwide crisis unleashed by COVID-19 gave priority to ensuring the stable supply of drugs to patients. Accordingly, we introduced measures to prevent the spread of infection among our employees and in our business activities. At the same time, we invested resources in activities to contribute to developing treatments for COVID-19 and preventing its spread.

The swift adoption of a response policy by our Emergency Headquarters and the rollout of the associated measures proved highly effective in combination with the measures taken under the existing corporate business continuity plan (BCP). As a result, there has been no disruption or other impact on the supply of active pharmaceutical ingredients (APIs) or other materials as of March 2021 and we have confirmed sufficient safety stocks of products manufactured at overseas plants.

We are working to contribute to the treatment of COVID-19 and to the prevention of its spread through a range of activities, from research and development and in- and out-licensing of technologies and products to various support initiatives.

In its R&D activities, specifically, as part of its policy to combat the COVID-19 pandemic, Chugai is collaborating with Roche and other pharmaceutical companies and research institutions to initiate development of therapeutic drugs using its proprietary technology and to conduct in-licensing to Japan of promising development items from other companies.

Main Initiatives to Develop COVID-19 Treatments and Prevent the Spread of Infection

Field of Activity	Outline of Initiatives
Research and development	● Domestic phase III clinical study of Actemra in hospitalized patients with severe pneumonia due to COVID-19 (J-COVACTA) (>Activity Report P7) ● Joint research between Chugai Pharmabody Research (CPR) and A*STAR (Agency for Science, Technology and Research) into a therapeutic antibody for COVID-19
Technology/product in- and out-licensing	● Out-licensing of antibody engineering technology to Eli Lilly and Company for research and development of therapeutic drugs for COVID-19 ● In-licensing from Roche of the development and exclusive marketing rights in Japan for an antibody cocktail therapy against COVID-19 developed by Regeneron Pharmaceuticals, Inc. (>Activity Report P7) ● In-licensing from Roche of the development and exclusive marketing rights in Japan for a new oral drug candidate against COVID-19 developed by Atea Pharmaceuticals, Inc.
Support activities (donations)	● Donation of RMB 1 million to the Red Cross Society of China to support COVID-19 response activities in the People's Republic of China ● Donation of a total of ¥50 million to The Nippon Foundation and the Tokyo metropolitan government for healthcare professionals in Japan working to provide treatment and prevent infection
Other	● Posting on Chugai's official YouTube channel of a podcast series created to provide "medicine for the mind" during the COVID-19 pandemic in a joint project with a former stage actor

Note: The page numbers indicated in parentheses above show where in this Activity Report to find more detailed information.

Main Initiatives Affecting Employees and Business Activities

● Swift adoption of response policies and rollout of measures by the Emergency Headquarters
● Policies to regulate the work and activities of all employees and rollout of a range of measures to promote hygiene and prevent infection
● Promotion of innovative workstyles for the new normal (>Annual Report P69)

Note: The page number indicated in parentheses above shows where in the Annual Report to find more detailed information.

Research

Strategic Points

- Expansion following success with mid-size molecule drug discovery ahead of global competition
- Progress in the discovery of therapeutic antibodies with a competitive advantage and development of new modalities
- Creation of innovative drug discovery projects aimed at realizing cures through intensified biological research
- Enhancement of the drug discovery process through digital technology
- Pursuit of innovation in drug discovery through external alliances

Performance in 2020

16
In-house projects in the development pipeline
(As of February 4, 2021)

62
Publications in academic papers and presentations at scientific conferences regarding Chugai's innovative proprietary antibody engineering technologies
(2016–2020)

100
Publications in academic papers regarding Chugai's research findings
(2016–2020)

14.4%
R&D expenditures to revenues (%)
(2020)

Business Model and Core Themes

To respond to the increasingly diverse range of unmet medical needs, we are committed to developing a succession of innovative new drugs with first-in-class/best-in-class status. To do so, as well as effectively utilizing our external networks, we are working to further strengthen our in-house drug discovery platform consisting of antibodies, small molecules, and mid-size molecules.

To focus resources on the creation of innovative drugs, in addition to building a stable revenue base through efficient development in Japan of products in-licensed from Roche, we have established a system for collaboration with Roche in the late-stage clinical development of in-house projects. Sharing the Roche Group's global research resources, including its large-scale, high-quality chemical library and its state-of-the-art infrastructure, enables us to carry out drug discovery on the scale of the pharmaceutical giants.

Bioethics and Animal Welfare

Chugai takes seriously the issues of bioethics and animal welfare and has responded with the measures outlined below.

To ensure that research using human-derived samples is carried out appropriately, Chugai has established Ethical Guidelines for Research That Uses Human-Derived Samples and a Research Ethics Committee. More than half of the members of this committee are from outside the Company, enabling fair evaluations from a pluralistic frame of reference.

When handling laboratory animals used in research, Chugai acts in accordance with the Guidelines for the Care and Use of Laboratory Animals it has established to respect their lives from the standpoint of animal welfare, and to minimize pain, keeping in mind the scientific conditions. Chugai's measures, which are based on the principles of the 3Rs (Replacement, Reduction, and Refinement), were positively evaluated by AAALAC International,[1] a global third-party evaluation organization, and the Company has maintained full accreditation since 2007.

1. The Association for Assessment and Accreditation of Laboratory Animal Care International, a private nonprofit organization (NPO) that promotes the humane treatment of animals in scientific research through voluntary inspection and accreditation programs. More than 900 facilities in 39 countries have obtained AAALAC accreditation.

Strategy and Progress

Uncompromising commitment to manufacturing as well as enhancement and expansion of the drug discovery platform

Having further enhanced our in-house antibody engineering technology to develop adenosine triphosphate (ATP) Switch-Ig and FAST-Ig/ACT-Ig, we have now begun clinical studies of antibodies to which this technology was applied.

In the field of drug discovery through chemical synthesis, in addition to our existing use of the small molecule modality, we are building a platform in the modality of mid-size molecules, where we have begun screening candidates for use with a number of target molecules. Mid-size molecules represent a particularly useful drug discovery tool for intracellular targets difficult to tackle with antibodies and small molecules, and we believe that this technology will broaden the scope of drug discovery. In 2020, we achieved major progress in the establishment of a technology platform for the creation of hit-to-lead compounds. Having spent more than 10 years in the development of this technology, we plan to commence our first clinical study using mid-size molecules in 2021.

Founded in Singapore in 2012, Chugai Pharmabody Research (CPR) has worked on creating therapeutic antibodies. It has now expanded the scale of its research activities after designing and launching a system able to carry out high-throughput screening of mid-size molecules.

Application of digital technology to drug discovery

In line with the rapid advances in science and technology centered on the fields of digital and information and communications technology (ICT), we believe that the drug discovery process will also undergo marked changes. In July 2018, Chugai entered into a comprehensive partnership agreement with Preferred Networks, Inc. (PFN), a global leader in artificial intelligence (AI) technology. We are currently conducting multiple cooperative projects with the aim of creating innovative drugs and new value through the application of PFN's cutting-edge deep learning technology and Chugai's expertise, technologies, and data.

As part of initiatives to boost the efficiency of drug discovery, we are progressing with laboratory automation and the introduction of robotic technology. The use of robots will enable a dramatic increase in the volume of experimental data obtained and more integrated data analysis, resulting in higher-quality drugs.

Healthcare in the future is expected to center on personalized healthcare (PHC), which provides optimal solutions tailored to individual patient needs, and will need to provide comprehensive value in a sustainable form that encompasses prevention and prognosis in addition to diagnosis and treatment, which are the focus of the current model. Using digital technology will allow us to gauge each patient's degree of satisfaction with their treatment so that we can tailor drug discovery to the individual patient's unmet medical needs.

Pursuit of innovation in drug discovery through external alliances

In April 2017, the Collaboration Promotion Laboratory began operating under our comprehensive agreement with Osaka University Immunology Frontier Research Center (IFReC) to conduct ongoing assessment and introduction of new candidate compounds from its cutting-edge immunology research. Immunity is involved not only in diseases of the immune system itself, but also in cancer and various other diseases, and immune-mediated therapies are now becoming mainstream cancer treatments. Combining the global top-class research in immunology at IFReC and Chugai's expertise in drug discovery research, accumulated through its proprietary technologies, is expected to result in the creation of innovative new drugs.

We are also looking to innovate the drug discovery process itself, including for next-generation PHC, by applying the highly advanced genomic analysis techniques and other capabilities of Foundation Medicine, Inc. (FMI),[2] which joined the Roche Group in 2015.

Additionally, we are engaged in the out-licensing of antibody engineering technologies developed in-house. In 2020, we concluded licensing agreements relating to Chugai antibody engineering technology with Eli Lilly and Company and three other companies. By making our innovative drug discovery technology available to other operators, we hope to stimulate innovation across the pharmaceutical industry that will result in solutions to unmet medical needs, creation of innovative new drugs, and other benefits.

2. FMI was established in Massachusetts, U.S.A. in 2010. In 2015, Roche took a majority stake, and then acquired the remaining outstanding shares in 2018 to make FMI a wholly owned subsidiary. Chugai carries out commercialization and product value maximization of FMI's Comprehensive Genomic Profiling Service in Japan.

Comparison of Drug Discovery Modalities

	Small Molecules	Mid-Size Molecules	Biologics
Molecular weight	Below 500	500–2,000	10,000 and above
Target specificity	Fair	High	High
Intracellular targets	Wide range	Numerous	Limited
PPI[3] inhibition	Fair	Good	Good
Administration route	Oral/Injection	Oral/Injection	Injection
Manufacturing method	Organic synthesis	Organic synthesis	Cell culture

3. PPI: Protein–protein interaction

Development

Strategic Points

- Establishment of development methods for Chugai products with new modalities and mechanisms of action
- Further acceleration of development through use of data assets
- Maximization of product value based on value-based healthcare (VBHC)

Performance in 2020

54
Pipeline projects
(As of February 4, 2021)

30
New products launched and new indications
(2016–2020)

39
Projects being co-developed with the Roche Group
(As of February 4, 2021)

20
Projects in-licensed from Roche
(2016–2020)

Business Model and Core Themes

The Translational Research (TR) Division acts as a bridge between preclinical and early clinical development. The division undertakes integrated project implementation from the initial research stage of drug discovery through to the early clinical development stage, in this way ensuring that clinical studies are conducted on a scientifically valid basis and working to establish proof of concept (PoC) at an early stage.

In October 2020, the Clinical Development Division consolidated its own clinical science and operational functions to establish a system that increases operational efficiency from planning through to operation.

By also integrating management functions for strategic planning and execution of clinical studies, including early clinical development, we aim to achieve strategically appropriate and efficient rollout and boost quality improvement. At the same time, sharing clinical development expertise and platforms with the Roche Group will assist us in accelerating global development.

Additionally, we utilize FMI and other partners to generate evidence from the clinical development stage that will contribute to personalized healthcare (PHC) and help to realize patient-centric medicine.

Strategy and Progress

A well-stocked pipeline

In 2020, all projects progressed steadily. We filed applications in nine projects and received approval in 11. The pipeline was also further enhanced, with clinical development starting in six projects based on items developed in-house or in-licensed from Roche.

Speedy global development

Chugai has been working to speed up global development by following a development model with a high probability of success and by making efforts to prove the value of in-house projects from the early stages of research and development. As a result, Alecensa took just seven years from concept to launch, and Hemlibra, for which we filed for approval simultaneously in Japan, the United States, and Europe, in collaboration with Roche, obtained approval in less than five years from initiation of clinical development, far ahead of our initial plan. This has dramatically transformed treatment strategies for hemophilia.

Enspryng (satralizumab) represents the first application of Chugai's proprietary recycling antibody engineering technology. Based on the results of Chugai-led global studies, we received approval for the product in 2020 in more than 10 countries around the world including Japan and the United States following applications filed in collaboration with Roche. In late-stage development projects, nemolizumab (CIM331), crovalimab (SKY59), and other in-house items progressed steadily through global phase III studies.

Initiatives in pharmaceutical development for COVID-19

As part of our initiatives to develop drugs for the treatment of COVID-19, Actemra entered domestic phase III clinical studies in May 2020. Overseas, Roche is engaged in a number of phase III global studies. We also obtained Japanese development and exclusive marketing rights to an antibody cocktail therapy (casirivimab and imdevimab) developed by Regeneron Pharmaceuticals and in-licensed from Roche in December 2020.

Evolution of clinical development using digital technology

We are also accelerating digital initiatives through partnerships. In collaboration with NTT DATA Corporation, we carried out a demonstration test of a clinical trial efficiency solution based on AI technology. Meanwhile, we are currently working with Biofourmis on digital solutions aimed at co-developing an objective assessment of pain associated with endometriosis. The utilization of real-world data (RWD) is expected to help realize more efficient and effective clinical studies with shorter development periods by allowing late-stage results to be predicted at the early stage, and to bring higher success rates by enabling more precisely formulated clinical development plans. In order to realize patient-centric healthcare, we will proceed with initiatives to promote the utilization of RWD.

Pharmaceutical Technology and Production

Strategic Points

- Acquisition of PoC with world-class speed and establishment of mid-size molecule manufacturing technology
- Strengthening of commercial production through outsourcing of manufacturing and building of an efficient production system through utilization of digital technology and robotics
- Action to mitigate environmental burden toward mid-term environmental goals

Performance in 2020

Began stable operations of facilities that can handle multiple antibody development projects simultaneously

Upgraded world-class system for pharmaceutical quality management

55
Research papers and other publications from the Pharmaceutical Technology Division
(2016–2020)

Business Model and Core Themes

Our pharmaceutical technology and production functions play a range of roles, from establishing manufacturing processes for investigational candidates—whether developed in-house, in-licensed from Roche, or originating elsewhere—to ensuring the stable supply of these products. By ensuring continuous evolution of our technologies and working to maintain and strengthen the supply chain, we aim to become a top innovator maintaining the trust of patients and healthcare professionals.

Strategy and Progress

Improving flexibility and speed

In its pharmaceutical technology and production operations, Chugai is aiming for simultaneous development of multiple products for the quickest launches possible. Specifically, the Ukima Plant has achieved a significant increase in capacity utilization by employing single-use plastic bioreactors. For development candidates based on next-generation antibody engineering technologies, the plant has also begun full-scale operation of UK3, an antibody API facility capable of high-mix, low-volume production from late-stage development to initial commercial products. At the Utsunomiya Plant, we have increased production flexibility by installing tray fillers that can handle filling of liquid medicines without making line changes or modifications, regardless of the syringe type.

At the Fujieda Plant, we will introduce an API manufacturing facility for investigational drugs for mid-size molecules, which are a next-generation modality, with the aim of starting operations in 2022.

Evolution of pharmaceutical technology and production functions through DX

In collaboration with IBM Japan, Ltd., we have started work on the digital transformation (DX) of production functions. By realizing “digital plants” through DX focused on human functions, we are driving improved productivity and reliability and innovation in workstyles. Implementation will begin first at the Ukima Plant’s UK3 facility, which will serve as a model, with rollout to other production bases planned for the future.

Evolving supply chain management

To minimize risks related to the supply and price of raw materials, we promote the globalization of our suppliers of raw materials and intermediate products in tandem with the globalization and establishment of two production bases for each finished product.

Thorough quality assurance

Quality assurance functions have diversified in recent years in response to the increasing complexity of supplying products and accelerated development with the introduction of the fast-track review system to support the early launch of innovative new drugs. In view of these trends, Chugai is working to further strengthen GMP* management oversight to promote more rigorous and high-level quality assurance. As part of these efforts, Chugai promotes the building and operation of a world-class system for pharmaceutical quality management.

* Good Manufacturing Practice: Standards for pharmaceutical production management and quality control

Biological API Production: Our Facility Portfolio

Plant	Target	Bioreactors	Features	Products
Utsunomiya	Commercial production (Large-scale)	10,000 L x 8 (UT1, UT2: Stainless steel tanks)	• Competitive low-cost production • Dedicated facilities	Actemra
Ukima	Commercial production/Production of investigational APIs (Medium-scale)	6,000 L x 6 (UK3: Stainless steel tanks)	• Emphasis on flexibility • Can handle high-mix, low-volume production	Future development projects
Ukima	Commercial production/Production of investigational APIs (Small-scale)	2,000 L x 4 (UK1, UK2: Single-use plastic bags)	• Improved capacity utilization through the application of single-use bioreactor technology	Hemlibra and future development projects

Marketing

Strategic Points

- Maximization of the value of growth drivers (innovative drugs and services)
- Quick and accurate value delivery to customers through optimized use of digital technology and strengthening of alliances for specialized functions

Performance in 2020

22.5%[1]
Share of sales in the Japanese therapeutic antibody market

15.2%[1]
Share of sales in the Japanese oncology market

1[2]
Satisfaction ranking based on healthcare professionals' assessments
(Oncology; hospitals with 100 or more beds)

1[3]
Adequacy ranking for provision of safety information based on healthcare professionals' assessments
(Hospitals with 100 or more beds)

1. Copyright © 2021 IQVIA. Source: JPM 2020 (calendar year). Reprinted with permission. The scope of the market is defined by Chugai.
2. Source: INTAGE Healthcare Inc., CS Survey of Oncology, 2020. Based on a survey of overall assessments of companies by physicians, as defined by Chugai.
3. Source: INTAGE Healthcare Inc., 2020 questionnaire about safety information needs.

Business Model and Core Themes

With growing interest in more sophisticated and individualized medical treatments such as cancer immunotherapy and genomic testing as a way to address unmet medical needs, healthcare professionals will be expected to promptly provide high-quality information. Chugai is responding to this need through three different approaches under the general heading of "consulting."

For patients
We conduct patient-centric consulting activities that give the highest priority to patients, including proposing the optimal drug treatment according to each patient's condition, providing relevant information on proper use and safety, and follow-up activities.

For regional healthcare
We provide liaison services for regional healthcare with the aim of solving medical issues according to local area characteristics. We conduct consulting activities that improve patients' access to treatment by supporting regional healthcare coordination among healthcare professionals and medical institutions as well as collaboration among local governments, public entities, and other industries.

For stakeholders
Multidisciplinary team care has advanced in recent years, with various specialist healthcare professionals working in collaboration to carry out treatment according to each patient's condition. We conduct consulting activities to support our diverse stakeholders, while multidisciplinary teams follow up on treatment through proper management of adverse events.

Because consulting activities necessarily require extensive communication with relevant parties, our medical representatives (MRs) play a key role. In addition to MRs, we also have a system for providing solutions that meet medical need through participation in cross-functional teams by members of the Marketing & Sales, Medical Affairs, and Drug Safety divisions, who have high-level expertise.

We are also innovating business processes using the latest digital technologies such as AI and the Internet of Things (IoT) to build a system that can provide more efficient and effective solutions based on higher-quality consulting activities.

Strategy and Progress

Oncology

Sales in the cancer diseases area in Japan in 2020 decreased ¥11.0 billion (4.6 percent), year on year to ¥229.5 billion. Although the restriction of activities accompanying the COVID-19 pandemic had some impact on the market rollout of new products and additional indications, the anti-PD-L1 monoclonal antibody Tecentriq, which has been approved for the additional indication of hepatocellular carcinoma (HCC) in combination with Avastin, enjoyed major sales growth with a year-on-year increase of ¥16.9 billion (82.0 percent) to ¥37.5 billion. There were sales decreases however for some mainstay drugs, including Avastin, impacted by National Health Insurance (NHI) drug price revision, and Herceptin and Rituxan, affected by competition from biosimilars. These impacts were reflected in reduced revenues for the domestic oncology area as a whole. Following a price reduction for exports to Roche, sales of Alecensa outside Japan declined ¥1.0 billion (2.2 percent) year on year to ¥44.3 billion.

In 2021, we expect some products to continue to be impacted by competition from biosimilars. For new products and additional product indications, however, we are aiming for sales growth from increasing market penetration. This applies to Tecentriq, which has been approved for the indications of lung cancer and HCC, and Kadcyla, now approved for the indication of human epidermal growth factor receptor type 2 (HER2)-positive early-stage breast cancer.

Bone and Joint Diseases

In 2020, sales in the bone and joint diseases area in Japan decreased ¥16.0 billion (14.8 percent), year on year to ¥92.4 billion. Actemra, a first-line biologic for the treatment of rheumatoid arthritis (RA), was impacted by an NHI drug price reduction due to repricing based on market expansion. With the general effect of the reduction in inpatient numbers due to COVID-19, mainstay drugs, including Bonviva for osteoporosis and Edirol, which was additionally impacted by the launch of generics, saw reduced sales revenue overall. Sales of Actemra outside Japan received a major boost from exports to Roche for use against COVID-19 and posted a year-on-year increase of ¥46.1 billion (52.2 percent) to ¥134.4 billion.

In the Japanese market in 2021, Edirol, for which a marketing alliance with Taisho Pharmaceutical Co., Ltd., has ended, is expected to be impacted by the market penetration of generics, resulting in reduced sales revenue. In markets outside Japan, we will work to achieve further market penetration of the subcutaneous formulation of Actemra for RA and to promote its uptake for the additional indication of giant cell arteritis approved in 2017.

Renal Diseases

Sales in the renal diseases area in Japan in 2020 decreased ¥6.0 billion (17.3 percent), year on year to ¥28.6 billion. Mircera was impacted by the revision of medical fees for hemodialysis in April 2020 and by the switch to biosimilars at dialysis facilities, while Oxarol came under pressure from generics and other factors. As a result, both products again saw year-on-year falls in sales revenue.

In 2021, we aim to maintain the market presence of Mircera and Oxarol in the pre-dialysis and dialysis stages through ongoing provision of information and patient-centric activities rooted in our high level of expertise in the area of renal diseases.

Other Diseases

Hemlibra is a bispecific antibody created using Chugai's proprietary antibody engineering technologies. It obtained approval and was launched in May 2018 for routine prophylaxis in people with congenital hemophilia A with blood coagulation factor VIII inhibitors. In December 2018, we obtained approval of blood coagulation factor VIII for the additional indication of hemophilia A without inhibitors. Compared to existing therapeutic drugs, it allows longer dosing intervals, which will contribute to improved QoL for hemophilia A patients and their families. Despite a temporary delay in its market rollout due to COVID-19, the strong need among patients and healthcare professionals resulted in sales in Japan of ¥34.1 billion, a year-on-year growth of ¥8.9 billion (35.3 percent). Outside Japan, exports to Roche, which had previously been at the initial shipment price, switched to the regular shipment price in 2020. This and the continuing switch from existing therapeutic drugs, especially in the United States, were the main factors in the year-on-year surge of ¥22.5 billion (625.0 percent) in sales outside Japan to ¥26.1 billion. In 2021, we will devote energies to continuing with the collection of safety information, information provision and activities to promote proper use, working thus to make further contributions to the treatment of congenital hemophilia A.

Enspryng represents the first pharmaceutical product developed using Chugai's proprietary recycling antibody engineering technology. As a fourth growth driver after Actemra, Alecensa, and Hemlibra, it has been approved in 22 countries around the world (as of the end of April 2021), including Japan and the United States, for neuromyelitis optica spectrum disorder (NMOSD). Its Japanese sales launch in August 2020 marked Chugai's entry into the neurology field. Administered at four-week intervals, it is the first subcutaneous formulation for the treatment of NMOSD. We will be promoting its proper use so as to make therapeutic contributions through both reduced recurrence and improved convenience.

As the scale of the influenza epidemic in the 2019–2020 season was extremely limited compared to a regular year, and because the start of the 2020–2021 season was late, sales of Tamiflu were held to ¥4.5 billion.

Evolution of activities through use of digital technology

Toward delivering patient-centric services, Chugai is pursuing initiatives that make use of digital technology to provide optimal solutions.

0C (Organic Communication)

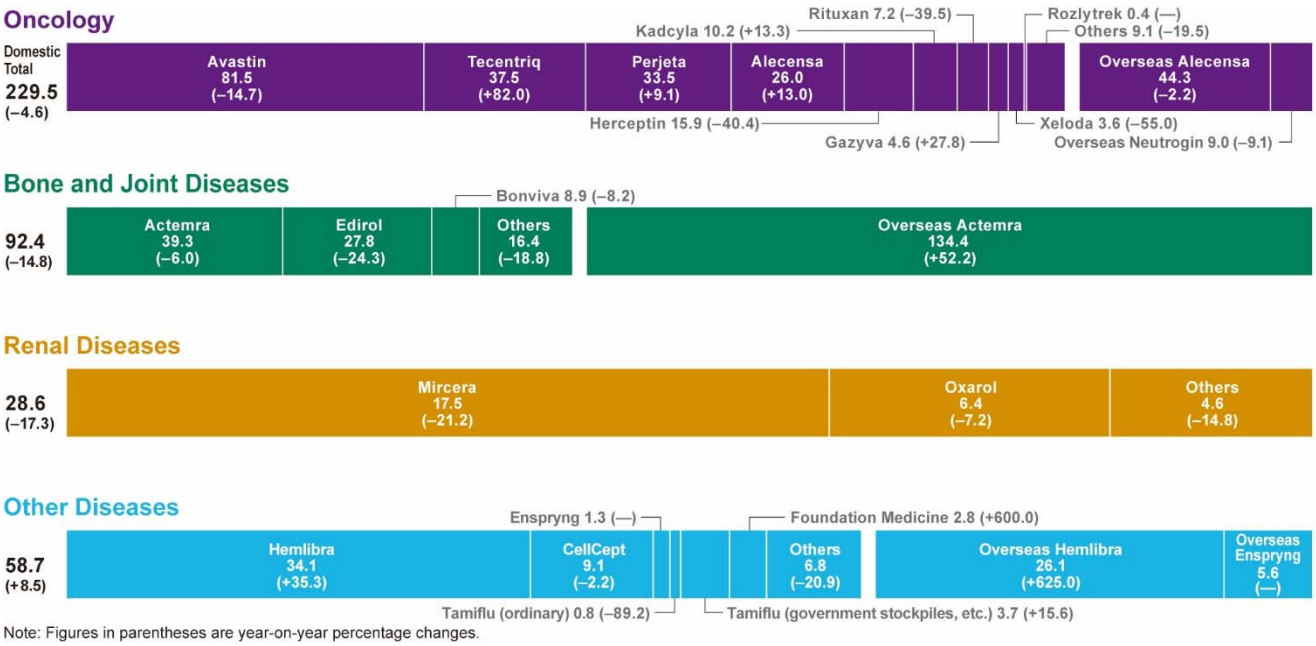
In order to respond flexibly to the needs of healthcare professionals, we have launched a cross-departmental project entitled 0C (Organic Communication), or Zero C, which aims to

build an integrated interface to realize customer-focused marketing. This will allow management via an integrated database of many different categories of data, from records of individual employee activity to market information on Chugai and competitors and customer and area information. In this way, we will create a system to support business activities through access to a range of analyses and an AI-based decision support engine.

MRs using LINE WORKS for their activities

In September 2020, we introduced LINE WORKS, which is the business version of the popular Japanese social media app LINE and is provided by WORKS MOBILE Japan Corp. During the COVID-19 epidemic, there has been a major change in how MRs communicate with healthcare professionals due to the limits on face-to-face contact. To continue responding smoothly and swiftly to the needs of healthcare professionals under these conditions, we are using LINE WORKS as a new tool, allowing us to provide optimal solutions without delay while also improving the productivity of MRs.

2020 Product Sales by Therapeutic Area (Billions of yen)



Note: Figures in parentheses are year-on-year percentage changes.

Medical Affairs

Strategic Points

- Acceleration and advancement of evidence generation to realize patient-centric healthcare
- Delivery of personalized healthcare (PHC) based on the characteristics and values of the individual patient
- Promotion of innovative medical affairs by strengthening collaboration with stakeholders and actively introducing digital and other new technologies

Performance in 2020

62
Contract-based post-marketing studies
(2020)

7 (as part of the above post-marketing studies)
Database research projects (including real-world data (RWD) research)
(2020)

150
Staff with GCP Passport (Japan Society of Clinical Trials and Research certification)
(As of January 31, 2021)

20
Number of non-clinical joint studies
(2020)

Business Model and Core Themes

The task of our Medical Affairs Division is to generate scientific evidence, focusing on the mode of action and other properties of the drug in non-clinical studies (basic research), as well as on its efficacy and safety in the clinical setting. Based on the evidence thus generated, we deliver appropriate information to healthcare providers.

Increasingly in recent years, the pharmaceutical industry has been called upon to ensure global-level compliance standards, for instance through appropriate separation of marketing and medical affairs[1] and transparency in funding, and to improve the quality and scientific level of research. It is important to respond to these concerns. With the aim of enhancing the quality and reliability of its research, Chugai has established a research support structure that conforms to the GCP[2] guidelines of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). Chugai has also acquired third-party accreditation[3] from the Japanese Association of Pharmaceutical Medicine (JAPhMed) for its medical science liaison (MSL) certification program. Additionally, in accordance with the Clinical Trials Act and the Next-Generation Medical Infrastructure Act, which came into force in 2018, we are working to upgrade systems, provide support for the implementation of clinical trials, conduct database research (including RWD[4] research), and meet the other requirements. Furthermore, in response to the Consensus Statement on Medical Affairs Activities and the Consensus Statement on Medical Science Liaison Activities, issued by the Japan Pharmaceutical Manufacturers Association (JPMA) in 2019, and the Guidelines for Prescription Drug Marketing Information Provision, issued by the Ministry of Health, Labour and Welfare in the same year, we have established an appropriate governance and compliance system.

Strategy and Progress

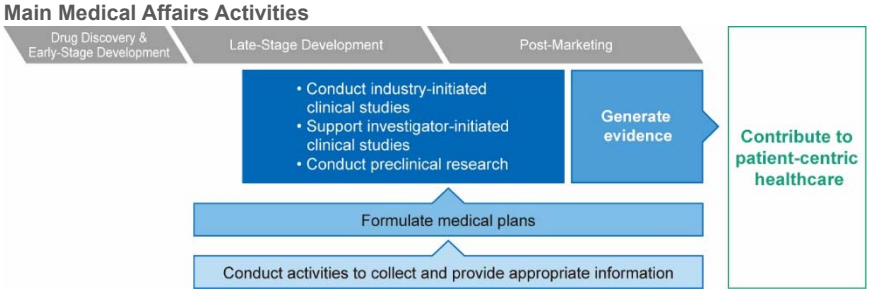
Enhancing intelligence functions and measures for PHC

In January 2019, we started operation of MI chat, an interactive program that uses AI to respond to inquiries from healthcare professionals. This program improves convenience such as reducing the time spent searching for information. We will continue to work on innovation, including the use of new digital technologies, to provide new solutions.

As a further digital initiative, we are engaged in prospective research into hemophilia through the TSUBASA study. People with hemophilia use the dedicated study app to provide information on their level of physical exercise, which is used to research the correlation with hemorrhagic events. Wearable devices are also used to collect physical data during exercise for analysis. Through this work with digital biomarkers, we aim to contribute to the progress of patient-centric medical research and the development of advanced medical treatments.

1. Activities that contribute to healthcare from a scientific standpoint
2. Good Clinical Practice: Standards for conducting pharmaceutical clinical trials
3. Composed of evaluation criteria (a total of 222 items in 42 categories) from the three perspectives of independence from promotional activities (compliance system), medical and scientific expertise, and the training system. In the accreditation examination, mail-in and on-site surveys of the evaluation criteria are conducted to evaluate whether the MSL certification program at the applicant company is being properly implemented.
4. Real world data

Main Medical Affairs Activities



Drug Safety

Strategic Points

- Maximization of the value of growth drivers through a commitment to promoting appropriate use
- Generation of unique evidence to contribute to personalized healthcare (PHC) and building of innovative customer engagement models
- Maximization of product value through enhancement of safety measures from the clinical development stage

Performance in 2020

201 thousand
Cases for which safety information was collected in clinical trials and post-marketing studies
(2020)

20
Lectures, papers, and conference presentations on drug safety
(2020)

15 products
Enforcement of risk management through RMPs
(As of January 20, 2021)

Business Model and Core Themes

In Japan and overseas, Chugai handles numerous therapeutic antibodies, molecular targeted therapies, and other pharmaceuticals with innovative modes of action. To promote the appropriate use of these pharmaceuticals around the world and gain acceptance from patients and healthcare providers, Chugai establishes pharmacovigilance protocols with Roche and other partners and collects safety information on a global level. We consider expert safety evaluation and speedy decision-making throughout the product lifecycle to be essential for timely provision of safety information and implementation of measures to ensure safety. Accordingly, we have established an independent Drug Safety Division and put in place a safety control system directly linked to management. Chugai sees pharmacovigilance activities as part of its mission as a pharmaceutical company and is committed to continuing with patient-centric activities in this area to build trust, provide truly valuable safety data, and contribute to patients and healthcare worldwide.

Strategy and Progress

Collecting and managing safety information

With the principal aim of collecting safety information from real-world clinical settings that is unobtainable from clinical trials, we gather reports from medical institutions and data from the literature and scientific conferences. We also collect safety information proactively from post-marketing surveillance, which includes all-case registration surveillance and database surveys. Data on safety collected from medical institutions is analyzed using diverse methods including epidemiology. Information on the results is provided to medical institutions and announced via scientific conferences, papers, and other means.

Chugai leads the industry in drug safety evaluation and safety measures through its additional wide-ranging and rigorous management methods, such as management of distribution and confirmation of conditions of use, for numerous anticancer agents, innovative new biopharmaceuticals, and other drugs.

Risk management based on pharmaceutical RMPs

Chugai has been ahead of its competitors in drawing up and applying risk management plans (RMPs), and discloses them on its website. Chugai considers RMPs to be part of its commitment to patients and healthcare professionals. In applying RMPs, we believe we need to strengthen our ability to analyze data from an epidemiological standpoint. This is another area where we have led the industry. To help upgrade Japan's epidemiological database, a group of Chugai experts with responsibility for epidemiological functions has collaborated with specialized enterprises and other bodies in a range of active initiatives, including formulating recommendations and guidance on database research for presentation to the regulatory authorities. We have additionally launched an initiative to apply database research at the practical level to pharmacovigilance for Chugai products in order to ensure swift and effective collection of safety information, which will enhance and strengthen the operation of RMPs.

Communications on safety

Chugai provides information on noteworthy adverse events to medical institutions and academic societies. We also distribute information leaflets for patients, post information on our website, and present a variety of lectures. In particular, our ability to rapidly provide information according to patient characteristics through the post-marketing surveillance database tool (PMS DB tool) and safety information database tool (SAFETY DB tool) that we began operating in 2016 has won praise from healthcare professionals.* With these tools, which include domestic post-marketing safety data, we can respond in a timely manner to urgent needs for safety information. Starting in 2018, we have additionally rolled out a clinical studies database tool that presents the clinical study safety data submitted for regulatory approval, allowing healthcare professionals to use new products with confidence from immediately after their sales release. In 2020, we continued to enhance the provision of information through database tools, launching an adverse event database tool on our dedicated website for healthcare professionals in May. This has further broadened our

Welby MyKarte ONC

Reference: Welby MyKarte ONC patient introduction webpage
https://oncology.welby.jp/ (in Japanese only)

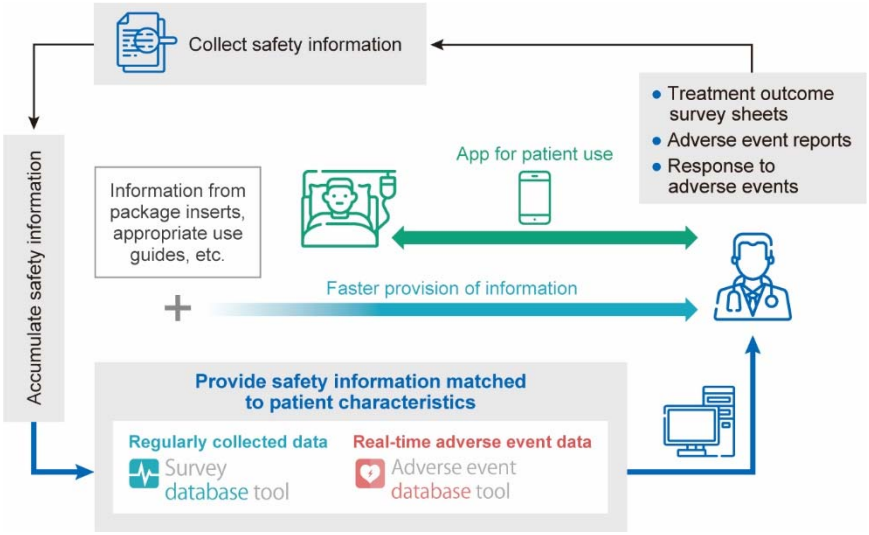
contribution to patient treatment by putting in place a system that enables healthcare professionals to directly access adverse event information on Chugai Pharmaceutical products whenever needed.

At Chugai, we are also concerned with ensuring smooth communication between patients and healthcare professionals so that patients can undergo treatment free of anxiety. In October 2020, in a joint project with Welby Inc., we began operating a patient support program based on Welby MyKarte ONC, a free personal health record (PHR) service provided by our project partner. This program, designed for breast cancer patients being treated with the immune checkpoint inhibitor Tecentriq, performs simple integrated management of information on day-to-day symptoms and treatment status to provide information optimized in line with the type of cancer and the symptoms. These functions support patients to achieve a better understanding of their treatment and are also designed to lead to better outcomes by keeping healthcare professionals constantly informed of the patient's condition, including adverse events and worsening of symptoms.

Meanwhile, to ensure that safety measures are closely attuned to patient needs, we operate a team of some 30 professionals with the job title of Safety Expert—a role unique to Chugai dedicated to handling safety information—who are posted to locations throughout Japan, where they provide safety consultations to meet the needs of healthcare providers and work continuously to build networks with local doctors and pharmacists.

* Source: Online article by Nikkei Medical Publishing, Inc. on AGING Web "Chugai's Ideal Information Prescription: 'PMS and SAFETY Database Tools' Providing Necessary Information to Those Who Need It, When They Need It" (in Japanese only)
Part 1 (November 10, 2017)
https://project.nikkeibp.co.jp/atcl21f/innovator/2017111001/
Part 2 (November 17, 2017)
https://project.nikkeibp.co.jp/atcl21f/innovator/2017111701/

Cycle of Safety Information Collection, Accumulation, and Provision under PV 2.0



Quality and Regulatory Compliance

Strategic Points

- Upgrading and strengthening of overseas subsidiaries' governance and compliance systems
- Building of Chugai's quality system to provide total assurance for all schemes including new modalities and new businesses in anticipation of joint projects and expansion of contracting
- Strengthening and embedding of digital compliance to accelerate implementation of digital strategy

Performance in 2020

10
Inspections by GMP regulatory authorities
(2020)

56
GMP/GDP quality audits
(2020)

31
GCP/GVP quality audits
(2020)

7,817
Number of examinations of information and lecture materials
(2020)

* Contract Development and Manufacturing Organizations

Business Model and Core Themes

The Quality & Regulatory Compliance Unit is responsible for ascertaining trends in pharmaceutical regulations within and outside Japan and ensuring the soundness of the quality management system spanning our business processes. It confirms, improves, and verifies the validity of business processes through audits and other activities throughout the product lifecycle and ensures the quality and regulatory compliance of data by operating a global IT system. By additionally leading activities to foster a self-sustaining quality mindset in organizations across the Chugai Group, it drives product and service quality under the slogan "Quality That Inspires."

Strategy and Progress

Initiatives to promote appropriate information Provision activities

To further promote appropriate information provision activities by our medical representatives (MRs) and other staff, we have introduced AI to analyze the content of activity reports. Additionally, following the issue in March 2020 by the Ministry of Health, Labour and Welfare of the notification "Key points to note for pharmaceutical manufacturers and distributors when providing information on ethical pharmaceuticals in response to patient inquiries," we established guidelines for information provision activities in response to inquiries from the public, including patients and their families, based on the Chugai core value of a patient-centric approach.

Further development of digital compliance system

In 2019, we established a digital compliance system for human-derived data such as genomic data and real-world data (RWD), as part of which we began operating the Digital Compliance Committee. The cases handled in the two years to 2020 showed a great variety and case numbers have continued to increase with the progress of the CHUGAI DIGITAL project. Meanwhile, Chugai is taking the lead in the use of digital technology for compliance, including by establishing guidelines to promote the appropriate use of genomic information and providing appropriate training for employees on an ongoing basis.

Alliances with external partners and ensuring quality and regulatory compliance

Alliances with contractors and other external partners have become increasingly important in connection with the continuous creation of new drugs and expansion of operations into new modalities and businesses. In 2020, Chugai established the Requirements for GxP Service Provider Management, a set of general quality requirements applicable to all GxP, through which we are working to strengthen alliances with external partners and roll out the Chugai quality brand. To meet requirements in terms of quality assurance and prevention of irregularities, we believe that the quality awareness of individual employees is particularly important. We therefore hold regular Quality Meetings as forums for considering and discussing quality issues with internal departments and selected external partners.

Development of electronic signature system applicable to GxP documents

To adapt to the teleworking recommended during the COVID-19 crisis, we have developed and begun operating a global electronic signature system that can be used with GxP documents and meets the regulatory requirements of different countries regarding electronic records and electronic signatures. This system, which removes the barrier of physical distance from the signing of contract and GxP documents and greatly reduces compliance-related worries over loss of documents and similar issues, is a practical example of increased efficiency and enhanced compliance from the utilization of digital technology.

Intellectual Property

Strategic Points

- Utilization of antibody engineering technology patents through licensing and other means
- Expansion of the patent portfolio in mid-size molecule drug discovery technology and mid-size molecule development projects
- Formulation and execution of a scenario for combating biosimilars and generics

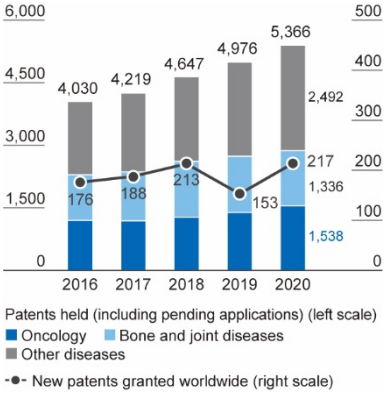
Performance in 2020

5,366
Number of patents held (including pending applications)
(As of December 31, 2020)

217
New patents granted worldwide
(2020)

Continued to provide value through resolution of disputes with manufacturers of branded products and manufacturers of biosimilars

Number of Patents Held (Including Pending Applications) and New Patents Granted



Business Model and Core Themes

Chugai views its global intellectual property (IP) strategy as the foundation for creating innovative new drugs. By integrating it with our business and R&D strategies, we protect the competitive advantage of our products and ensure operational flexibility. We focus resources on and secure IP rights for high-priority R&D projects. At the same time, we actively work to secure rights outside Japan with a view to global co-development with the Roche Group. When we apply for patents for products, we include filings for lifecycle patents related to formulation, production method, diagnostic method, and PHC in addition to those for the substance and use. We also work to establish rights globally for significant drug discovery technologies, such as those related to innovative antibody engineering and mid-size molecules. Additionally, we are building a competitor database to identify opportunities for utilization of Chugai's drug discovery technology patents and are formulating and implementing strategies for the utilization of the associated IP. In 2020, initiatives to utilize antibody engineering technology patents through licensing and other means resulted in the conclusion of licensing agreements with four companies.

Strategy and Progress

Integration of IP and research strategies (Strategic mix)

At Chugai, we view our antibody engineering technologies as a core drug discovery technology platform, and we are deploying R&D strategies both to cultivate basic technologies and to apply them to product development. We have been dispatching IP liaisons to the Fuji Gotemba Research Laboratories and Kamakura Research Laboratories since 2018, and to the Collaboration Promotion Laboratory at IFReC since 2019, to strengthen collaboration from the initial stage of research. The objective is to promote a stronger strategic mix by building an independent portfolio of technology and development candidates that exploits current gaps in the network of technologies and rights. IP liaisons hold monthly meetings to review IP with the Pharmaceutical Technology Division, which is also promoting the same strategic mix.

Current patent portfolio

Supported by technological development, we have structured a well-balanced patent portfolio that reflects the diversity of products and development projects generated through Chugai's own research and development. Bone and joint diseases account for approximately 25 percent of patents by therapeutic area, oncology for approximately 29 percent, and other diseases including chronic disorders, hematologic diseases, and drug discovery technology for approximately 46 percent. In 2020, Chugai acquired 217 patents in Japan, the United States, and major European countries, as well as other countries worldwide.

Maximizing product value in response to changes in the competitive environment

With the globalization of our portfolio of products developed in-house and the expansion of our portfolio of development projects and drug discovery and manufacturing technologies, our competitive environment is becoming increasingly intense. This requires more sophisticated IP activities to maximize the value of Chugai's IP while respecting the effective rights of other parties. This in turn will help to maximize the value of our products, development projects, and technologies.

We carry out IP activities in close cooperation with internal and external stakeholders including Roche, Genentech, and other affiliated companies, outside attorneys, and our business and legal departments. So far, patent disputes relating to Hemlibra, Herceptin, and other major products have been highly effective in maximizing product value. In 2020, we filed patent infringement lawsuits in the United States and Japan relating to generics of Alecensa and Edirol, respectively. By rolling out IP activities of this kind to maximize product value, Chugai will continue to deliver value to society.

Human Resources

Strategic Points

- Assignment of the right people to the right positions and provision of growth opportunities through position management and talent management
- Promotion of talent management to quickly identify and develop leaders and highly competent specialists to accelerate strategy execution and innovation
- Maintenance and deepening of employee engagement, fostering of an organizational culture for the pursuit of innovation, and accelerating the success of women

Performance in 2020

14.6%
Ratio of female managers[1]
(2020)

13.0%
Ratio of female managers[2] (with subordinates)
(2020)

194
Number of employees posted through the Roche Human Resource Exchange Program
(2004–2020)

1. Percentage of all managers on a Chugai Pharmaceutical non-consolidated basis.
2. Percentage based on Chugai Pharmaceutical (non-consolidated) and affiliated companies in Japan.

Chugai was selected as a Nadeshiko Brand for the fifth time in 2021 for its exceptional record in promoting the success of women.

Basic Approach

Chugai recognizes that its people are its most important asset. That is because human resources are the generators of innovation and the driving force of value creation. We believe that assigning the right people to the right positions and conducting talent management will recognize individuals with independent thinking ability and motivation for self-improvement and support them to take on challenges and demonstrate to the fullest their strengths and expertise. We seek to create workplaces that bring together innovative people regardless of nationality, gender, or other attributes to work enthusiastically together in a diverse environment.

The All-Employee Survey

Chugai carries out regular employee surveys to identify organizational issues requiring reform and to support the formulation of strategy. The survey consists of two parts: Employee engagement, an indicator of employee commitment to performance and self-motivation; and environment for utilizing employees, an indicator of whether the right people are in the right positions and whether there is a supportive work environment. In the survey results for 2020, our score for “employee engagement” was three points higher than in the previous survey and 10 points above the global average, placing Chugai in the global top ranks. In “environment for utilizing employees,” we advanced by three points to reach the global average. For Chugai to join the global top ranks, some areas require further improvement, notably resource optimization and work process efficiency. Going forward, as we implement our new growth strategy, TOP I 2030, we will shift resources to value-creating operations and ensure the comprehensive rollout of our new personnel system. Alongside these and other strategies to resolve issues across the Company, we will work to identify personnel and structural issues within each department and organization and will seek to resolve them through the plan-do-check-act (PDCA) cycle and other measures.

Key Points of 2020 Survey Results

- Chugai scored above the Japanese corporate average in all question categories and achieved overall improvement from the previous survey.
- In “employee engagement,” Chugai was in the global top ranks.
- For further improvement in “environment for utilizing employees,” Chugai will address areas including resource optimization, interdepartmental cooperation, and creating opportunities for highly competent specialists.

Outline of Survey

Number of Eligible Respondents and Response Rate
Eligible respondents: 7,318 / Respondents: 6,644 / Response rate: 91%

Question Categories
Employee engagement: Strategy and direction; leadership; quality and customer orientation; respect for individuals; opportunities for growth; and compensation and benefits
Environment for utilizing employees: Performance indicators; authority and discretion; resources; education and training; framework for collaboration; business processes and organizational structure; and innovation

Benchmark Data
Global average for strongly performing companies, global average for all companies, global average for pharmaceutical companies, and average for Japanese companies

Strategy and Progress

Position management and talent management based on management strategy

To realize our management strategy and create innovation, we use position management and talent management to assign the right people to the right positions. In position management, we delineate the duties and human resource requirements for realizing corporate strategy and assign staff with the corresponding experience, skills, competencies, or other qualities. In talent management, we work to identify and develop

managerial talent and highly competent specialists at an early stage based on how their competencies, performance, and potential correspond to requirements and expectations. In this way, we are creating a talent pool[3] of future management candidates in each department and visualizing and selecting successor candidates for major positions in Japan and overseas. Medium- to long-term policy for cultivating successors is formulated in discussions between executive management and department managers, and includes off-the-job training programs to drive strategic assignment of human resources and reinforce leadership skills. Executive management takes the lead in implementing this plan-based human resource development and works to accelerate development.

3. A group from which next-generation leaders are drawn

Strategic focus on core businesses and securing and strengthening of highly competent specialists

Leveraging its unique strength in science and technology, and its strategic alliance with the Roche Group, Chugai delivers innovative drugs and works to develop sophisticated solutions by driving advances in personalized healthcare (PHC). Chugai strives to realize growth by linking its core businesses with human resources. Specifically, we are focused on the recruitment and development of human resources who have strong expertise in medical science, DX, and other fields and who are motivated by a frontier spirit to take on challenges. Chugai in return supports the growth of these human resources by offering them opportunities to demonstrate their individual expertise and a wide range of career possibilities.

Establishing a personnel system that encourages a spirit of challenge regardless of age or other attributes

Following its revision in April 2020, our new personnel system puts in place a competitive remuneration system based not on individual abilities and past contribution but on the value of duties performed in each position. In this way, it shifts the deciding factor from the individual to the role and the relevant duties and realizes a pay-for-position approach.

The job profile of all positions is now made available company-wide and all personnel are eligible for appointment regardless of age, thus abolishing age limits for managerial posts and supporting self-directed career development toward a future vision under the concept of “Career for Future.” Setting and strictly implementing rules for assignment and dismissal will further promote the rejuvenation of the organization.

The accompanying evaluation system sets indicators both for the performance required for a job (commitments) and for taking on challenges beyond that (targets). By doing so, we will improve satisfaction with evaluations and promote a spirit of challenge among employees. By setting indicators at the level of both commitments and targets and specifying their relative weight, the system allows a balanced evaluation in line with performance. It also provides appropriate and timely feedback from superiors, which encourages employees to challenge themselves.

To ensure fully effective operation of the new personnel system, managers receive regular training to enhance their skills for feedback and dialogue with team members. We also carry out continuous employee surveys and implement the PDCA cycle to improve not only the system content but also the operational rules.

Supporting self-directed learning and growth

Chugai implements a range of human resource development measures and provides a variety of training programs to deepen and widen employee expertise, reinforce skills, and support career planning. Level-specific training consists of programs to impart the mindset, knowledge, and skills required for the particular position or role. Our leadership competency program strengthens the seven competencies required of all Chugai human resources through a training package to build conceptual, human, and technical skills and improve English-language ability. To promote self-directed career development, we offer a career design program as a regular opportunity for employees in all age groups to take stock of their career. Additionally, we support self-improvement by enabling employees to set their own goals and pursue them through continuous self-directed learning.

In 2021, we introduced a new learning management system based around on-demand programs. The resulting learning environment enables employees to work on their own development by pursuing continuous self-motivated study and growth toward their individual career aims. In this way, we are fostering a learning culture that encourages self-directed activity in the area of learning, re-skilling, and career development.

Establishing new workstyles for improved productivity and work-life synergy

The COVID-19 pandemic is driving a shift to new workstyles, among them the rise of remote working. Against this background, Chugai has addressed the issue of new workstyles by gathering opinions in employee surveys, holding discussions within each organization and between labor and management, and examining the issue at the management level. Workstyle reform based on cooperation between labor and management has already produced a range of initiatives, but we see the changes accompanying the pandemic as a major opportunity to further accelerate existing workstyle reforms to realize new ways of working.

As workstyles vary depending on factors such as the character of the organization, job type, and specific work duties, our declared vision is to realize through digitalization a range of workstyles that are highly flexible in response to these factors. This “smart working” will meet the demands of both productivity improvement and work-life synergy, and result in continuous innovation. The implementation of new workstyles will be guided by four themes: (1) Introduction of the Telework System based on work-from-home (WFH) and satellite offices, (2) Creation of workplace environments that operate highly flexible workstyles yet still maintain and improve productivity, (3) Review of office-related systems coordinated with the introduction of the Telework System, and (4) Realization of personnel evaluation and management methods adapted to the Telework System.

By reconciling productivity improvement with work-life synergy, the introduction of new patterns of work offers a way forward to generating continuous innovation. In this way, continued initiatives for workstyle reform will enable us to go on contributing to patient wellbeing worldwide as a top innovator in the healthcare industry.

Creating a culture of innovation through D&I and health and productivity management

Chugai has identified diversity and inclusion (D&I) as a key management issue. We believe that D&I is essential in order for employees to generate new value—in other words, diversity is necessary for generating innovation. As such, in 2010 we launched a working team led by the president, and in 2012 we established a dedicated organization that has since been conducting initiatives to promote diversity.

Amid demands for more active participation by diverse human resources, we provide e-learning on the topic of unconscious bias for managers, who play a key part in promoting D&I, as a way of enhancing their practical workplace skills. We also conduct annual training for managers and leader candidates to help women plan and develop their careers. In 2020, as part of an ongoing program of initiatives, we held task management training to equip managers to facilitate career planning and growth for team members navigating major life events. We will continue our focus on promoting the success of women, with a target for the end of 2023 of achieving 17 percent for both female management position ratio and female manager ratio.

Meanwhile, we are seeking to provide a variety of work arrangements and support systems so that all employees can benefit from work-life synergy. A healthy and vital organizational culture that supports both the mental and physical wellbeing of diverse human resources is essential to innovation. By rolling out health and productivity management based on workstyle reform and employee health management, we will work to further enhance the workplace environment.

Moreover, in 2020 we held Chugai Diversity DAYS with the aim of firmly establishing the practice of D&I to build an inclusive organizational culture that fosters innovation. As part of this initiative, the president delivered to employees a message emphasizing that the active participation of human resources who are diverse in terms of gender, age, cultural background, and other attributes is essential to implementing corporate strategy. In his message, the president named three activities key to inclusion: Spreading the message, talking to one another, and acceptance. By firmly establishing these practices, we will work to actively create a culture of innovation.

Examples of initiatives by executives and department managers to promote the success of women

- Messages from senior management on the importance and significance of D&I and female success delivered in the annual New Year’s address and at diversity-related events
- Commitment to activities for female success, with key performance indicators (KPIs) established to drive the appointment of women to managerial positions and a committee

consisting of senior management, executives with relevant responsibility, and all departmental managers that meets every year to check progress toward female advancement, discuss issues toward achieving the KPIs, and investigate career development plans and other relevant measures

- Nomination of women as successor candidates for all key positions in talent management (division head or equivalent)

Creation of network for former employees through alumni system

With the aim of building a two-way network between Chugai and its former employees and also of securing human resources for immediate effective deployment, Chugai introduced an alumni system in May 2020. The system makes it possible to respond to arising corporate recruitment needs by re-deploying alumni, in principle with regular employee status. Currently, around 100 former staff members are registered as alumni, and three have been redeployed. The network is a forum for lively interaction, with regular news bulletins from Chugai, sponsored events, and email contact between alumni.

Establishing Systems and Environments to Promote the Success of Diverse Employees

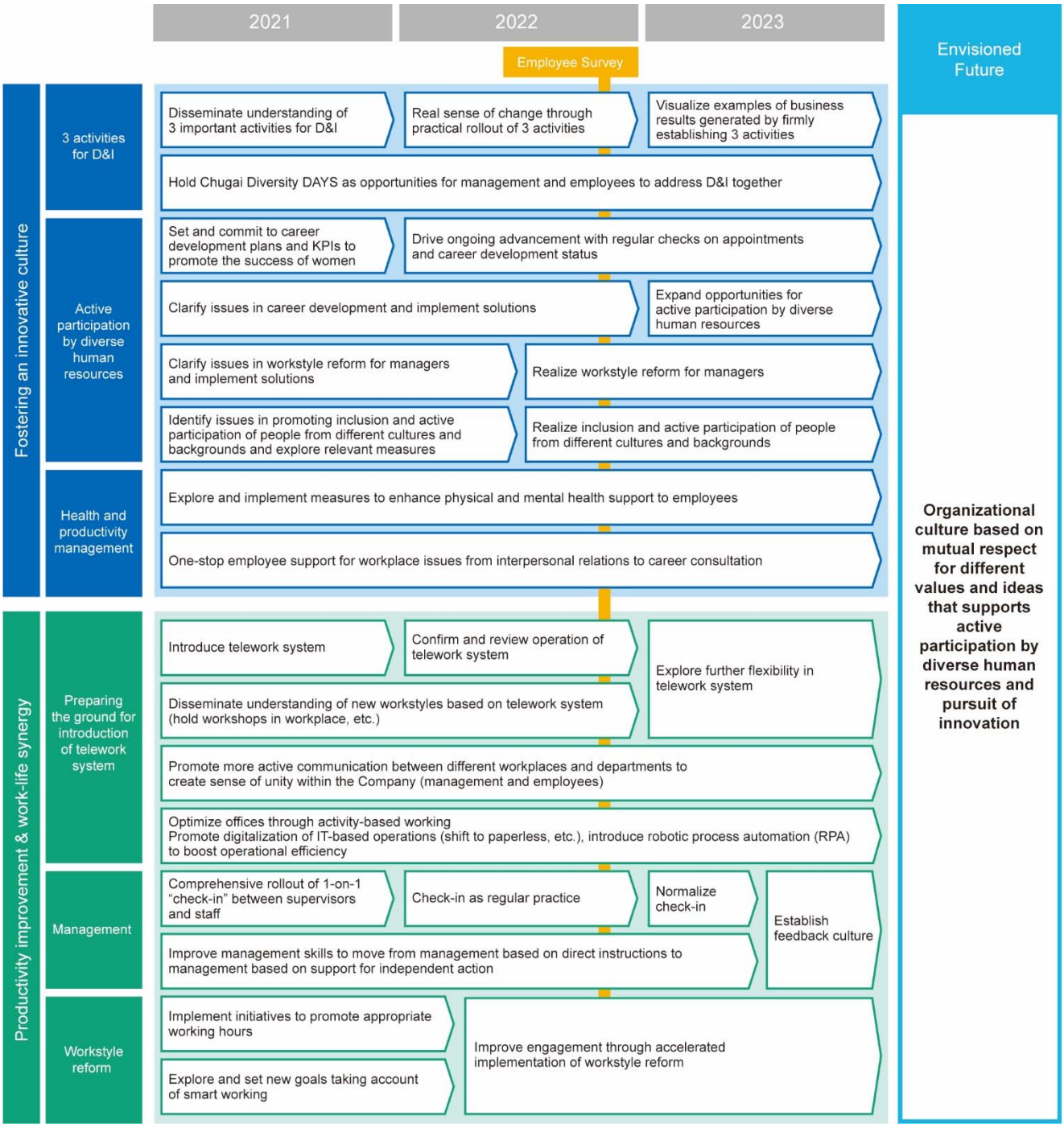
More flexible workplaces	• Introduction of the Telework System • Introduction of satellite offices • Introduction of free address workspace (Head Office)
More flexible work schedules	• Super-flextime system (no core time) (including for MRs and other remote workers) • Discretionary work system (for researchers) • Paid leave system in units of half-days or hours
Support for work-life balance	• Support plan for living with spouse who is transferred (MRs) • Use of Company vehicles to take children to/from childcare • Consortium-managed childcare center (Head Office) • Leave system for employees whose partner gives birth • Leave system to nurse sick children (preschool age) • Introduction of concierge for finding nursery care
Support for career planning	• Career consulting service • Career reporting • In-house job posting system • Out-of-house job posting system • Alumni system • Re-employment system (transfer from contract to regular employment) • Joint or secondary employment (where certain criteria are met) • Leave for education and acquisition of qualifications • Volunteer leave system • Interviews and e-learning offered before childbirth leave and after childcare leave

Results of Workstyle Initiatives (Non-consolidated)

	Performance
Percentage of annual paid leave taken (Average days taken) (April 2019–March 2020 results)	65.6% (14.7 days)
Average overtime hours/month[4] (April 2019–March 2020 results)	2.6 hours/month
Percentage of male employees taking childcare leave (Average days taken) (2020 results)	77.0% (15.3 days)
Percentage of employees using the WFH system	WFH as norm due to the COVID-19 pandemic

4. Excluding employees on a de facto or discretionary working hours system

Roadmap for Implementing D&I



Human Rights

Strategic Points

- Continue to conduct human rights awareness training
- Conduct human rights due diligence, including for suppliers
- Identification of human rights issues and implementation of solutions in cooperation with third-party organizations

Performance in 2020

Continued to conduct human rights awareness training

8
Supplier evaluations conducted based on the PSCI Principles*

Continued to exchange opinions with third-party organizations

* The Pharmaceutical Industry Principles for Responsible Supply Chain Management established by the Pharmaceutical Supply Chain Initiative (PSCI), a non-profit group of global pharmaceutical companies

Employee training (2019)

Note: The 2020 training was conducted via e-learning.

Roundtable dialogue (Online meeting)

Basic Approach

At Chugai, we declare our respect for human rights in the Chugai Group Code of Conduct, which is based on our shared Core Values. In respecting human rights, we aim to realize workplaces that prize diversity, where each person values their own feelings and accepts the values of others—allowing everyone to fully demonstrate their abilities, based on an organizational climate of appreciation for oneself and others. In such a workplace, people are empowered to work creatively with enthusiasm and engagement, which leads in turn to improved levels of achievement and increased productivity for the organization as a whole. We also believe that a workplace culture of this kind that encourages all employees to become more sensitive to human rights and to act with greater respect for the individual can help to eliminate social discrimination and infringements of human rights in society in general through corporate activities and their private lives.

In the increasingly important social issue of business and human rights, we believe that companies need to ensure respect for human rights not only in their own activities but throughout the supply chain. As an operator in the healthcare industry, we are committed to acting with a greater awareness of respect for human rights.

Chugai Group Human Rights Statement
https://www.chugai-pharm.co.jp/english/sustainability/humanrights/policy.html

Issues and Initiatives

Chugai conducts ongoing human rights initiatives for its employees in areas such as prohibition of workplace discrimination and harassment, respect for diversity, and safety and health. In 2020, we provided training to impart an understanding of the main points of the revision to the law on prevention of harassment as well as training to help eliminate discrimination from a variety of perspectives, including those forms that have become more conspicuous during the COVID-19 pandemic. Meanwhile, based on the United Nations' Guiding Principles on Business and Human Rights, we formulated the Chugai Group Human Rights Statement, which commits us, in the framework of supplier management, to conducting human rights and environmental risk assessments in addition to the existing assessments of stable supply and quality management. To do this, we have formulated guidelines based on the PSCI Principles, in which we call on our business partners to comply with laws and social norms. The guidelines also specify other requirements including eliminating child labor and forced labor; prohibiting all forms of discrimination by race, gender, or other attribute; respecting the dignity of individual employees; and maintaining safety and health. The guidelines thus establish due diligence on human rights including attention to working conditions. In October 2020, Chugai participated for the third consecutive year in the international Business and Human Rights Conference in Tokyo, an event in its ninth year which is sponsored by the Caux Round Table Japan, where we engaged in individual dialogue with overseas experts. These experts stated that it was important for companies, when conducting human rights due diligence for suppliers, to add to the existing assessment items an analysis of the impact of COVID-19 on business and human rights issues. We also exchanged opinions on the creation of a trusted and user-friendly mechanism for handling complaints.

Due to the impact of COVID-19, the number of supplier assessments so far has been limited to eight, with no significant human rights-related risk identified. We were able to secure the understanding of suppliers regarding the need for human rights due diligence and their agreement to cooperate in addressing human rights issues. In 2021, we will continue with human rights due diligence focused on the contract manufacturing operators who are among our major suppliers.

In addition, Chugai has established an Anti-Bribery Policy as part of the proper management of its corporate activities. As well as setting our own code of conduct, it prohibits our business partners from engaging in bribery of government officials, civil servants, corporate staff, and other parties, whether corporations or individuals. We will continue our comprehensive efforts to prevent bribery.

Environment, Health, and Safety (EHS)

Strategic Points

- Implementation of plan toward achieving new mid-term environmental goals
- Strengthening of global EHS promotion system with emphasis on cross-departmental functions
- Execution of priority items for health and productivity management and reassessment of evaluation indicators

Performance in 2020

–17%[1]
Energy consumption per employee compared with 2010
(2020)

–20%[1]
CO_2 emissions per employee compared with 2010
(2020)

97%[1]
Waste recycling ratio
(2020)

1. Chugai Group in Japan

Certification as a "White 500" Health and Productivity Management Organization 2021 (Large Enterprise Category)

2021 健康経営優良法人 Health and productivity ホワイト500
(Large Enterprise Category)

Basic Approach

As an R&D-driven pharmaceutical company, Chugai is engaged in many specialized scientific activities. One aspect of these activities involves handling numerous antibodies and highly active pharmaceutical substances, which means that ensuring environmental protection and maintaining health and safety are extremely important for us.

At the same time, the demands of society have grown more diverse and sophisticated. Integrated management of EHS is required worldwide because of the close connection between environmental protection and health and safety. Accordingly, in 2016, Chugai developed an integrated management system for EHS and has been implementing the plan-do-check-act (PDCA) cycle for ongoing improvement of its EHS promotion activities based on a consistent policy company-wide, from top management to each facility. Having established an EHS risk assessment system in 2017, we are now working to eliminate EHS risk in the workplace. Since 2008, we have implemented a Group-wide assessment system to reduce the risk of occupational injuries from exposure to all substances handled, not only restricted substances.

EHS management extends throughout the value chain, from the procurement of raw materials and manufacture of products through to their supply to patients and healthcare professionals. We are therefore working in cooperation with customers and suppliers, partners, and industry organizations to broaden our activities to cover the whole of the value chain.

Strategy and Progress

Outline of previous mid-term environmental goals

Chugai's aims encompass not only its own sustainable development but also environmental protection in local communities and globally. We have set priority items to be addressed as well as medium- to long-term targets.

The priority items of the previous mid-term environmental goals, which were set in 2014 to cover the period up to 2020, were climate change countermeasures, energy conservation, resource conservation, waste management, biodiversity protection, prevention of environmental pollution, and improvement of environmental literacy. Placing particular focus on the management of energy consumption and waste, we set the four mid-term environmental goals indicated in the table below, with corresponding goals for each individual year, and worked toward meeting each of these targets.

We have been progressing steadily with initiatives toward meeting the mid-term environmental goals by their final year of 2020. The reduction in energy consumption per employee compared with 2010 was held to 17 percent, but in CO_2 emissions per employee, we achieved a 20 percent reduction. In energy consumption per employee, we aim to use renewable energy certificates to reach a 20 percent reduction in non-renewable energy consumption.

Mid-Term Environmental Goals (Target Year: 2020)

Item	Target	Performance in 2020
Energy consumption per employee	20% reduction from 2010	17% reduction from 2010[3] (20% reduction in CO_2 emissions per employee from 2010)
Average fuel efficiency of MR fleet	16 km/L or higher	27 km/L
Specified fluorocarbons (CFCs, HCFCs)	Eliminate use	Achieved
Zero emissions of waste[2]	3 facilities	2 facilities

2. A waste recycling ratio of 99 percent or higher
3. We aim to reach a 20 percent reduction in non-renewable energy consumption by using renewable energy certificates to cover the equivalent of 3 percent.

Performance in Environmental Goals for 2020

Item	Target	Achieved
Energy consumption	Year-on-year reduction of 2% or more	6% reduction
CO_2 emissions	Year-on-year reduction of 2% or more	6% reduction
Ratio of eco-friendly cars[4]	80% or higher	85%
Average fuel efficiency of MR fleet	16 km/L or higher	27 km/L
Industrial waste recycling ratio	99% or higher	97%
Final disposal ratio	Lower than previous year (2019: 1.1%)	0.5%
On-site verification of waste disposal contractor facilities	100% over a three-year period	71%
Plain paper copier (PPC) paper purchased	Lower than previous year (2019: 126 tons)	71 tons
Recycling ratio for PPC paper	80% or higher	78%
Whole effluent toxicity (WET) tests: Conduct at each plant and research laboratory	Once every year	Conducted once every year

4. Includes hybrids and fuel-efficient vehicles

Formulation of mid-term environmental goals 2030

In 2020, to reflect analysis results from the previous mid-term environmental goals and changes in the expectations and aspirations of society, Chugai formulated a more comprehensive set of mid-term environmental goals for 2030 from a longer-term perspective. In the items selected for inclusion in the new targets, the four items of the previous mid-term environmental goals are increased to 10, including items such as water risk and chemical substance management, to enable us to address material issues from a medium- to long-term perspective. For many of these items, we have designated 2025 as a milestone on the way to 2030. In the area of climate change, to respond to the need for long-term and large-scale countermeasures, we have selected zero CO_2 emissions as a long-term goal with a target year of 2050.

New Mid-Term Environmental Goals (Target Year: 2030)

Area	Item	KPI (Base year 2019)
Climate change countermeasures (prevention of global warming)	Scope 1+2[5] CO_2 emissions	40% reduction by 2025 60–75% reduction by 2030 Zero emissions by 2050
	Scope 1+2[5] Energy consumption	5% reduction by 2025[6] 15% reduction by 2030[6]
	Sustainable electricity ratio	100% by 2025
	Fuel consumption by MR vehicles	35% reduction by 2025 75% reduction by 2030
	Halogenated hydrocarbons	25% reduction by 2025 100% reduction by 2030 (Base year 2020)
Use of renewable/ recycled resources (resource conservation, waste management)	Industrial waste reduction	5% reduction by 2025[6] 10% reduction by 2030[6]
	Plastic waste reduction	5% reduction by 2025[6] 10% reduction by 2030[6]
	Water resource conservation (water withdrawal)	15% reduction by 2030[6]
Biodiversity protection (environmental burden mitigation)	Chemical substance management (SVHC)[7]	After 2021, manufacturing processes without using SVHC-listed chemicals are established for all Chugai original candidate molecules by commercial productions.
	Hazardous waste reduction	5% reduction by 2025[6] 10% reduction by 2030[6]

5. Scope 1: Direct emissions, Scope 2: Indirect emissions from the generation of purchased energy
6. Per total floor area (Excluding leased properties)
7. Substances of very high concern

Climate change countermeasures

Viewed with increasing seriousness worldwide, climate change is an important issue for which reinforced regulation of fluorocarbons is envisaged. Given this situation, it is essential that we step up to initiatives at a higher level, as simply continuing with the current course of action will have limited effect. By 2025, we aim to realize a sustainable electricity ratio of 100 percent by opening a new research facility at Chugai Life Science Park Yokohama and relocating research laboratories, reducing and making more efficient

use of energy, and switching to sustainable electric power sources. As direct CO_2 emissions from fuel consumption (Scope 1) also need to be reduced, we are studying options in this area as well, including conversion, rationalization, and redesign of our existing facilities.

Use of renewable/recycled resources
With the current emphasis on the circular economy, businesses need to take a proactive approach to efficient resource utilization rather than simply meeting their fixed obligations. As well as making essential progress toward zero waste emissions, Chugai has designed its own unique business activities to promote the circular economy. In the area of water risk, although we have relatively low exposure due to our business activities being located mainly within Japan, we will respond to increasing expectations from society by ensuring comprehensive risk assessment and management.

Biodiversity protection
Stronger initiatives are required to manage not only substances covered by Pollutant Release and Transfer Register (PRTR) Law and specially controlled industrial waste, but also substances of very high concern (SVHC) under the European Union's Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) regulations. In addition to reinforcing measures to reduce harmful chemical substances, including wastewater management and verification of the product manufacturing plan, we will also enhance partnership with local communities.

Scenario analysis to assess climate change risk

As the effects of climate change become more severe year after year, stakeholders, including investors, have been calling for adequate disclosure of its impact on corporate business activities. To respond to these stakeholder expectations and aspirations, Chugai conducted a scenario analysis applying the steps outlined below based on the framework in the recommendations of the Task Force on Climate-related Financial Disclosures (TCFD).[8]

STEP 1 Qualitative assessment of risks and opportunities
- Survey of a range of published information and interviews with experts
- Identification of physical risks, transition risks, and opportunities
- Assessment and classification of each risk

STEP 2 Risk scenario analysis
- Setting of scope of risk scenario analysis
- Analysis of storm and flood risk now and after climate change
- Estimate of financial impact

The analysis results and qualitative assessment did not identify any major climate-related risk requiring large-scale business conversion and investment over the long term, which is the TCFD characterization of a high-risk sector. However, the results did indicate climate-related risks common to the manufacturing industry in general which make ongoing analysis essential, such as risks to manufacturing bases and product procurement from climate-related disasters, water shortages, and carbon taxes in the value chain. Moreover, some research indicates that the pharmaceutical manufacturing sector may have a relatively high level of greenhouse gas (GHG) emissions (Scope 1 and 2), and we therefore think that the possibility of regulatory strengthening across the industry needs to be considered. (See table on next page for an outline of the qualitative assessment of climate change-related risks and opportunities.)

The qualitative assessment consisted of climate change scenario analyses of our main product manufacturing and distribution bases in Japan assuming a 2°C and a 4°C temperature rise scenario. The estimated results indicated that, compared to the current estimate of ¥3.96 billion/year, the fall in sales revenue from storm and flood risk would be approximately 37 percent greater under the 2°C scenario (¥5.41 billion/year) and approximately 60 percent greater under the 4°C scenario (¥6.33 billion/year).

The analysis was carried out using the procedure indicated below.
- The probability distribution of floodwater depth for each building was calculated using the global coordinates of each business site to access data on plan scale and floodwater depth.
- Current storm and flood risk was calculated in terms of the expected reduction in sales revenue based on the number of days of business suspension at each floodwater depth and the frequency of such events.
- Distribution data was adjusted to account for climate change-related change in the frequency of high-intensity rainfall events.
- Storm and flood risk after climate change was estimated in terms of the expected reduction in sales revenue for each scenario.

The risk items included in the TCFD scenario analysis correspond to the items covered by the business continuity plan and other existing provisions, and the countermeasures associated with the latter resulted in a reduction in the financial impact estimated in the analysis of climate change-related risk. Specifically, the construction of the third facility (UK3) at the Ukima Plant included the provision of a five-meter-high defense against earthquake and flood damage, while the new distribution center to which operations relocated in January 2021 included flood defense measures based on a disaster map.

Going forward, we will continue applying the results of the scenario analysis to manage climate change-related risks and opportunities and working to further enhance information disclosure.

8. Disclosure of climate-related information that has a financial impact on a company
TCFD https://www.fsb-tcfd.org/

Outline of the Qualitative Assessment of Climate Change-Related Risks and Opportunities

Physical Risks		
Acute risk	✓ Increased risk of interruption of the supply chain, including raw material procurement and product shipment and distribution, due to increased frequency of localized torrential rain and major typhoons ✓ Increased frequency of damage to facilities and increased repair costs from abnormal weather and meteorological disasters, suspension of business activities due to damage to manufacturing facilities	General
Chronic risk	✓ Risk of relocation of plants and other bases becoming necessary due to rising sea levels	General
	✓ Risk of lower staff productivity and increased rates of absence due to heat and cold waves causing deterioration of the workplace environment and diseases with increased incidence due to climate change	General
	✓ Risk of increased temperature control expenses in drug manufacturing, storage, and distribution, and risk of deterioration in product quality, due to rising outdoor temperature	Pharmaceutical
	✓ Risk of water shortage and deterioration of water quality due to drought, etc.	Pharmaceutical
Transition Risks		
Official policy and laws	✓ Risk of increase in manufacturing-related energy costs and price of procured products due to rising carbon taxes ✓ Risk of capital investment costs arising from facility replacement to meet GHG emissions reduction targets set by national governments, industry organizations, etc.	General
Technology	✓ Risk of growing capital investment costs arising from the introduction of new technologies (in-house power generation, storage batteries, etc.) accompanying the spread of clean energy technology	General
Markets	✓ Risk of reduced demand due to rise in product prices following rise in market price of procured products ✓ Risk of change in consumer behavior	General
Reputation	✓ Risk of impact on share price due to delay in implementing climate change countermeasures	General
Opportunities		
Resource efficiency	✓ Manufacturing cost reduction driven by improved resource efficiency in areas including energy use, water consumption, and waste management	General
Energy	✓ More stable energy costs and energy supply due to improvement in distributed clean energy technology	General
Products and services	✓ Opportunity for expansion of demand for pharmaceuticals due to diseases arising from climate change (existing drugs)	Pharmaceutical
Markets	✓ Opportunity for expansion of demand for pharmaceuticals to treat infectious diseases caused by rising temperatures and abnormal weather (new market)	Pharmaceutical
Resilience	✓ Minimization of physical risk-related damage due to plan-based implementation of countermeasures ✓ Greater operational stability due to climate-related risk assessment and risk diversification measures	General

Pharmaceutical: Risk with high specificity to the pharmaceutical manufacturing sector
General: Risk for enterprises in general, particularly in manufacturing industry

2020: Initiatives and progress in environmental protection activities

As measures to conserve energy, we are reducing energy consumption by introducing highly energy-efficient facilities, switching fuels, introducing eco-friendly cars, and conducting an energy conservation program in daily business activities while curbing GHG emissions,[9] which is the key to combating climate change. Before proceeding toward our

mid-term environmental goals for 2030, we have entered into an agreement with an electric power company to begin installing sustainable power sources at the Utsunomiya Plant, Ukima Representative Office, Kamakura Research Laboratories, and Fuji Gotemba Research Laboratories from 2021. To prevent environmental pollution, we are also working to reduce the use of chlorofluorocarbons (CFCs) and hydrochlorofluorocarbons (HCFCs) to halt the destruction of the ozone layer, and to prevent the leakage of environmental pollutants. Meanwhile, the Ukima Plant, which is covered by the Tokyo Cap-and-Trade Program, received a certificate of appreciation from the Tokyo governor dated January 4, 2021, in recognition of the plant's cooperation in 2020 with the metropolitan government's efforts toward a Zero Emissions Tokyo.

In waste management, we aim to increase the waste recycling ratio and further reduce landfill waste to achieve zero emissions of waste, and our initiatives are yielding results.

We are conducting risk management for water, given its importance as a raw material in pharmaceutical manufacturing and as a crucial global resource. As water-related risks, Chugai considers raw material procurement risks and water damage risks in distribution. Although Chugai believes its procurement-related risks to be low at present, it monitors the volume of water it uses and the wastewater it discharges each year, and is building awareness of the effective use of water resources. Chugai's countermeasures for the risks to stable supply posed by water damage include diversification of risk such as by storage and management at multiple storage facilities. Moreover, from the standpoint of protecting biodiversity, we began conducting WET tests[10] in 2013 to ascertain the ecological impact of wastewater discharged from our facilities. The purpose of this additional test is not only meeting the effluent standards of laws and regulations, but also making a general judgment of the ecological impact of chemicals involved in wastewater. In 2020, we again conducted a WET test once at each plant and research laboratory, and confirmed that there were no problems.

Meanwhile, our production bases continued with the water resource conservation activities begun in 2019. In 2020, we collaborated in forest maintenance activities with a local NPO in the wooded highlands of Kawanehoncho in Shizuoka Prefecture, which is the Fujieda Plant's water source. As well as minimizing the environmental impact of production activities, we want to help conserve the water resources Chugai shares with local residents. In our business activities, we use water with care and release it in a clean state, and we will continue with activities to maintain forests that sustain clean water.

9. In Sustainability Policy and Data 2020, which will be released separately, we intend to receive independent verification for 2020 energy consumption, GHG emissions (Scope 1, Scope 2, Scope 3, Categories 1, 4, 5, and 6), and industrial waste generated.
10. A method for comprehensive evaluation of the safety of wastewater and the aquatic environment by determining the impact on crustaceans (*Daphnia*), algae, and fish (*Oryzias latipes* and others) immersed in diluted wastewater

Promotion and progress of health and safety activities

Chugai engages in health and safety activities as one aspect of its health and productivity management, in the belief that sound employee physical and mental health and a satisfying and rewarding work environment where all employees can do their jobs with enthusiasm are the foundation for growth.

To create such an environment, we established a company-wide health and safety promotion framework in 2017 based on a policy of cooperating with the health insurance society and the labor union in simultaneous pursuit of both individual and organizational health. We also established six priority items: support for employees with cancer, measures to prevent and treat lifestyle diseases among employees, measures for employee mental health, measures to address employee presenteeism (working while sick), improvement of health literacy, and workplace safety measures. In September 2019, as part of activities to promote health and productivity management, we decided to further strengthen measures against smoking, which is strongly linked to cancer and lifestyle-related diseases. With the aim of reducing the employee smoking rate to zero by the end of 2030, we issued the Chugai Group Non-Smoking Declaration and were able to declare all Company premises smoke-free in September 2020 after a concerted company-wide effort. We are also working with corporate departments to offer support to employees identified as having high stress levels in a stress check questionnaire. At the same time, we are seeking to improve organizational health based on the results of organizational analysis. Of course, in addition to these preventive measures, we continue to conduct our existing programs to support employees during cancer treatment and after they return to work, as well as mental health awareness activities.

In 2021, we plan to formulate new mid-term health and safety goals.

Mid-Term Health and Safety Goals

Item	Target	Performance in 2020
Cancer screening participation rate[11, 12]	90% or higher	Gastric cancer 83%, colorectal cancer 85%, lung cancer 95%, breast cancer 86%, cervical cancer 64%
Percentage of employees at high risk for lifestyle-related diseases	2% or lower by 2020	4.7%[12, 13]
Awareness of Company programs	90% or higher	63%
EHS risk assessment	Conduct at each site at least once every three years	Conducted at 8 out of 16 sites

11. Screening rate for lung cancer, gastric cancer, colorectal cancer, breast cancer, and cervical cancer in the eligible age group
12. Based on medical checkup data from April 2019 to March 2020
13. High-risk criteria are under review for a more proactive approach

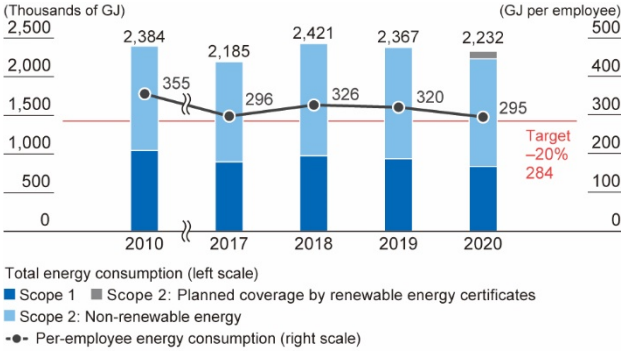
Initiatives by Theme

Theme	Details of Initiatives
Employee health management Improvement of health literacy	Maintain a support system based on cooperation with the health management organization and related departments. Improve health literacy as the basis for all health and safety activities, and conduct training for all employees.
Countermeasures against cancer	Step up recommendations for screening for early detection of cancer and provide enhanced support for continuing to work while undergoing cancer treatment.
Measures to prevent and treat lifestyle-related diseases among employees	Encourage high-risk individuals to take appropriate treatment and strengthen health guidance for them to reduce leaves of absence, job departures, and accidents caused by lifestyle-related diseases.
Measures for employee mental health	Conduct return-to-work programs and countermeasures to improve working environments based on the results of stress checks in cooperation with relevant departments.
Measures to address employee presenteeism (working while sick)	Plan, implement, and determine the effectiveness of measures based on health survey results.

Performance by EHS indicators

Total and per-employee energy consumption

Total and per-employee energy consumption in 2020 decreased by 6 percent and 17 percent, respectively, compared with the base year of 2010. The goal of a 20 percent reduction in per-employee energy consumption was not met, but we plan to use renewable energy certificates to reach a 20 percent reduction in non-renewable energy consumption.



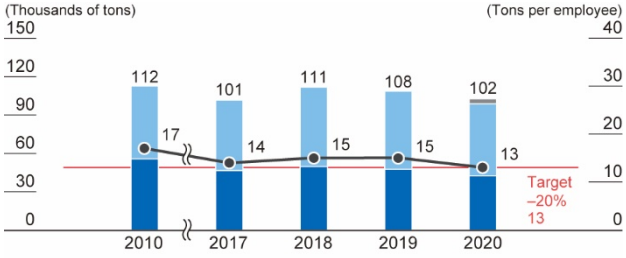
Total energy consumption (left scale)
Scope 1 Scope 2: Planned coverage by renewable energy certificates
Scope 2: Non-renewable energy
Per-employee energy consumption (right scale)

Per-employee energy consumption after utilization of renewable energy certificates in 2020: 284 GJ

Note: The year 2010 is the base year for mid-term environmental goals.
Overseas energy consumption (electricity and heat) is included from 2018.

CO_2 emissions and CO_2 emissions per employee

Total CO_2 emissions decreased 6 percent from 2019 to 101,663 tons. CO_2 emissions per employee decreased 20 percent compared with 2010. The main factor was a reduction in direct CO_2 emissions from fuel consumption (Scope 1), achieved through measures such as introducing highly energy-efficient facilities, fuel switching, and promoting energy-saving measures.



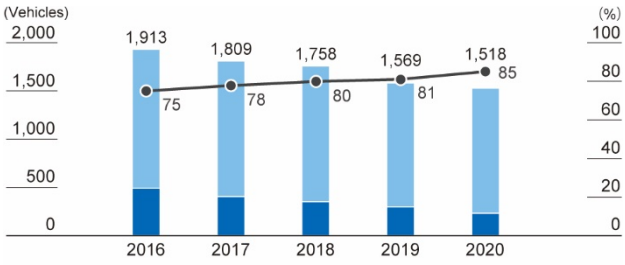
CO_2 emissions (left scale)
Scope 1 Scope 2: Planned coverage by renewable energy certificates
Scope 2: Non-renewable energy CO_2 emissions per employee (right scale)

CO_2 emissions per employee in 2020 after utilization of renewable energy certificates: 13,000 tons

Note: The year 2010 is the base year for mid-term environmental goals.
Figures from 2018 include overseas emissions (electricity and heat).

Ratio of eco-friendly cars

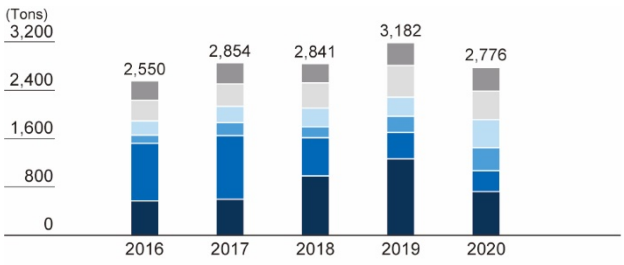
As of December 31, 2020, Chugai had introduced a cumulative total of 1,294 hybrid and fuel-efficient vehicles in its MR fleet. The ratio of eco-friendly cars was 85 percent, meeting the year's target of 80 percent or higher.



Number of gasoline and diesel vehicles (left scale)
Number of eco-friendly vehicles (left scale)
Ratio of eco-friendly cars (right scale)

Industrial waste

Industrial waste generated decreased by 406 tons from 2019 to 2,776 tons. The main factor was the decrease in sludge generation due to the decline in production accompanying the decrease in production lines at the Utsunomiya Plant. The Fujieda Plant, which had the highest waste oil emissions, is progressing with measures to reduce waste, including introduction of an oil-water separation process in its waste treatment facilities to reduce the volume of waste oil.

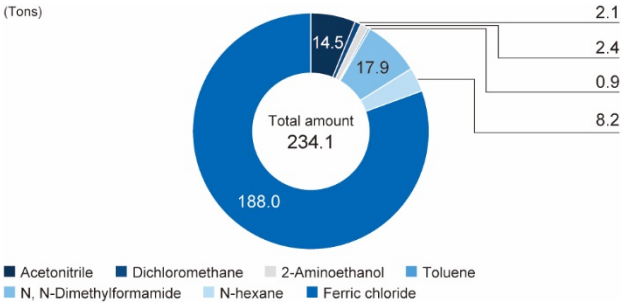


Sludge Waste oils Waste acids Waste alkalis
Waste plastics Others

Note: The amount of waste generated overseas is included from 2018.

Volume of substances covered by PRTR Law[14] (Statistical period: April 2019–March 2020)

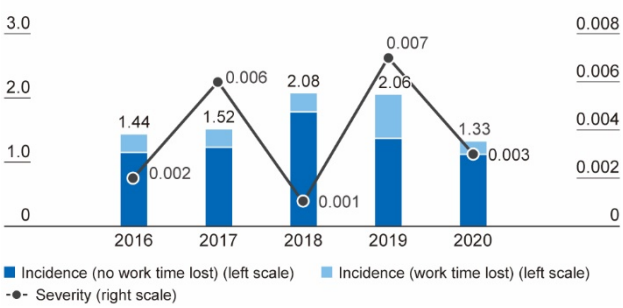
The volume of substances was 234 tons. Of this figure, 188 tons consisted of ferric chloride, which is used to treat the wastewater generated in the biopharmaceutical manufacturing process. The volume therefore increases with production amount.



14. Handled amounts of chemical substances covered by PRTR Law

Incidence and severity[15] of occupational injuries

Based on the principle that employee safety comes before business, we work actively to ensure safety, prevent occupational injuries, maintain and enhance employee health, and create a comfortable workplace environment.



15. Incidence: Indicator of frequency showing the number of occupational deaths and injuries per million hours worked (Incidence = Number of occupational deaths and injuries / Total number of hours worked × 1,000,000)
Severity: Indicator of severity of occupational injuries showing number of working days lost per thousand hours worked (Severity = Number of working days lost / Total number of hours worked × 1,000)

Note: Figures from 2020 include employees of contractors engaged in joint operations with Chugai employees at the same plant or research facility.

GHG Emissions (Tons)[16]

Scope 1: Total 42,771				Scope 2: Total 59,935	
Energy-related: 41,728 (Direct emissions)		Non-energy-related: 1,043 (Fluorocarbons, etc., from business activities)		Indirect emissions from the generation of purchased energy (Electricity, heat)	
Plants	29,070	Fluorocarbons	959	Plants	31,178
Research laboratories	11,192	• Japan	959	Research laboratories	23,984
Branches	1,446	• Overseas	0	Branches	913
Head Office	21	CO_2, etc.	84	Head Office	528
Distribution	0	• Japan	72	Distribution	561
Overseas	0	• Overseas	12	Overseas	2,770

Scope 3: Total 1,052,337 (excl. calculations in progress) (Other indirect emissions)				
Classification		Category	Scope of Calculation	Emissions Volume
Upstream	1	Purchased goods and services	Raw materials, procurement from Roche/CMOs	811,546
	2	Capital goods	Capital investment	212,816
	3	Fuel- and energy-related activities not included in Scope 1 or Scope 2	Scope 1 and 2 energy purchase	19,883
	4	Upstream transportation and distribution	Transport from logistics centers to wholesalers and airports, and from airports in Japan to overseas airports	4,594
	5	Waste generated in operations	Industrial waste	237
	6	Business travel	Business travel by aircraft in Japan and overseas	774
	7	Employee commuting	All employees	2,352
	8	Upstream leased assets	Not covered	—
Downstream	9	Downstream transportation and distribution	Transport from wholesalers to hospitals	Calculation in progress
	10	Processing of sold products	Not covered	—
	11	Use of sold products	Not covered	—
	12	End-of-life treatment of sold products	Packaging materials sold	84
	13	Downstream leased assets	Not covered	—
	14	Franchises	Not covered	—
	15	Investments	Joint research activities with academia	51

16. In Sustainability Policy and Data 2020, which will be released separately, we intend to receive independent verification for 2020 energy consumption, GHG emissions (Scope 1, Scope 2, Scope 3, Categories 1, 4, 5, and 6), and industrial waste generated.

Social Contribution

Strategic Points

- Contribution to health in local communities
- Promotion of understanding of diversity to realize an inclusive society

Performance in 2020

Promoted awareness of and supported para-sports

3
Number of SPOTLIGHT events
(2020)

Basic Concept of Social Contribution Activities

As a member of society, Chugai engages in social contribution activities to help solve social issues, contributing our resources and professional capabilities without seeking direct compensation. We actively promote activities that contribute to society while maintaining partnerships with society. We also encourage and support the engagement of individual employees in social contribution activities. Chugai keeps its stakeholders informed properly about its efforts in social contribution activities. Based on this approach, we have identified five priority areas: healthcare, social welfare, creating an inclusive society, next-generation development, and local community.

Basic Concept of Social Contribution Activities
https://www.chugai-pharm.co.jp/english/sustainability/community/concept.html

Main Initiatives for Social Contribution

Disease Awareness

SPOTLIGHT

We have been engaged since November 2019 in SPOTLIGHT, a project for patient-centric activities to help resolve social issues in the field of rare diseases. Many of these diseases are difficult to treat and patients may struggle to receive adequate understanding and support from society for their condition and the associated challenges. Our aim in launching SPOTLIGHT was to share information on its activities with stakeholders in and outside the Company to highlight the situation of patients whose voices would otherwise go unheard and thereby help resolve the social issues related to rare diseases.

One of the regular activities is a seminar for the media designed to promote improved understanding of social issues in the area of neuromuscular diseases through lectures and discussions with patients, healthcare professionals, and experts. The theme in 2019 was “Neuromuscular Diseases and Employment: Towards Improvement” and in 2020 “Definite Diagnosis and Emotional Support.” These events spread the message that, when people with disabilities receive the appropriate support to enable them to participate in society, it not only enhances their QoL but also improves sustainability for the whole of society.

In 2020, to coincide with World Hemophilia Day, we launched a dance video for children with hemophilia, who often experience deterioration of muscular strength through lack of physical activity. The video introduces a range of enjoyable dance exercises accessible to everyone. We also held an in-house workshop with the participation of a certified genetic counselor. Through sharing of information on the current state and issues of genetic disease counseling and the experiences of patients and their families, the session provided an opportunity for renewed reflection on the meaning of the “patient-centric” approach that we advocate.

Patient-Centric Activities to Help Resolve Social Issues in the Field of Rare Disease
https://www.chugai-pharm.co.jp/english/sustainability/patient/spotlight.html

Initiatives for generation AYA

In March 2017, Chugai launched AYA Life, a website for young cancer patients offering regularly updated content. Recognition of generation AYA* has been growing gradually, but there are still many patients facing a wide range of issues in areas from higher education and employment to marriage. To help even in a small way to relieve these anxieties and issues, in 2020 we held the online AYA Roundtable, a series of open discussions among people affected, whose content has been published on the website six times. As a leader in the area of oncology, Chugai will continue improving the website to provide a space that supports generation AYA cancer patients to face their treatment with peace of mind.

*AYA stands for Adolescent and Young Adult and is aimed at the 15 to 39 age group.

AYA Life
https://aya-life.jp/ (in Japanese only)

ART FUNK BREAKIN

Supporting children's activities
We provide support as a top program partner to the CP Adaptive Sports Class, a regular exercise class designed mainly for children who are wheelchair users. To give children with disabilities and their families the opportunity to participate in outdoor activities, we also sponsor kayak and handcycling classes for parents and children to enjoy together, thus encouraging the children to challenge themselves with activities that are sometimes considered difficult for them.

A new addition to our wide range of support activities is our sponsorship of ART FUNK BREAKIN, Japan's first breakdance competition exclusively for people with disabilities, organized by the Japan Adapted Breakin Association and the Agency for Cultural Affairs.

Raising awareness of para-sports
With the aim of promoting understanding of diversity, we provided support for the making of a booklet to raise awareness of hearing disabilities and a handbook for wheelchair softball.
- *What Does Being Deaf Mean?*, published by the Japan Deaf Football Association
- *Wheelchair Softball Handbook*, published by the Japan Wheelchair Softball Association

Action to assist an evacuation center operated by a support group
(Kuma district, Kumamoto Prefecture)

Disaster relief

Support to areas hit by torrential rains in July 2020
To provide emergency relief following the torrential rains that hit especially the Kyushu and Chubu regions in July and to support regional recovery, Chugai made financial donations to the Association for Aid and Relief, Japan, and the AMDA Group. Both groups provided daily living assistance and support for recovery to local people through evacuation centers, where appropriate measures were taken to prevent COVID-19 infection.

Support to areas of western Japan hit by torrential rains
Chugai is a regular participant in the Roche Group charity event Roche Children's Walk. Chugai matches the funds raised by employees with an equal sum and the total amount is donated to associations in Malawi and other countries and disaster-hit areas of Japan. In 2020, we supported Nozomi, an NPO based at Kurashiki in Okayama Prefecture that provides assistance in areas including employment, child development, and after-school day service facilities. Following the destruction of the organization's facilities in the torrential rains of July 2020, it relocated its activities to the neighboring city of Soja. The donation will be used to cover the cost of moving its office back to Kurashiki.

Para-transit vehicle donations

Chugai's program to donate specially equipped para-transit vehicles began in 1985 as part of activities to commemorate the Company's 60th anniversary. The program marked its 36th year in 2020. A total of 263 vehicles have been donated since the start of the program. Securing the means for senior citizens and disabled people living at home to go to places such as hospitals, day service centers, and day care centers and for staff from these facilities to visit homes to perform in-house care is significant from the viewpoint of enhancing welfare services. The para-transit vehicle donation program is conducted in cooperation with the Japan National Council of Social Welfare and Central Community Chest of Japan, and through it vehicles have been donated to recipients in all of Japan's 47 prefectures.

Global Health

Strategic Points

- Rolling out global health activities that contribute to both the creation of corporate value and the resolution of social issues
- Contributing to the sustainable improvement of healthcare, mainly in low- and middle-income countries
- Prioritizing local needs and promoting activities that utilize Chugai's capabilities

Performance in 2020

Held workshop on multidisciplinary team care in Cambodia in February as part of activities to support childhood cancer treatment

Entered into partnership with City Cancer Challenge Foundation (C/Can) in July

Chugai's Basic Approach to Global Health

Chugai has adopted creating shared value with stakeholders as its basic management policy and is rolling out global health activities that contribute to both the creation of corporate value and the resolution of social issues, with the aim of "the realization of advanced and sustainable patient-centric healthcare". These activities will be continued in our new growth strategy "TOP I 2030".

Basic Policy for Creating Shared Value
https://www.chugai-pharm.co.jp/english/sustainability/sharedvalue/policy.html

There are still many people around the world who suffer from diseases without a cure, or who, despite the availability of treatment, are denied access due to poverty or institutional reasons, etc. Chugai has adopted creating shared value with stakeholders as its basic policy. We identified 25 material issues that should be given priority, one of which is improving access to healthcare. In this area, we aim to generate corporate value and at the same time contribute to resolving social issues through a range of activities including partnerships with public bodies, NGOs, industry organizations, and other entities. Our Basic Approach to Global Health, issued in 2019 to outline this strategy, sets the following priority initiatives: developing and improving access to new products for diseases with no treatments, and improving access to sustainable healthcare. Before launching specific activities, we undertake detailed research into local needs with the emphasis on activities that make the best use of Chugai's capabilities in terms of strengths, technologies, and expertise, and activities that can contribute to sustainable improvement of healthcare mainly in low- and middle-income countries.

Chugai's Basic Approach to Global Health
https://www.chugai-pharm.co.jp/english/sustainability/globalhealth/concept.html
Activity Reports: Global Health
https://www.chugai-pharm.co.jp/english/sustainability/activity/index.html?year=&category=2

Main Initiatives for Global Health

Main Projects We Participate In

GHIT Fund

Jointly established with funding from Japanese pharmaceutical companies, the Japanese government, the Bill & Melinda Gates Foundation, and the United Nations Development Programme, the Global Health Innovative Technology Fund (GHIT Fund) is Japan's first public-private partnership to support and promote research and development of drugs, vaccines, and diagnostics for infectious diseases in developing countries. Chugai joined the GHIT Fund in December 2014. In addition to making donations, Chugai is active on the fund's council and contributes to its administration.

GHIT Fund
https://www.ghitfund.org/

Access Accelerated (AA)

AA was established in January 2017 by 22 global pharmaceutical companies including Chugai and follows a strategy decided jointly by members. In partnership with the World Bank Group, the City Cancer Challenge Foundation, and other organizations, AA is working for the prevention, diagnosis, and treatment of noncommunicable diseases (NCDs) in low- and middle-income countries. Its aim is to contribute to the target set in the United Nations Sustainable Development Goals (SDGs) of achieving a one-third reduction in premature deaths from NCDs by 2030.

Access Accelerated
http://www.accessaccelerated.org/

Khmer staff attending the workshop

Chugai Independent Initiatives

Target disease areas: cancer, hemophilia, and other non-communicable diseases

Activities to support childhood cancer treatment (Cambodia)

The Cambodian economy has been growing in recent years, particularly in urban areas. In the field of healthcare and hygiene, however, equal access to quality medical care remains a challenge for reasons including the shortage of healthcare professionals, insufficient medical knowledge, and the lack of a well-developed health insurance system. One of the issues that needs to be addressed is how to enhance coordination between doctors, nurses, and the numerous other healthcare professionals to deliver high-quality medical care within the constraints of the limited human resources and facilities available to frontline services. To help resolve this issue, Chugai, bringing together the expertise in supporting team care it has accumulated over many years as a leader in the area of oncology, held a workshop on multidisciplinary team care in Cambodia for local healthcare professionals in February 2020. The workshop, which took place at the Children's Medical Center operated by the NPO Japan Heart, welcomed twenty-one participants. We aim to host a total of 50 healthcare professionals at the workshop over the next three years.

Enhancing the Quality of Patient-Centric Cancer Care (Yangon, Myanmar)

In Myanmar, the therapeutic approach adopted for cancer patients is not based on multidisciplinary coordination, and no standard therapy has been established. To contribute to enhancing the quality of patient-centric cancer care in Yangon, we entered into a partnership in July 2020 with the NGO City Cancer Challenge Foundation (C/Can), which supports cancer treatment in units of cities in the developing world. Specifically, we provided support for the formulation of cancer treatment guidelines tailored to local conditions, and education and training to support implementation of the guidelines by multidisciplinary teams of healthcare professionals including doctors, nurses, and caregivers, with training for approximately 400 staff planned over a period of three years. The aim is to promote team care based on multidisciplinary coordination for types of cancer with strong treatment needs locally, and to encourage the consolidation and further dissemination of this practice. So far, guidelines for breast cancer and cervical cancer have been formulated and received approval from the Myanmar Ministry of Health and Sports.

Treatment in a developing country
(provided by WFH)

World Federation of Hemophilia (WFH) Humanitarian Aid Program

The WFH Humanitarian Aid Program, comprising a network of patient organizations in 140 countries, aims to improve access to care and treatment for people with inherited bleeding disorders in developing countries, where there is a severe lack of access to healthcare. Chugai, the originator of the hemophilia A agent Hemlibra, is participating together with Roche as a member of the Roche Group. The Roche Group will provide prophylactic treatment to approximately 1,000 people with hemophilia A in developing countries by donating supplies of Hemlibra over a course of five years. Additionally, the Group is providing support to put in place the infrastructure and conditions required for healthcare professionals to make proper use of treatments.

Mobile medical clinic in Myanmar

Support for Safer Childbirth and Health Camps Against NCDs (Rural areas of Myanmar)

In partnership with the NPO AMDA Multisectoral and Integrated Development Services (AMDA-MINDS), Chugai is engaged in rural areas of Myanmar in projects to promote safer hospital-based childbirth and maternity healthcare and to combat NCDs. In the latter project, healthcare professionals traveled to villages and set up mobile clinics, with a target of examining more than 4,000 people at 48 locations throughout Meiktila Township. People in rural areas face hurdles to outpatient consultation and treatment due to the distances and cost burden, resulting in the issue of delayed initial treatment and progression to serious illness. In 2020, of some 2,500 villagers examined, 30 percent were diagnosed as having an NCD, for which treatment and follow-up care were arranged. We also provided education and training to prevent the spread of COVID-19 infection as well as protective masks and gowns. To gain an accurate understanding of local needs for each project, we listen carefully to the opinions and requests of patients, healthcare professionals, and local health departments in such a way that we can continue helping to improve access to healthcare even after the project is completed.

Basic Information

Basic Information on the Pharmaceutical Industry

Drug Discovery Research

Research and Development Aims

Drug discovery research is the activity of creating new drugs by first identifying target molecules and then developing them into drug candidates. To respond to unmet medical needs,* Chugai aims to successively create innovative new drugs that can achieve first-in-class*/best-in-class* status. This series of pre-clinical processes is said to normally require five to eight years. Chugai conducts its research activities making efficient use of its research infrastructure, including unique drug discovery and AI technologies, its external networks, including links with academia, and the infrastructure of the Roche Group.

Unmet medical needs
Medical need that is not adequately met due to a lack of effective treatments.

First-in-class
An original drug that is highly novel and useful, and will significantly change the therapeutic system.

Best-in-class
A drug that offers clear advantages over other existing drugs in the same category, such as those with the same molecular target.

Drug Discovery Modalities

Modality refers to the material classification of a drug. Until the 1990s, small molecule drugs were virtually the only modality, but the options are now increasing. New modalities open up new approaches in areas of disease where there is no effective treatment. To add to its world-leading therapeutic antibodies* and small molecule drugs,* Chugai is therefore working to establish mid-size molecule drugs* as a third modality.

Therapeutic antibody
A type of biopharmaceutical, which is a drug created by applying biotechnology such as genetic recombination. It is an artificially created antibody used as a medicine to prevent or treat diseases. Therapeutic antibodies are designed to act only on the specific molecule (antigen) that causes the disease, and therefore can be expected to provide high therapeutic efficacy and reduce side effects.

Small molecule drug
A drug created by chemical synthesis with a low molecular weight of 500 or less.

Mid-size molecule drug
This modality is thought to offer a promising new approach to reaching intracellular targets inaccessible with antibodies and small molecules.

Clinical Drug Development

Basic Clinical Development Process

In clinical development, the efficacy and safety* of drug candidates are demonstrated based on the evidence obtained in the research stage. To do this, clinical trials* with an optimal design based on the latest scientific findings are conducted to gather the data required for regulatory approval. Chugai achieves efficient and speedy clinical development by contributing from Japan to joint multinational clinical studies as part of global development projects sponsored by the Roche Group.

PoC / Early PoC
Proof of concept (PoC) is confirmation that the therapeutic effect conceived in the research stage is effective in humans. Early PoC means that in addition to safety, signs of efficacy or pharmacological effect have been confirmed in a limited number of cases.

Clinical trial
A study to verify the safety, efficacy, and other characteristics of a drug in human subjects. Studies conducted for the purpose of filing an application for approval are called clinical trials.

Phase I: Performed on a small number of healthy volunteers (or, for certain disease areas and diseases, on patients) to assess the drug's safety and the process by which it is absorbed, distributed, metabolized, and eliminated by the body.

Phase II: Performed on a small number of consenting patients to determine the safest and most effective dosage and the dosing regimen.

Phase III: Performed on a large number of consenting patients to verify the efficacy and safety of the new drug in comparison with existing drugs or placebo.

Phase IV: Post-marketing clinical surveillance. Performed on a larger number of consenting patients than in phase III studies to verify the drug's safety and efficacy for its approved indication(s).

Application for Approval

When a new drug candidate has demonstrated efficacy and safety in a range of clinical trials, pharmaceutical companies file an application for manufacturing and marketing approval with the regulatory authorities. In Japan, the Minister of Health, Labour and Welfare grants manufacturing and marketing approval to substances deemed appropriate as pharmaceuticals based on reviews by the Pharmaceutical and Medical Devices Agency (PMDA) as well as academic and other experts in the Pharmaceutical Affairs and Food Sanitation Council. To expedite the practical application of a drug, there is a system* in place enabling breakthrough therapies and other drugs that fulfill certain conditions to be given priority in consultation and review for regulatory approval.

Breakthrough therapy designations
This is a designation granted by the U.S. Food and Drug Administration (FDA) to expedite the development and review of drugs for the treatment of serious or life-threatening diseases and symptoms. A drug must be highly innovative to receive the designation, but receiving it is valuable for various reasons. For example, a drug with this designation receives priority review, which shortens the development period, bringing the drug to patients as quickly as possible. Chugai has received this designation for five products and eight projects originating from in-house research (as of February 4, 2021), an indication of the strength of its drug discovery capabilities.

Drug Lifecycle Management

Basic Lifecycle Management System

Chugai operates an integrated lifecycle management (LCM) system. In this process, customer needs and product management perspectives are incorporated from the early stage of each clinical development project. The management process continues as the product is launched and matures right through to the end of the lifecycle. To maximize the product's value potential, Chugai pursues a range of objectives, from shortening the development period, expanding sales, and extending product lifespan to acquiring additional indications,* ensuring appropriate cost management, and implementing an appropriate patent strategy.

Additional indication
A new indication for a previously approved drug.

Drug Patents

Patents are crucial to the value of a drug. As they operate in combination with the regulatory system, relatively few patents are required for product protection compared to other industries. Patent rights are normally valid for 20 years from the date of application, but to compensate for the length of the pharmaceutical R&D period, some governments may allow an extension of patent rights for a maximum of five years. As the market release of generics is not permitted during the term of the

patent, it is an important part of the LCM strategy to progressively acquire patents for additional indications, additional dosing and administration options, and others.

Overview of Domestic Pharmaceutical Market and National Health Insurance (NHI) Drug Prices

Trends in National Medical Expenses

Without medical system reforms, Japan's national medical expenses will increase at an annual rate of approximately 2 to 4 percent going forward. In fiscal 2019 (the year ended March 2020), national medical expenses[1] totaled ¥43.6 trillion, a ¥1.0 trillion or 2.4 percent increase from the previous year. The accelerating pace of aging of Japan's society presents serious challenges to efficiently managing the increase in medical expenses for the elderly.

1. Source: Trends of recent medical expenditure (fiscal 2019) by Ministry of Health, Labour and Welfare

Promotion of the Use of Generics

The Japanese government is promoting the use of generics with the primary objective of reducing the cost burden on patients and improving the finances of the health insurance system. Various measures have been carried out under the action program announced in October 2007 to promote the worry-free use of generics. In April 2013, the new "Roadmap to Further Promote the Use of Generics" was formulated. A Cabinet decision in June 2017 set the new goal of raising the volume market share of generics, which was 78.3 percent[2] as of September 2020, to 80 percent by the end of September 2020. Based on the result achieved, a new target for promoting the use of generics is now being considered. For biosimilars, the government aims to double the number of items in use by the end of 2023 compared to July 2010, based on the number of active ingredients.[3]

2. Preliminary results of 2020 Drug Price Survey
3. New Economic and Fiscal Revitalization Plan, 2020 Reform Schedule

NHI Drug Price Revision

The Ministry of Health, Labour and Welfare (MHLW) generally reviews drug reimbursement prices every two years and sets new standard prices (reimbursement prices) so that the official prices of pharmaceuticals prescribed under the health insurance system approximate their actual market price. The MHLW does this by investigating the prices and volumes of all prescription drug transactions during a given period.

Due to the growing public financial burden caused by the situation at the time, in which drug prices were maintained for up to two years even if the actual market price fell, it was decided in the fiscal 2018 fundamental reform of the NHI drug pricing system that drug price survey and revision should also take place in interim years, when, ordinarily, there would be no revision. The government has since been considering the specific details of this policy.

Fiscal 2021 will be the first year in which the interim price revision is conducted. With the aim of achieving a wide-ranging reduction of the public financial burden, the revision will be applied to all product items showing a price difference from the market average of more than 0.625 times (5 percent). Moreover, to take into account the impact of COVID-19 infection, the drug price revision will be based on actual market prices so as to soften by 0.8 percent the extent of the price reduction.

In concrete terms, it has been decided that the revision of April 2021 should bring a drug price reduction of ¥100.1 billion when measured in terms of government spending.

NHI Drug Price Revision Rate (%) 4. Adjusted to account for consumption tax increase 5. Pending release by the MHLW Source: Chugai data

	2008	2010	2012	2014[4]	2016	2018	2019/10[4]	2020	2021
Industry average	(5.2)	(6.5)	(6.25)	(2.65)	(7.8)	(7.48)	(2.4)	(4.38)	—[5]
Chugai	(7.2)	(6.8)	(6.0)	+0.8	(5.5)	(6.7)	(0.2)	(9.2)	(2.5–3.0)

Repricing Based on Market Expansion

Under this repricing rule introduced in 1994, drugs priced by the cost calculation method with annual sales exceeding ¥10.0 billion and more than 10 times the original forecast at the time of price revision, or with annual sales exceeding ¥15.0 billion and more than two times the original forecast, are subject to a price reduction of up to 25.0 percent. Drugs priced by methods other than the cost calculation method (including the similar efficacy comparison method) with annual sales exceeding ¥15.0 billion and more than two times the original forecast at the time of the price revision are subject to a price reduction of up to 15.0 percent. In addition, the prices of drugs that have pharmacological action similar to a drug subject to this repricing rule are reduced by the same rate. In the NHI drug pricing system fundamental reforms of fiscal 2018, it was decided to use the NHI listing of new drugs that takes place four times a year as an opportunity for repricing of drugs with annual sales exceeding ¥35.0 billion. The purpose of this change is to respond more quickly when sales expand rapidly due to an additional indication or other reasons.

Special Market-Expansion Repricing

In the reforms to the drug pricing system in fiscal 2016, an additional repricing rule for drugs with very high annual sales was introduced as a special measure from the standpoint of balancing reward for innovation with the sustainability of the NHI system. This rule lowers prices by up to 25.0 percent for drugs with annual sales of ¥100.0–150.0 billion and more than 1.5 times the original forecast, and lowers prices by up to 50.0 percent for drugs with annual sales exceeding ¥150.0 billion and more than 1.3 times the original forecast. In addition, the prices of drugs that have pharmacological action similar to a drug subject to the special repricing rule and were comparator drugs at the time of the NHI price listing are reduced by the same rate. In the NHI drug pricing system fundamental reforms of fiscal 2018, it was decided to use the NHI listing of new drugs that takes place four times a year as an opportunity for repricing under this scheme.

Premium to Promote the Development of New Drugs and Eliminate Off-Label Use

As part of the NHI drug pricing system reforms of fiscal 2010 (the year ended March 2011), a new pricing scheme was implemented on a trial basis to promote the creation of innovative medical products and solve the drug lag[6] problem. In this scheme, at the time of the NHI drug price revisions, prices are maintained on drugs for which no generics are available (provided that they have been in the NHI price list for no more than 15 years), and which satisfy certain conditions.

This premium pricing for new drugs was continued on a trial basis in subsequent NHI drug pricing system reforms. However, in the NHI drug pricing system fundamental reforms of fiscal 2018, the decision was made to revise the requirements for

companies and products and list them in the drug repricing rules. Companies that do not respond appropriately to development requests from the MHLW will continue to be excluded from eligibility for premium pricing. In addition, indicators have been set for (A) creation of innovative drugs and treatments for antimicrobial-resistant bacteria, (B) drug lag countermeasures, and (C) development of novel drugs ahead of other countries, and the pricing premiums may vary according to the level of achievement or fulfillment of these indicators. Healthcare-related ventures are expected to play an important role in the creation of innovative drugs, and will be evaluated accordingly, irrespective of the company indicators.

Regarding the product requirements, the percentage price difference requirement will be abolished, and the price premium will be limited to novel drugs during their patent period, and drugs that are truly innovative and useful. More specifically, it will be limited to orphan drugs; drugs for which development was publicly requested; drugs to which the premium was applied because of their usefulness, such as at the time they were newly listed; drugs with novel mechanisms of action that are innovative or useful (limited to the top three first-in-class drugs within three years from listing) or that have newly added efficacy or effectiveness deemed equivalent to novel modes of action; drugs that have Sakigake designation; and treatments for antimicrobial-resistant bacteria.

Among new drugs subject to premium pricing, including those for which generics (including biosimilars) have been launched or 15 years have elapsed since their drug price listing, the cumulative amount of premium pricing is deducted from the NHI drug price in the subsequent initial drug price revision. Furthermore, a reduction or other adjustment due to the actual market price of the new drug during the fiscal year is made to the NHI drug price less the cumulative amount.

6. The inability of Japanese patients to gain access to global standard or most advanced treatments because the drugs are not developed in Japan

Solving the Drug Lag Problem

In January 2005, the MHLW established the Investigational Committee for Usage of Unapproved Drugs as one means of helping solve the drug lag problem. The committee is charged with investigating the clinical necessity and the appropriateness of usage of drugs already approved in Europe and the United States, but not yet approved in Japan. The aim of these investigations is to promote the development of those drugs in Japan. In February 2010, the MHLW established the Review Committee on Unapproved Drugs and Indications with High Medical Needs. This committee evaluates the medical necessity of drugs and indications that are not yet approved in Japan and investigates matters such as the applicability of filings for approval based on evidence in the public domain. As a result of continuous efforts to strengthen the review function of the PMDA, an independent administrative institution responsible for reviewing drugs and medical devices for approval, the median total review time for new drugs in fiscal 2019 was 11.8 months. In fiscal 2019, the difference between Japan and the United States in the median total review period for approved new drugs was 0.1 years, while for new drug applications filed in Japan, the median lag compared to the time of filing in the United States was 0.5 years. Based on the total of these two figures, the fiscal 2019 drug lag amounted to 0.6 years.

Response to Requests from the MHLW Review Committee on Unapproved Drugs and Indications with High Medical Needs
(As of January 30, 2021)

Development Request	Product	Indication	Development Status
First development request	Xeloda	Advanced or recurrent gastric cancer	Approved in February 2011
	Tarceva	Advanced or recurrent pancreatic cancer	Approved in July 2011
	Avastin	Advanced or recurrent breast cancer	Approved in September 2011
	CellCept	Pediatric renal transplant	Approved in September 2011
	Herceptin	Q3W dosage metastatic breast cancer overexpressing HER2	Approved in November 2011
		Neoadjuvant breast cancer overexpressing HER2	
	Kytril	Gastrointestinal symptoms associated with radiotherapy	Approved in December 2011
	Pulmozyme	Improvement of pulmonary function in patients with cystic fibrosis	Approved in March 2012
	Bactramin	Treatment and prevention of pneumocystis pneumonia	Approved in August 2012
	Avastin	Ovarian cancer	Approved in November 2013
Second development request	Avastin	Recurrent glioblastoma	Approved in June 2013 (Malignant glioma)
	Herceptin	Q1W dosage postoperative adjuvant breast cancer overexpressing HER2	Approved in June 2013
	CellCept	Lupus nephritis	Approved in May 2016
Third development request	Tamiflu	Additional dosage for neonates and infants younger than 12 months	Approved in March 2017
	Xeloda	Adjuvant chemotherapy in rectal cancer	Approved in August 2016
	Avastin	Additional Q2W dosage and administration for ovarian cancer	Submitted company opinion and waiting for evaluation by committee

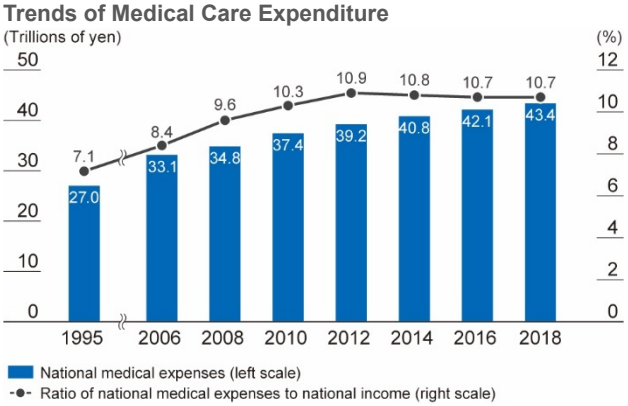
Fourth development request	Copegus	Improvement of viraemia associated with genotype 3 chronic hepatitis C or compensated cirrhosis related to hepatitis C when administered in combination with sofosbuvir	Approved in March 2017
	Xeloda	Neuroendocrine tumor	Submitted company opinion and waiting for evaluation by committee
	Avastin	Cerebral edema induced by radiation necrosis	Submitted company opinion and waiting for evaluation by committee
	Neutrogin	Combination therapy with chemotherapy including fludarabine for relapsed/refractory acute myeloid leukemia	Submitted company opinion and waiting for evaluation by committee
	CellCept	Prevention of graft-versus-host disease in hematopoietic stem cell transplantation	Evaluated by the Review Committee in December 2020 as eligible for public knowledge-based application; application approved January 27, 2021, by the First Committee on New Drugs, Pharmaceutical Affairs and Food Sanitation Council

Creation of a System for Cost-Effectiveness Assessments

A system of price adjustments based on cost-effectiveness assessments has been approved by Chuikyo, and was implemented in April 2019. The system primarily applies to products that meet the requirements of the selection criteria at the time of their NHI price listing. Cost-effectiveness assessments will be conducted for a certain period after the listing, and the price will be adjusted according to the results. The extent of the price adjustment is the portion corresponding to the amount of the corrective premium for usefulness applied at the time of the drug's initial pricing (for products with a degree of disclosure under 50 percent, as calculated by the cost calculation method, the portion corresponding to operating profit is also subject to adjustment). Price adjustments will be made according to the incremental cost effectiveness ratio (ICER).[7] The corrective premium will be maintained if the ICER is less than ¥5 million (less than ¥7.5 million for anticancer agents), but will be reduced in stages by up to 90 percent if the ICER is ¥5 million or more. The price adjustment will be limited to 10–15 percent of the total drug price.

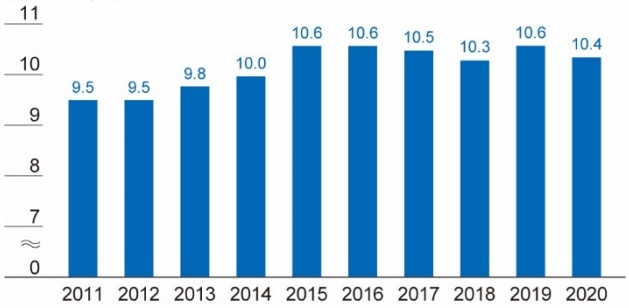
7. The ICER indicates the extent to which additional investment would be necessary to obtain the additional benefit from replacing existing drug (technology) B with new drug A.

Trends of Medical Care Expenditure



Source: Overview of Estimates of National Medical Care Expenditure, FY2018 by Ministry of Health, Labour and Welfare
Note: National income is based on the actual results of the System of National Accounts announced by the Cabinet Office.

Prescription Drug Market



Source: JPM, based on 2011–2020 (calendar year). Reprinted with permission.

Note: The status of products and drug candidates under development is as of February 4, 2021.

Oncology

Overview of Disease and Treatment Methods

Leading Cause of Death in Japan

Cancer has been the single most common cause of death in Japan since 1981.

In 2019, 376,425 people[1] died of cancer, accounting for 27.3 percent[1] of all deaths in that year and the highest number since government surveys began in 1899.

1. Source: Outline of Vital Statistics (2019) by Ministry of Health, Labour and Welfare

Establishment of the Basic Act for Anticancer Measures and Improvement in the Healthcare Environment

The Cancer Control Act was enacted in June 2006 to establish a system so that patients can receive appropriate treatment based on scientific knowledge regardless of the region in which they reside and with respect paid to their wishes, as well as to implement the Basic Plan to Promote Cancer Control Programs (the "Basic Plan"). Since the enactment of the Cancer Control Act, some results have been obtained, including establishment of designated cancer hospitals and a reduction of the cancer mortality rate and improvement of the five year survival rate owing to advances in cancer treatment. The goal of reducing the age-adjusted cancer mortality rate by 20 percent over the 10-year period from fiscal 2007 was judged difficult to achieve, and therefore, in December 2015, the Plan for Acceleration of Cancer Control Programs was formulated. This plan specified concrete measures that should be implemented intensively in a short period of time.

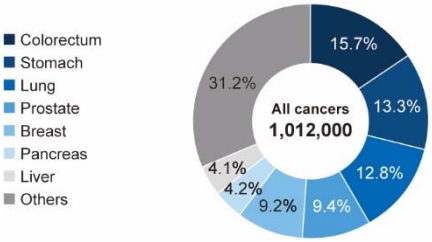
In recent years, it has become apparent that new measures are

necessary to fight rare cancers, difficult-to-treat cancers, childhood cancers, and cancers in adolescents and young adults (AYA); to promote new treatments such as genomic medicine; and to address societal problems including employment. The principles of the Cancer Control Act revised in 2016 require that the national and local governments make effective use of healthcare and welfare resources and implement cancer control measures from the viewpoint of serving the public in order to achieve the stated goal of creating a society in which cancer patients can live with peace of mind and dignity. In the 3rd Basic Plan to Promote Cancer Control Programs released in March 2018, measures are being implemented to educate the public, including patients, about cancer and help them to overcome it. These measures are based on four pillars: cancer prevention, improvement of cancer care, living with cancer, and deployment of infrastructure to support those measures.

Changes in Treatment Methods

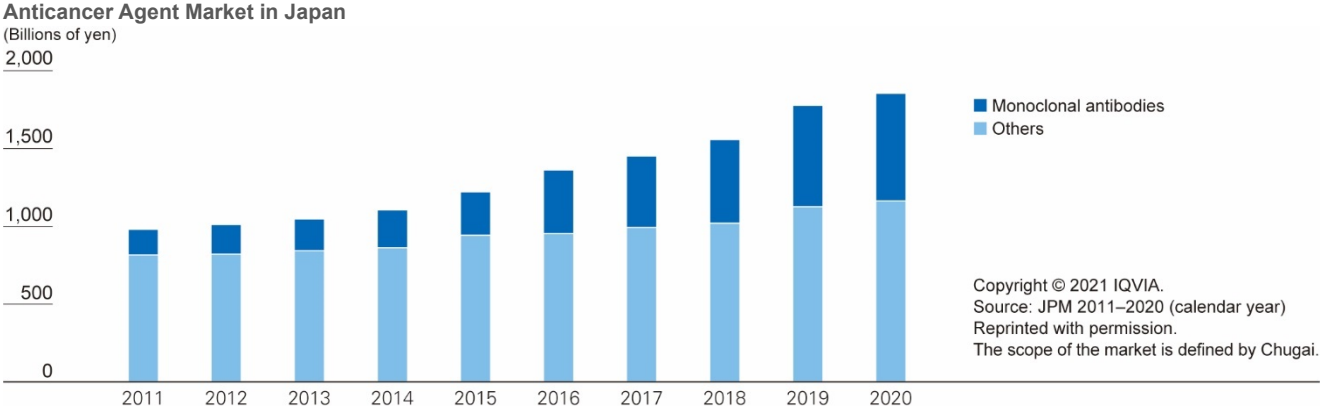
Cancer treatment is increasingly being based on a multidisciplinary approach that combines surgery, radiation therapy, and drug therapy. In particular, the field of anticancer agents is evolving, and highly innovative medicines such as molecular targeted drugs have been introduced. This has brought dramatic improvement in treatment outcomes for various types of cancer. Advances are being made in personalized healthcare (PHC), which involves testing patients with companion diagnostics when administering molecular targeted drugs to identify patients who are likely to benefit with minimal strain on the body and few side effects. In addition to enabling physicians to propose the optimal treatment tailored to each patient, this approach offers a number of other benefits. For example, it can reduce national healthcare expenditures by reducing the administration of drugs when their effect cannot be determined. Diagnosis with comprehensive genomic profiling (CGP), such as genomic testing using next-generation sequencing, is also becoming important. In improvement of cancer care, one of the pillars of the abovementioned Basic Plan, cancer genomic medicine heads the list of measures, and practical application of CGP testing was promoted as an important government-led initiative. As a result, in June 2019 CGP, which entails comprehensive analysis and profiling of genes in a single test using solid tumor tissue from the patient, became eligible for health insurance coverage. The provision of optimal treatments based on each patient's genomic profile has thus become a reality. Genomic medicine started in the oncology field, but is now being promoted for intractable diseases and other diseases, in line with the "Action Plan of the Growth Strategy," "Follow-up on the Growth Strategy," and "Action Plan for Innovative Business Activities in Fiscal 2019," which were approved by the Cabinet in June 2019. This is expected to further advance precision medicine in ways such as promoting the development of treatment approaches that utilize genomic information obtained not only through genomic analysis of cancer tissue, but through entire genome analysis. Cancer immunotherapy, which takes advantage of the body's own immune cells to fight cancer, is another important emerging field of treatment. Immune checkpoint inhibitors, one type of immunotherapy now in use, are a promising new direction in cancer treatment. Cancer has the ability to suppress (apply brakes to) immune functions to avoid attack from the immune system, but immune checkpoint inhibitors block the immune "brakes" (the binding of PD-1 to PD-L1, etc.) known as the immune checkpoint, thereby awakening immune cells to attack cancer cells. In clinical study results, immune checkpoint inhibitors have shown promise for long-term survival and cure, even in advanced cancer. Their high therapeutic efficacy is recognized in clinical settings, and they are increasingly used as treatments for a wide range of cancers. However, some patients do not respond to cancer immunotherapy, so screening to select patients for whom this therapy is likely to be effective is also being examined, as are various combinations with existing anticancer agents and development candidates, and development for use in early-stage cancer. CAR T-cell therapy, another immunotherapy using gene delivery technology, is also in use in Japan. In this approach, T cells collected from the patient are engineered to produce chimeric antigen receptors (CAR) that recognize specific cancer cell antigens. The T cells are then multiplied and returned to the patient to attack the cancer cells.

Projected Cancer Incidence (2020)



Source: National Cancer Center Cancer Information Service, "Cancer Registries/Statistics"
* Intraepithelial cancer not included in projection.
Note: The projection of cancer incidence was calculated by using future estimates of population by age bracket for 2020 to adjust the incidence by age bracket and cancer type according to the national cancer register (2017 recorded statistics). The total may not add up because projections have been performed by cancer type and figures have been rounded.
Reference: Japanese Journal of Clinical Oncology 2014, 44: 36-41

Anticancer Agent Market in Japan



Source: JPM 2011–2020 (calendar year)

The scope of the market is defined by Chugai.

FoundationOne CDx Cancer Genomic Profile

FoundationOne CDx Cancer Genomic Profile (F1CDx), developed by U.S.-based Foundation Medicine, Inc., is a next-generation sequencing-based diagnostic device. It detects substitutions, insertion and deletion alterations, and copy number alterations in 324 genes and select gene rearrangements, as well as genomic signatures including microsatellite instability (MSI) and tumor mutational burden (TMB). The program is available as a companion diagnostic for multiple molecular-targeted drugs approved in Japan. Chugai launched the program and began providing testing services in June 2019. In March 2021, Chugai received approval for FoundationOne Liquid CDx Cancer Genomic Profile, a liquid biopsy test for solid tumors using blood samples. As it detects tumor DNA circulating in blood (ctDNA), it can be used in cases where tumor tissue is difficult to sample. The product is expected to bring further advances in PHC, including by allowing tissue samples and blood samples to be used selectively at different stages of treatment.

Tecentriq (RG7446)

Engineered anti-PD-L1 monoclonal antibody
(Generic name: atezolizumab)
Launch in Japan: April 2018

Tecentriq is an engineered anti-PD-L1 monoclonal antibody in-licensed from Roche. One way that tumor cells evade the immune system is by expressing a protein called programmed death-ligand (PD-L1) on their surface, which is believed to shield them from immune system attacks by binding to T cells. Tecentriq restores and maintains the immune response of T cells by binding to PD-L1, and is expected to demonstrate efficacy against cancer cells. Its mode of action differs from conventional treatments that attack cancer cells directly. Since it takes advantage of the patient's own immune response, it is also promising for use in combination with existing drugs and for various cancer types. Chugai obtained approval in January 2018 for the treatment of unresectable, advanced, or recurrent nonsquamous non-small cell lung cancer (NSCLC), and obtained approval in December 2018 for the treatment of chemotherapy-naïve people with unresectable, advanced, or recurrent nonsquamous NSCLC in combination with Avastin and chemotherapy. In 2019, Chugai obtained approval for the additional indications of extensive-stage small cell lung cancer (SCLC) in August, PD-L1-positive inoperable or recurrent triple-negative breast cancer (TNBC) in September, and unresectable, advanced, or recurrent NSCLC (new dosage/form) in November. Characterized by rapid progression and poor prognosis, SCLC and metastatic TNBC are diseases with high unmet medical needs. SCLC is an area that has long had limited therapeutic options, and Tecentriq received orphan drug designation as the first new drug in 17 years that improved treatment outcomes. The additional dosage forms for NSCLC, some of them approved for the first time worldwide, enable a regimen that does not limit combination with other anticancer agents in first-line treatment. In September 2020, approval was received for use in combination with Avastin for unresectable hepatocellular carcinoma (HCC). The MHLW had granted priority review designation on the grounds of improved prognosis and gave approval seven months after filing. Additionally, in December of the same year, Tecentriq was approved for monotherapy in chemotherapy-naïve cases of PD-L1-positive unresectable, advanced, or recurrent NSCLC. Tecentriq is the first immune checkpoint inhibitor to be approved in Japan, the United States, and Europe in the areas of SCLC, breast cancer, and HCC. Chugai is also participating in global phase III studies for a range of further indications: neoadjuvant and adjuvant therapy for NSCLC; urothelial carcinoma; renal cell carcinoma; renal cell carcinoma (adjuvant therapy); early breast cancer; ovarian cancer; HCC (adjuvant therapy); head and neck carcinoma (maintenance therapy); and esophageal cancer. A number of these studies involve the co-development with Takeda Pharmaceutical Company Limited, of combination therapy with CABOMETYX® tablets. Chugai is also engaged in global phase I studies for pancreatic cancer.

Review of 2020 Performance

Sales of Tecentriq increased ¥16.9 billion, or 82.0 percent, year on year to ¥37.5 billion, substantially higher than expected. This result was driven partly by expansion of the product's use in prescription for unresectable, advanced, or recurrent NSCLC, extensive SCLC, PD-L1-positive, inoperable, or recurrent TNBC, and unresectable HCC.

Avastin (RG435)

Anti-VEGF humanized monoclonal antibody
(Generic name: bevacizumab)
Launch in Japan: June 2007

Avastin is a humanized monoclonal antibody targeting vascular endothelial growth factor (VEGF). It is the first therapeutic agent in the world that inhibits angiogenesis, which is the growth of the network of blood vessels that supply nutrients and oxygen to the cancer. Unlike conventional anticancer agents that act directly on cancer cells, Avastin acts on the cancer microenvironment. In Japan, Avastin was launched in 2007 for the treatment of unresectable, advanced, or recurrent colorectal cancer. In 2009, Chugai obtained approval for a new dosage and administration for colorectal cancer and the additional indication of unresectable, advanced, or recurrent NSCLC, followed in 2011 by inoperable or recurrent breast cancer. Chugai also obtained approval for the additional indications of malignant glioma and ovarian cancer in 2013, and advanced or recurrent cervical cancer in May 2016. In September 2020, Chugai obtained approval for the additional indication of unresectable HCC in combination with Tecentriq.

Review of 2020 Performance

Sales of Avastin decreased ¥14.1 billion, or 14.7 percent, year on year to ¥81.5 billion. Performance was impacted by a 15.7 percent drug price reduction in April due to the loss of premium pricing status and by the launch of biosimilars in some of its indications. Development is progressing in global phase III studies of combination therapy with Tecentriq in HCC (adjuvant therapy) and SCLC.

Perjeta (RG1273)

HER2 dimerization inhibitory humanized monoclonal antibody
(Generic name: pertuzumab)
Launch in Japan: September 2013

Perjeta is a humanized monoclonal antibody and is the first molecular targeted therapy that inhibits the dimerization of HER2. The combination of Perjeta and Herceptin, which also targets HER2, provides a more comprehensive blockade of HER signaling pathways associated with the proliferation of tumor cells. Chugai launched Perjeta for the indication of HER2-positive inoperable or recurrent breast cancer in September 2013, after obtaining approval in June 2013. In 2018, Perjeta obtained approval for the additional indication of neoadjuvant and adjuvant therapy for HER2-positive breast cancer.

Review of 2020 Performance

Sales of Perjeta increased ¥2.8 billion, or 9.1 percent, year on year to ¥33.5 billion. Although repricing based on market expansion led to a 15 percent price reduction in April 2020, the combination of Perjeta and Herceptin with a chemotherapy agent

as neoadjuvant and adjuvant therapy for HER2-positive early breast cancer, an additional indication approved in October 2018, achieved good market penetration. Chugai is also engaged in a global phase III study of RG6264 (subcutaneous injection), a fixed-dose combination of Herceptin and Perjeta for HER2-positive breast cancer.

Alecensa (AF802/RG7853) (In-house development)

ALK inhibitor
(Generic name: alectinib)
Launch in Japan: September 2014

Alecensa, an oral, small molecule targeted molecular therapy created by Chugai, inhibits the activity of the tyrosine kinase anaplastic lymphoma kinase (ALK) with *EML4-ALK* fusion gene expressed in about 2 to 5 percent of NSCLC. It was designated as an orphan drug in Japan in September 2013 for the treatment of *ALK* fusion gene-positive unresectable, advanced, or recurrent NSCLC. In October 2013, Chugai filed an application for approval. Following approval in July 2014, Alecensa was launched first in Japan in September 2014. In addition to being the first product from Chugai research to be granted breakthrough therapy designation by the U.S. FDA as a second-line treatment in 2013, Alecensa received the same designation as a first-line treatment in 2016, and it is contributing to the treatment of patients around the world. Outside Japan, after obtaining approval in the United States in December 2015 and in Europe in February 2017 for the indication of ALK-positive metastatic (advanced) NSCLC in patients whose disease has progressed or who are intolerant to crizotinib, Alecensa obtained approval as a first-line treatment in the United States in November 2017 and Europe in December 2017.

In February 2020, Alecensa obtained approval for the additional indication of recurrent or refractory *ALK* fusion gene-positive anaplastic large cell lymphoma (ALK-positive ALCL).

Review of 2020 Performance

Market penetration proceeded further with the announcement of positive results that led to the early stopping for benefit of a study comparing the efficacy and safety of Alecensa and a competing product on patients in Japan (J-ALEX study). Sales of Alecensa in Japan increased ¥3.0 billion, or 13.0 percent, year on year to ¥26.0 billion, due to a high rate of continuation of treatment. Overseas sales of Alecensa (including exports to Roche) decreased ¥1.0 billion, or 2.2 percent, year on year to ¥44.3 billion due to a reduction in the export price. In development, a global phase III study for adjuvant therapy of ALK-positive NSCLC is under way.

Herceptin

Anti-HER2 humanized monoclonal antibody
(Generic name: trastuzumab)
Launch in Japan: June 2001

Herceptin is a humanized monoclonal antibody that targets human epidermal growth factor receptor type 2 (HER2),[8] which contributes to tumor cell growth. The earliest PHC-based anticancer agent, Herceptin has built a solid reputation as an essential treatment for HER2-positive breast cancer since its launch in 2001.

Overexpression of HER2 is found in about 15 to 20 percent of breast cancers. Such cancer is diagnosed as HER2-positive. HER2-positive breast cancer progresses rapidly, and has been associated with a poor prognosis. However, treatment outcomes have improved significantly with the emergence of Herceptin and other medicines that target HER2. In 2011, Herceptin obtained approval for the additional indication of advanced or recurrent gastric cancer overexpressing HER2, not amenable to curative resection, bringing PHC to the field of gastric cancer.

8. A diagnostic test can determine if a patient's breast or gastric cancer cells have overexpression of a protein called HER2. Herceptin, Perjeta, and Kadcyla target HER2 and are administered only to patients whose tumors are identified as HER2-positive.

Review of 2020 Performance

Sales of Herceptin decreased ¥10.8 billion, or 40.4 percent, year on year to ¥15.9 billion due to the impact of biosimilars. It is used in combination with Perjeta for HER2-positive advanced or recurrent breast cancer. Since October 2018, it has been widely used in combination with Perjeta, after Perjeta became available as a neoadjuvant and adjuvant therapy in HER2-positive breast cancer. For gastric cancer, although Herceptin maintained its established position in first-line treatment, sales decreased slightly due to competition in second-line treatment.

Kadcyla (RG3502)

Anti-HER2 antibody-tubulin polymerization inhibitor conjugate
(Generic name: trastuzumab emtansine)
Launch in Japan: April 2014

Kadcyla is an antibody-drug conjugate of the anti-HER2 humanized monoclonal antibody trastuzumab (product name: Herceptin) and the potent chemotherapeutic agent DM1, joined together with a stable linker. Chugai filed an application for approval for HER2- positive inoperable or recurrent breast cancer in January 2013, obtained approval in September 2013 after priority review, and launched the product in April 2014.

Review of 2020 Performance

Sales of Kadcyla increased ¥1.2 billion, or 13.3 percent, year on year to ¥10.2 billion. Kadcyla is widely used as a second-line treatment for HER2-positive advanced or recurrent breast cancer that has progressed following first-line treatment with Herceptin and Perjeta plus chemotherapy. In August 2020, it was approved for adjuvant therapy of HER2-positive breast cancer.

Rituxan

Anti-CD20 monoclonal antibody
(Generic name: rituximab)
Launch in Japan: September 2001

Rituxan is a monoclonal antibody targeting the CD20 antigen found on the surface of lymphocytes. As a standard therapy for CD20-positive, B-cell non-Hodgkin's lymphoma (hematological cancer), it has substantially improved clinical outcomes in combination with chemotherapy or in monotherapy. In Japan, Rituxan is marketed jointly by Chugai and Zenyaku Kogyo Co., Ltd. In recent years, the usefulness of Rituxan has been recognized in treating CD20-positive, B-cell lymphoma in immunosuppressed patients, granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA), refractory nephrotic syndrome with frequent relapses or steroid dependence, suppression of antibody-mediated rejection in ABO-incompatible kidney and liver transplantation, and idiopathic thrombocytopenic purpura (ITP). It has also become a valuable treatment option for patients with autoimmune diseases and other conditions. Rituxan obtained approval for the additional indications of CD20-positive chronic lymphocytic leukemia (CLL) in 2019 and acquired thrombotic thrombocytopenic purpura in February 2020.

Review of 2020 Performance

Sales of Rituxan decreased ¥4.7 billion, or 39.5 percent, year on year to ¥7.2 billion. The decrease was due to more intense competition resulting from the launch of biosimilars.

Gazyva (GA101)

Glycoengineered type II anti-CD20 monoclonal antibody
(Generic name: obinutuzumab)
Launch in Japan: August 2018

Gazyva is a glycoengineered type II monoclonal antibody in-licensed from Roche that, like Rituxan, targets CD20. A study that directly compared its efficacy and safety with Rituxan, currently the most widely used monoclonal antibody, in patients in Japan and overseas (the GALLIUM study) was terminated early for benefit after positive results were reported. Gazyva obtained approval for the indication of CD20-positive follicular lymphoma in July 2018, and was launched in August 2018. In November 2012, Chugai entered into an agreement with Nippon Shinyaku Co., Ltd. to co-develop and co-market this agent in Japan.

Review of 2020 Performance

Sales of Gazyva increased ¥1.0 billion, or 27.8 percent, year on year to ¥4.6 billion, reflecting steady sales expansion on market penetration for both initial and recurrent disease.

Xeloda

Antimetabolite, 5-FU derivative
(Generic name: capecitabine)
Launch in Japan: June 2003

Xeloda is a 5-fluorouracil (5-FU) anticancer agent developed at the research laboratories of the former Nippon Roche. Orally administered Xeloda is absorbed by the body, then gradually metabolized by certain highly active enzymes in liver and tumor tissue, and is eventually converted into active 5-FU within tumor tissue. Xeloda has obtained approval for the treatment of inoperable or recurrent breast cancer, colorectal cancer, and gastric cancer.

Review of 2020 Performance

Sales of Xeloda decreased ¥4.4 billion, or 55.0 percent, year on year to ¥3.6 billion. The sharp decline in sales resulted partly from the loss of premium pricing status, which led to a drug price cut of 27.4 percent in April 2020. Additionally, the uptake of a generic launched in January 2019 was greater than expected. However, in adjuvant therapy performed to inhibit recurrence after surgery for colon cancer, Xeloda is the most prescribed drug because of its recommendation in the guidelines for the treatment of colorectal cancer and the results of a large-scale global study.

Rozlytrek (RG6268)

ROS1/TRK inhibitor
(Generic name: entrectinib)
Launch in Japan: September 2019

Rozlytrek, in-licensed from Roche, is an orally bioavailable central nervous system (CNS)-active tyrosine kinase inhibitor that potently and selectively inhibits ROS1 and the TRK family, and also acts on brain metastases. Targeting *NTRK* fusion gene-positive solid tumors, RG6268 has been granted breakthrough therapy designation in the United States, PRIorityMEdicines (PRIME) designation in the EU, and Sakigake designation in Japan. Chugai obtained the world's first approval for the treatment of *NTRK* fusion gene-positive advanced/recurrent solid tumors in Japan in June 2019, and launched the product in September 2019. Rozlytrek is a tumor-agnostic therapy that uses a next-generation sequencing-based companion diagnostic to identify target genomic alterations that drive cancer, thus embodying the advanced PHC that Chugai is promoting. F1CDx obtained approval in June 2019 as a companion diagnostic for Rozlytrek. Chugai obtained approval for *ROS1* unresectable, advanced, or recurrent fusion gene-positive NSCLC in February 2020.

Review of 2020 Performance

Sales of Rozlytrek totaled ¥0.4 billion. Although market penetration was delayed by the spread of COVID-19 infection, sales expanded steadily following the start of its administration for *ROS1* fusion gene-positive unresectable, advanced, or recurrent NSCLC.

Neutrogin (In-house development)

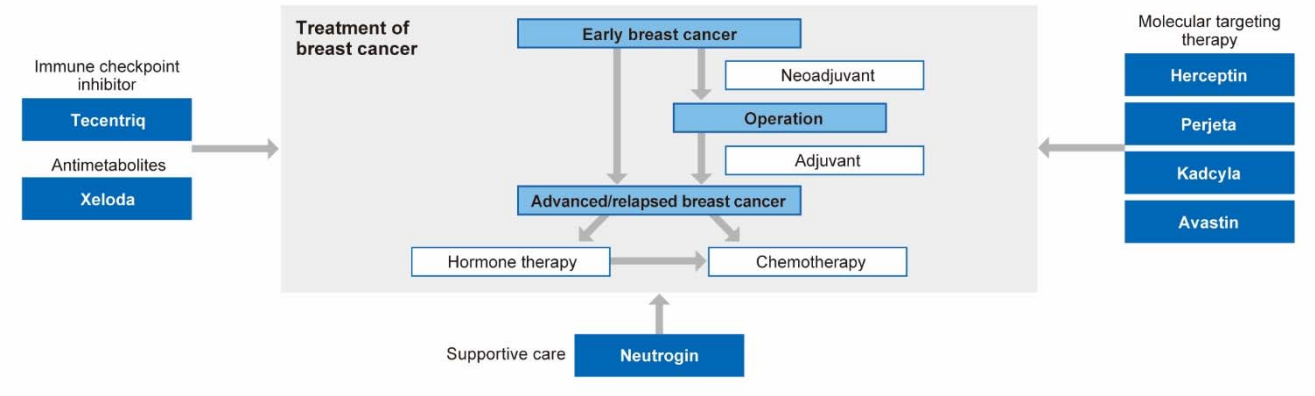
Recombinant human granulocyte colony-stimulating factor (G-CSF)
(Generic name: lenograstim;
overseas product name: Granocyte)
Launch in Japan: December 1991

Neutrogin is a recombinant human granulocyte colony-stimulating factor (G-CSF) created by Chugai. One common side effect of anticancer drugs is neutropenia, a decrease in the white blood cell count that heightens the risk of developing serious infections. Neutrogin stimulates the differentiation and growth of neutrophils, enabling the safer use of chemotherapy, thus helping to improve treatment outcomes. Neutrogin is also essential in hematopoietic stem cell transplantation, which is performed for illnesses that affect production of normal blood cells, such as leukemia.

Review of 2020 Performance

Overseas sales of Neutrogin decreased ¥0.9 billion, or 9.1 percent, year on year to ¥9.0 billion due to intensified competition.

Extensive Contribution to Cancer Treatment (Breast Cancer)



RG7596 Development project

Anti-CD79b antibody-drug conjugate
(Generic name: polatuzumab vedotin)

RG7596 is an antibody-drug conjugate of an anti-CD79b monoclonal antibody and the microtubule inhibitor MMAE, joined together with a linker. In-licensed from Roche, the conjugate is designed to deliver MMAE directly into B cells via CD79b, which is expressed on B cells, so that the inhibitor can act. To demonstrate a cytostatic effect on tumor cells, a global phase III study for previously untreated diffuse large B-cell lymphoma (DLBCL) started in November 2017. In addition, a phase II clinical study for relapsed or refractory DLBCL started in Japan in October 2018 and achieved a primary endpoint in February 2020.

In November 2019, RG7596 received orphan drug designation for the treatment of DLBCL, and in June 2020 Chugai filed an approval application for the treatment of recurrent or intractable DLBCL.

RG7440 Development project

AKT inhibitor
(Generic name: ipatasertib)

RG7440 is an AKT inhibitor in-licensed from Roche. Global phase III studies started in June 2017 for prostate cancer and in January 2018 for breast cancer.

Of the various breast cancer studies, global phase III studies for triple-negative breast cancer and hormone-positive breast cancer, begun in 2018, failed to meet the primary endpoint, while a global phase III study of combination therapy with atezolizumab for triple-negative breast cancer, initiated in 2020, was discontinued before completion. In progress at present is a global phase III study in hormone-positive breast cancer launched in 2019.

RG6058 Development project

Anti-TIGIT fully humanized monoclonal antibody
(Generic name: tiragolumab)

RG6058 is an anti-TIGIT monoclonal antibody in-licensed from Roche. TIGIT is an immune checkpoint expressed on the surface of NK cells and T cells that binds to poliovirus receptors (PVR) expressed on tumor cell surfaces. This binding is thought to allow the cancer cells to evade attack by immune cells. RG6058 restores and maintains the immune response of NK cells and T cells by blocking the binding of TIGIT to PVR, and is thus expected to demonstrate efficacy against cancer cells. In November 2019, Chugai began a phase I clinical trial of RG6058 for solid tumors in Japan. Additionally, Chugai launched a series of global phase III studies: for SCLC in February 2020, for NSCLC in March, for NSCLC (Stage III) in August, and for esophageal cancer in September.

RG6171 Development project

SERD
(Generic name: giredestrant)

RG6171 is a selective estrogen receptor degrader (SERD) in-licensed from Roche. In October 2020, Chugai initiated a global phase III study for the treatment of breast cancer.

OBP-301 Development project

Oncolytic type 5 adenovirus
(Generic name: undetermined)

OBP-301 is a type 5 adenovirus genetically engineered to specifically replicate within and thereby destroy cancer cells. The type 5 adenovirus is also present in the natural world, where it causes cold-like symptoms. It is expected to display powerful antitumor activity by specifically proliferating within cancer cells to dissolve them and also to demonstrate clinical safety due to its very low ability to proliferate within normal cells. In April 2019, Chugai acquired exclusive licensing rights in Japan and Taiwan in an agreement with Oncolys BioPharma Inc. In March 2020, Chugai began a phase II clinical study of combination with radiotherapy for esophageal cancer, followed in January 2021 by the start of a phase I clinical study of combination therapy with Tecentriq and Avastin for hepatocellular carcinoma. In April 2019, OBP-301 received Sakigake designation from the MHLW.

GC33 (RG7686) Development project (In-house development)

Anti-glypican-3 humanized monoclonal antibody
(Generic name: codrituzumab)

GC33, a humanized monoclonal antibody created by Chugai, targets glypican-3 (GPC3), which is specifically expressed in hepatocellular carcinoma. GC33 did not meet the primary endpoint in a global phase II monotherapy study started in March 2012. A phase I clinical study for hepatocellular carcinoma in combination with Tecentriq has been under way since August 2016, and the study results were presented at the European Society of Medical Oncology (ESMO) 2018 Congress.

ERY974 Development project (In-house development)
Anti-glypican-3/CD3 bispecific antibody

ERY974 is the first T-cell redirecting antibody (TRAB) developed by Chugai. TRAB is a bispecific antibody that creates a short bridge between CD3 on T cells and tumor antigen on tumor cells to activate T cells in a tumor antigen-dependent manner, and is expected to demonstrate strong cytotoxicity against tumor cells.

GPC3, a tumor antigen targeted by ERY974, is reported to be expressed in multiple types of tumor cells including hepatocellular carcinoma, lung cancer, gastric cancer, and esophageal cancer. A phase I clinical trial is under way.

RG7421 Development project
MEK inhibitor
(Generic name: cobimetinib fumarate)

RG7421 is an MEK inhibitor in-licensed from Roche. Chugai started a phase I clinical study for the treatment of solid tumors in Japan in July 2017.

RG7802 Development project
Anti-CEA/CD3 bispecific antibody
(Generic name: cibisatamab)

RG7802, a bispecific antibody in-licensed from Roche, is expected to activate T cells and attack tumor cells by cross-linking CD3 on T-cells to carcinoembryonic antigen (CEA) on tumor cells. Chugai started a phase I clinical study of RG7802 for the treatment of solid tumors in Japan in January 2018.

RG7828 Development project
Anti-CD20/CD3 bispecific antibody
(Generic name: mosunetuzumab)

RG7828 is a bispecific antibody in-licensed from Roche. It is expected to activate T cells and attack tumor cells by cross-linking CD3 on T cells to CD20 on B cells. Chugai started a phase I clinical study for the treatment of hematologic tumors in Japan in March 2018.

RG6026 Development project
Anti-CD20/CD3 bispecific antibody
(Generic name: glofitamab)

RG6026 is a bispecific antibody in-licensed from Roche. By cross-linking CD3 on T cells with CD20 on B cells, it is expected to cause T-cell activation and proliferation and attack on the target B cells through cytokine release, resulting in antitumor effect. Chugai started a phase I clinical study for the treatment of hematologic tumors in Japan in March 2020.

AMY109 Development project (In-house development)

AMY109 is the third therapeutic antibody to apply the recycling antibody engineering technology created by Chugai. In March 2020, Chugai began a phase I clinical study for solid tumors.

STA551 Development project (In-house development)
Anti-CD137 agonist switch antibody

STA551, a “switch antibody,” is the first application of switch antibody technology, which was developed by Chugai. Switch antibodies bind to the target antigen only where there is a high concentration of a certain “switch” molecule, which is concentrated specifically at the diseased site. STA551 binds to CD137 and activates T cells in the presence of the switch molecule ATP, but not in the absence of ATP. It therefore promises to act selectively on tumors. Chugai started a phase I clinical study for the treatment of solid tumors in March 2020.

SPYK04 Development project (In-house development)

SPYK04 is a small molecule drug developed in-house by Chugai. In September 2020, Chugai began a phase I clinical study for solid tumors.

RG6194 Development project
Anti-HER2/CD3 bispecific antibody
(Generic name: undetermined)

RG6194, an anti-HER2/CD3 bispecific antibody in-licensed from Roche, is expected to act against HER2-expressing cancer cells by inducing and activating T cells. In November 2020, Chugai began participation in a global phase I study for the treatment of solid tumors.

Bone and Joint Diseases / Autoimmune Diseases

Osteoporosis

Osteoporosis is a disease in which the bones become weak due to advanced age or other factors, increasing the risk of fractures. Osteoporosis patients may incur fractures through normal daily activities. Among these, compression fractures of the spine and femoral neck fractures can decrease QoL by leaving patients bedridden and can also increase mortality risk. About 13 million people in Japan suffer from osteoporosis. However, the treatment rate stands at around only 20 percent of the estimated number of sufferers because there are usually no symptoms until a fracture occurs. The availability of superior new drugs that have higher efficacy, safety and convenience has brought promise for improvement in the QoL of patients.

Treatment Methods

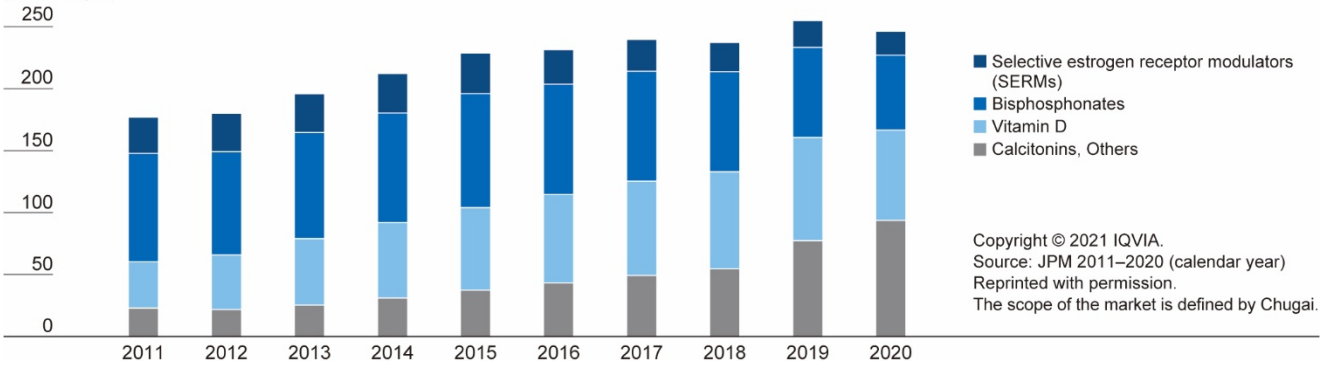
Osteoporosis drug therapies include active vitamin D_3 derivatives, which improve bone metabolism, bisphosphonates, which are bone resorption inhibitors, an anti-RANKL antibody, selective estrogen receptor modulators (SERMs), human parathyroid hormone (PTH), which is a bone formation agent, anti-sclerostin antibodies, and calcitonins.

Regulatory Trends

National prevention and treatment guidelines for osteoporosis were revised in October 2006. Subsequently, advances have been made in basic and clinical research into osteoporosis; evaluation of fracture risk and criteria for the initiation of drug treatment have been reviewed; and osteoporosis caused by lifestyle-related diseases has been addressed. In the interim, Edirol and other medicines have been approved for insurance coverage. Revisions issued in December 2011 added preventive and diagnostic items in light of the importance of early prevention to broaden the overall scope of osteoporosis treatment. Since then, the 2012 revised Diagnostic Criteria for Primary Osteoporosis and Management and Treatment Guidelines of Steroid-induced Osteoporosis have been adopted. Bonviva IV Injection and other medicines have been launched and covered by insurance, and revised guidelines were issued in July 2015.

Recently, an osteoporosis liaison service (OLS) initiated by the Japan Osteoporosis Society was introduced for the purpose of preventing osteoporosis and inhibiting bone fractures by coordinating the efforts of various healthcare professionals, including doctors, nurses, pharmacists, and physical therapists. Medical staff involved in liaison and possessing extensive knowledge related to osteoporosis are called osteoporosis managers. This education program has been ongoing since 2012, and approximately 3,600 osteoporosis managers were active as of April 2020.

Osteoporosis Market in Japan



Edirol (In-house development)

Active vitamin D_3 derivative
(Generic name: eldecalcitol)
Launch in Japan: April 2011

Edirol, a vitamin D_3 preparation born out of Chugai's many years of research in vitamin D, is an agent that improves bone metabolism in addition to calcium metabolism. Chugai started sales of Edirol in April 2011 as the successor drug to Alfarol for the indication of osteoporosis. Under an agreement signed in May 2008, Edirol was co-developed and co-marketed with Taisho Pharmaceutical Co., Ltd. Clinical trials have confirmed that Edirol has a similar safety profile to alfacalcidol with a statistically significant greater effect in preventing fractures. In the 2015 osteoporosis prevention and treatment guidelines, Edirol received a Grade A recommendation, the only one for an active vitamin D_3 derivative, for its effectiveness in increasing bone density and preventing vertebral fractures. The marketing alliance with Taisho Pharmaceutical terminated on April 10, 2021.

Review of 2020 Performance

Sales of Edirol decreased ¥8.9 billion, or 24.3 percent, year on year to ¥27.8 billion. Performance was impacted by the temporary reduction in medical consultations caused by the COVID-19 pandemic and by intensified competition due to the launch of generics.

In December 2020, Edirol received approval for the treatment of osteoporosis in China. Chugai is promoting its appropriate use by alerting to hypercalcemia as an adverse reaction.

Bonviva

Bisphosphonate anti-resorptive agent
(Generic name: ibandronate)
Launch in Japan: August 2013

Bonviva is a bisphosphonate in-licensed from Roche. Bonviva IV Injection was launched in August 2013. Under an agreement signed in September 2006, Bonviva is being co-developed and co-marketed with Taisho Pharmaceutical. Bonviva IV Injection can be given as a rapid intravenous injection once a month, and

thus may significantly reduce the burden on patients. It is also expected to benefit patients who have difficulty taking oral formulations or who tend to forget to take their medication. In addition, Bonviva Tablet, a once-monthly oral formulation, demonstrated non-inferiority to Bonviva IV Injection in a phase III clinical trial, and Chugai began sales in April 2016. By enabling drug selection according to patient lifestyle, monthly Bonviva IV Injection and Bonviva Tablet are expected to help improve patient adherence, convenience for healthcare providers, and the rate of continuation of treatment.

Review of 2020 Performance

Sales of Bonviva decreased ¥0.8 billion, or 8.2 percent, year on year to ¥8.9 billion, due partly to the reduction in medical consultations caused by the COVID-19 pandemic. The intravenous injection and oral formulations have the same high level of efficacy, and the ability to select the formulation according to the patient's condition has helped to differentiate Bonviva from other bisphosphonates.

Rheumatoid Arthritis/Osteoarthritis

Rheumatoid arthritis (RA) is a systemic disease characterized by painful inflammation and deformation of joints leading to dysfunction. Without appropriate treatment, the patient's condition deteriorates over time. There are currently an estimated 700,000 to 800,000 patients in Japan suffering from RA, of whom some 330,000 are currently receiving drug treatment. The aging of the patient population has also become a problem in recent years. On the other hand, there are about 8,000 patients in Japan with juvenile idiopathic arthritis (JIA), a form of RA suffered by children under 16 years of age.

Treatment Methods and Market Conditions

In drug therapy for RA, the introduction of biologics has made high remission rates a realistic treatment goal. Research in recent years suggests that the administration of biologics at the early onset stage is effective in inhibiting bone and joint damage. The global market for these agents is forecast to reach U.S.$56.7 billion[9] by 2024. The continuing change in the market is illustrated by the launch in the United States and Japan in 2013 of biological DMARDs, a new class of oral drugs, and the launch of biosimilars in Japan in 2014 following their earlier release in Europe. Actemra and other drugs are greatly expanding the therapeutic options for RA.

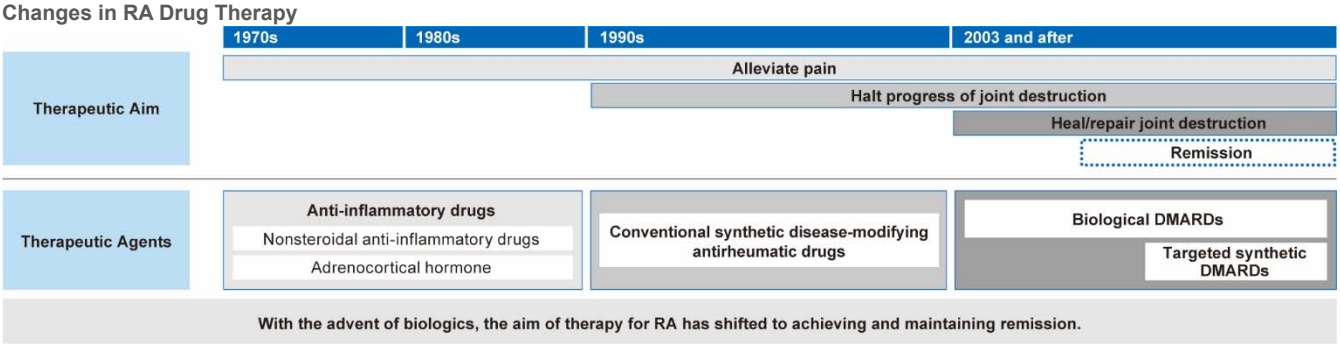
Systemic juvenile idiopathic arthritis (sJIA) accounts for 30 to 40 percent of all JIA cases, but steroids, the main treatment for sJIA, can cause growth impairment and other adverse reactions. Consequently, Actemra, approved for the additional indication of sJIA in April 2008, has provided a significant advance in therapy.

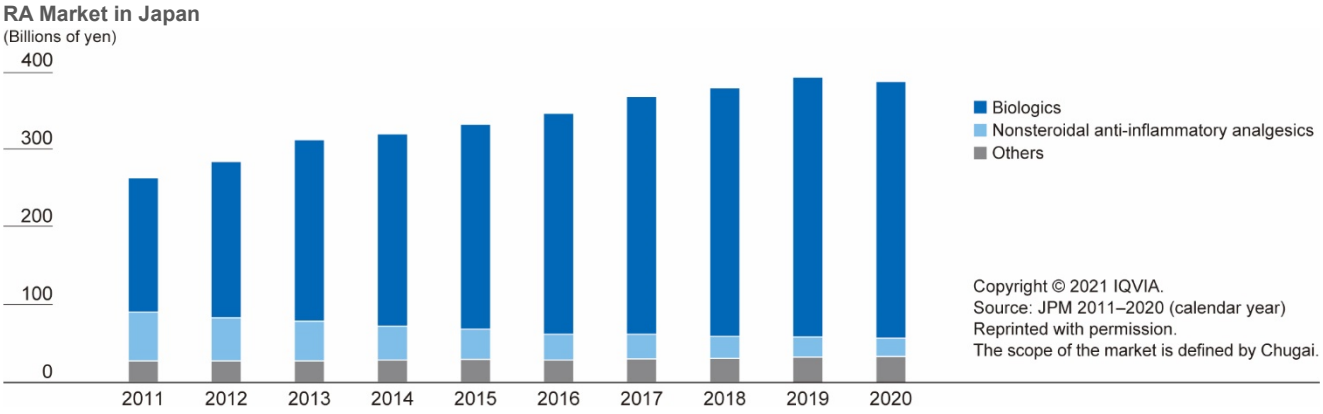
9. Source: Evaluate Pharma

Regulatory Trends

In November 2018, the MHLW released an update of the Report of the Rheumatism and Allergy Countermeasure Committee, which was previously issued in 2005 and 2011. To maximize long-term QoL of RA patients through appropriate treatment that controls disease activity, and to provide comprehensive support in daily life at workplaces and schools, and for life events such as pregnancy and childbirth, the report calls for (1) enhancement of medical service systems, (2) improvement of the patient environment, including consultation opportunities and access to information, and (3) promotion of research and development and other activities. In Europe, revised treatment recommendations in 2013 added Actemra and Abatacept to the biologic drugs recommended in first-line therapy, which were previously limited to anti-TNF agents. In 2015, a proposed update of clinical practice guidelines was announced at the American College of Rheumatology, with biologics including Actemra added as first-line therapy along with anti-TNF agents. Moreover, the updated European League Against Rheumatism (EULAR) recommendations that were announced in June 2016 state the superiority of interleukin-6 (IL-6) inhibitor therapy over other biologics in cases where MTX and other therapies cannot be used. In Japan, April 2021 saw the release of the Guidelines for the Management of Rheumatoid Arthritis, Japan College of Rheumatology 2020, which recommend regimens to reflect the advances in drug therapies of recent years and other factors such as Japan's falling birth rate and aging population.

Changes in RA Drug Therapy





Castleman's Disease

Castleman's disease is a lymphoproliferative disease characterized by symptoms such as systemic lymphadenopathy, fever, and general fatigue, as well as various abnormal laboratory test values including anemia, hypergammaglobulinemia, and hypoalbuminemia. It has been confirmed that these manifestations result from the excessive production of IL-6, one of the cytokines that causes inflammation. Castleman's disease is very rare, affecting approximately 1,500 people in Japan.

Large-Vessel Vasculitis

Large-vessel vasculitis belongs to a group of autoimmune diseases called vasculitis syndromes. It refers to vasculitis in the aorta and the major aortic branches to the limbs and head and neck, and includes Takayasu arteritis and giant cell arteritis (temporal arteritis).

Takayasu arteritis leads to inflammation of the aortic arch and its branch vessels. It affects women more than men, at a ratio of 9:1, and age of onset is between 20 and 50 years. It occurs most commonly in Asia, including Japan, and the Middle East. Initial symptoms are reduced head and cerebral blood flow related conditions, primarily dizziness, lightheadedness and headaches, as well as neck pain, chest pain, and vascular pain along the limb arteries.

Giant cell arteritis is a granulomatous vasculitis occurring primarily in the aorta and aortic branches, mainly the temporal arteries. It also affects women more than men, at a ratio of 1.6:1, and the age of onset is 55 years or older. It occurs most commonly in Western countries and is rare in Japan. Common initial symptoms include headache, systemic conditions such as fever, and loss of vision.

Adult Still's Disease

Adult Still's disease is an autoimmune disease that typically presents with a high spiking fever, aching joints, and a light-pink rash. Leukocytosis, increased C-reactive protein (CRP) levels, and elevated erythrocyte sedimentation rates are frequently observed in laboratory findings. Inflammation suppression with corticosteroids is the standard therapy, but until recently, no drug covered by the NHI was available for steroid-resistant patients.

Interstitial Lung Disease Associated with SSc

Systemic sclerosis (SSc), also known as scleroderma, is a progressive and potentially life-threatening disease. It is estimated to affect approximately 138,000 people worldwide, but with large regional differences in incidence. In SSc, abnormalities in the immune system cause fibrosis of the skin and various other organs. Of the organ damage accompanying SSc, interstitial lung disease (ILD) is the most frequently occurring and is the main cause of death related to SSc. ILD is a broad term covering more than 200 widely varying rare lung syndromes. ILD is characterized by coughing, shortness of breath, and other common symptoms, but the causes, treatment, and prognosis differ widely.

Actemra (MRA/RG1569) (In-house development)

Humanized anti-human IL-6 receptor monoclonal antibody
(Generic name: tocilizumab)
Launch in Japan: June 2005

Actemra, created by Chugai and the first therapeutic antibody originating in Japan, blocks the activity of IL-6, a type of cytokine. It was launched in Japan in June 2005 as a treatment for Castleman's disease. In April 2008, Chugai obtained approval in Japan for the additional indications of RA, polyarticular juvenile idiopathic arthritis (pJIA), and sJIA. In May 2013, Chugai launched a new subcutaneous formulation in addition to the existing intravenous infusion formulation with the aim of improving convenience. This subcutaneous formulation includes the first auto-injector in the Japanese RA market.

Actemra is marketed globally through Roche. In Europe, where the medicine is known as RoActemra, sales for the treatment of RA started in 2009. Chugai's marketing subsidiary co-promotes RoActemra with Roche in the United Kingdom, France, and Germany. In the United States, Actemra obtained approval in January 2010 for the treatment of adult patients with moderate to severe active RA who have had an inadequate response to one or more anti-TNF agents, and obtained approval in October 2012 as a first-line biologic treatment. In Taiwan and South Korea, where Chugai has marketing rights, Actemra obtained approval in July 2011 and April 2012, respectively. Following its launch in Japan, the subcutaneous formulation obtained approval in the United States in October 2013 and in Europe in April 2014, and has been launched in both markets. RoActemra was also approved for early RA in Europe in September 2014.

Furthermore, Actemra obtained approval for the additional indication of treatment of sJIA in the United States in April 2011 and in Europe in August 2011. Actemra also received breakthrough therapy designation from the U.S. FDA in 2016 for giant cell arteritis. In Japan, it became possible in June 2017 to reduce the dose interval of Actemra from two weeks to one week in patients with an inadequate response to use of the subcutaneous formulation for RA. Actemra obtained approval in Japan for the additional indications of Takayasu arteritis and giant cell arteritis in August 2017, and in the United States, in

November 2018 an autoinjector obtained approval as an additional formulation for the treatment of RA, giant cell arteritis, sJIA, and pJIA. Actemra also obtained approval in the United States in August 2017 and in Europe in August 2018 for the additional indication of chimeric antigen receptor (CAR) T-cell-induced cytokine release syndrome, and in Japan in March 2019 for the additional indication of cytokine release syndrome induced by tumor-specific T-cell infusion therapy. In May 2019, Chugai obtained approval for the additional indication of adult Still's disease where existing treatments provide insufficient efficacy.

In February 2020, Actemra obtained approval in the United States for the additional indication of interstitial lung disease associated with SSc.

Review of 2020 Performance

Sales of Actemra in Japan decreased ¥2.5 billion, or just 6.0 percent, year on year to ¥39.3 billion. This was despite an 18.5 percent price reduction due to repricing based on market expansion. Sales levels were maintained by the growth in new prescriptions for RA and by the strong performance of the subcutaneous formulation, which accounted for more than 60 percent of the total, following its approval for additional dosage and administration options with shorter dose interval and for the additional indications of Takayasu arteritis and giant cell arteritis.

Overseas sales of Actemra (including exports to Roche) increased ¥46.1 billion, or 52.2 percent, year on year to ¥134.4 billion on increased demand due to the COVID-19 pandemic. Roche's global sales also expanded by a considerable 30 percent.

RG7880 Development project
Human IL-22 fusion protein
(Generic name: efmarodocokin alfa)
RG7880 is a human IL-22 fusion protein in-licensed from Roche. It is expected to demonstrate efficacy in treating inflammatory bowel disease by directly promoting the regenerative and protective functions of IL-22 in epithelial tissue. A phase I clinical trial began in July 2019.

Renal Diseases

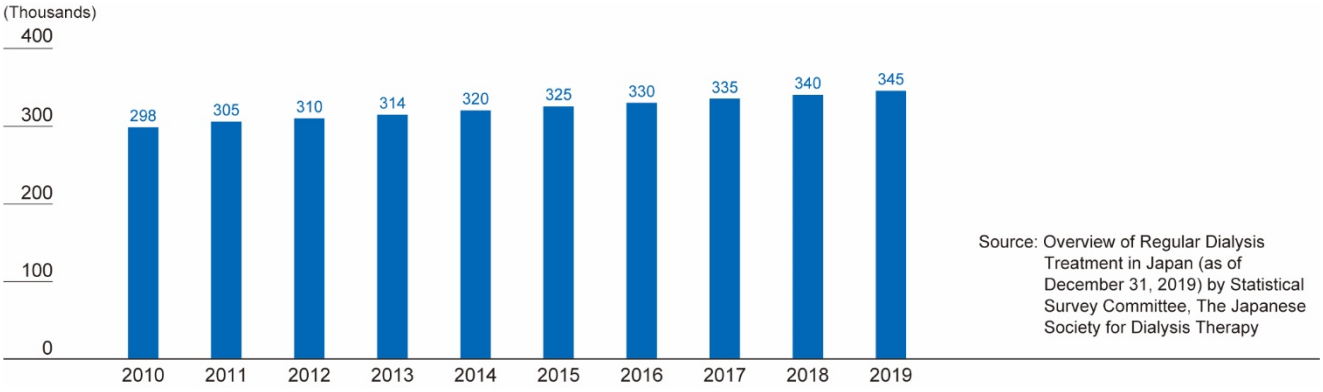
Renal Anemia

Complications of Renal Dysfunction

In dialysis patients and end-stage chronic kidney disease (CKD) patients, a key issue is treating the various complications of advanced renal dysfunction, such as renal anemia, secondary hyperparathyroidism, and abnormal calcium and phosphorus metabolism. Of these complications, renal anemia is one of the most frequent, occurring not only in renal disease patients undergoing dialysis but also in pre-dialysis CKD patients. Renal anemia is associated with reduced QoL, and is also a factor in the progress of organ damage, including decreased cardiac function and renal function.

The importance of treatment and the appropriate management of renal anemia and chronic kidney disease - mineral and bone disorder (CKD-MBD) were indicated in the Guidelines for Renal Anemia in Chronic Kidney Disease (2015) and the Clinical Practice Guidelines for the Management of CKD-MBD (2012) issued by the Japanese Society for Dialysis Therapy and in the Evidence-based Practice Guidelines for the Treatment of CKD (2018) issued by the Japanese Society of Nephrology.

Number of Dialysis Patients in Japan



Source: Overview of Regular Dialysis Treatment in Japan (as of December 31, 2019) by Statistical Survey Committee, The Japanese Society for Dialysis Therapy

ESA
Erythropoietin (EPO) is a hemopoietic factor produced mainly in the kidneys. It stimulates erythrocyte production by binding to EPO receptors on erythroid progenitor cells in bone marrow. An erythropoiesis-stimulating agent (ESA) is effective in treating renal anemia caused primarily by the decline in EPO production due to CKD, and is thought to help improve QoL. ESAs are currently used by approximately 80 percent of dialysis patients as well as by some predialysis CKD patients with renal anemia. ESAs are thus an essential drug for the treatment of renal anemia.

Flat-Sum Reimbursement System for ESAs
Since the 2006 revisions of medical fees, ESAs have been included in medical fee points for hemodialysis (artificial kidney). The integrated fee points are reviewed with each revision of medical fees, and were reduced in 2020, which has led to intensified price competition for ESAs in the dialysis market.

Mircera
Long-acting erythropoiesis-stimulating agent
(Generic name: epoetin beta pegol)
Launch in Japan: July 2011
Mircera is a drug that raises the stability of epoetin beta in the bloodstream through pegylation. It is a new type of renal anemia treatment with the longest serum half-life among ESAs, enabling stable and sustained control of anemia. It stimulates erythropoiesis through a different interaction with the EPO receptor on burst-forming unit erythroid (BFU-E) cells in the bone marrow. Mircera was launched in Japan in July 2011 as a treatment for renal anemia. Outside Japan, Mircera obtained approval in Europe in 2007 and is currently sold in more than 100 countries, including the United States.

The serum half-life of Mircera is virtually the same for intravenous or subcutaneous administration, and the drug demonstrates efficacy in relieving the symptoms of anemia when administered at four-week intervals during the maintenance period. Consequently, it is expected to reduce the burden of hospital visits on the aging population of patients with pre-dialysis CKD and to contribute to better treatment adherence. Furthermore, as a dialysis-related treatment, Mircera is expected to reduce the burden on medical staff and improve medical safety by dramatically reducing administration frequency, and is one of the options for the treatment of renal anemia.

Review of 2020 Performance
Sales of Mircera decreased ¥4.7 billion, or 21.2 percent, year on year to ¥17.5 billion. Despite its wide use in pre-dialysis CKD patients, it was impacted by the drug price revision and competition from authorized generics and biosimilars. There was also intensified price competition in the dialysis market after a medical fee revision that reduced the integrated fee points for hemodialysis (artificial kidney).

Others

Oxarol (In-house development)
Agent for secondary hyperparathyroidism
(Generic name: maxacalcitol)
Launch in Japan: September 2000
Originated by Chugai, Oxarol is the first intravenous active vitamin D_3 derivative agent in Japan. It treats secondary hyperparathyroidism, a result of conditions such as impaired vitamin D activation associated with renal dysfunction, by acting directly on the parathyroid gland to control parathyroid hormone synthesis and secretion, and by improving bone metabolic conditions. With its short serum half-life, Oxarol shows efficacy and enables treatment in patients who previously could not be treated adequately with oral active vitamin D_3 derivatives due to the onset of hypercalcemia.

Review of 2020 Performance
Sales of Oxarol, impacted by the market penetration of generics and the drug price revision, decreased ¥0.5 billion, or 7.2 percent, year on year to ¥6.4 billion.

EOS789 Development project (In-house development)
EOS789 is an oral drug created by Chugai with a molecular weight of over 500 g/mol. A phase I clinical trial of EOS789 for hyperphosphatemia has been completed.

Neurology

NMOSD
Neuromyelitis optica spectrum disorder (NMOSD) is a neurological autoimmune disorder characterized by severe optic neuritis and transverse myelitis. The disease affects 0.3 to 4.4 in 100,000 people, and there are about 4,000 patients in Japan. It is an incurable disease that typically appears around the age of 40 years and affects women more than men, at a ratio of 9:1. Symptoms include loss of vision (in some cases progressing to blindness) and impairment of motor function and sensation. In some cases, the disease results in death. NMOSD is an orphan disease with high unmet medical need. It is believed to occur mainly when aquaporin-4 (AQP4) in the central nervous system is attacked by autoantibodies called anti-AQP4 antibodies. Formerly, the diagnostic criteria of neuromyelitis optica (NMO) accompanied by optic neuritis and myelitis, and NMOSD accompanied by either optic neuritis or myelitis were proposed. Recently, however, it was proposed to reorganize and unify the definitions of both disorders under the term NMOSD. This term is now widely used to refer to a broader spectrum of disease.

Enspryng SA237/RG6168 (In-house development)
pH-dependent binding humanized anti-IL-6 receptor monoclonal antibody
(Generic name: satralizumab)
Launch in Japan: August 2020
Enspryng is a next-generation therapeutic antibody that has shown success in blocking IL-6 receptors with a longer duration of action. Chugai created Enspryng by applying its novel antibody engineering technology (Recycling Antibody engineering technology) that enables a single antibody molecule to block the target antigen repeatedly. As a result, a prolonged

serum half-life has been demonstrated in clinical trials, which will make a lower dosing frequency possible. Because IL-6 promotes the production of the anti-AQP4 antibodies that are the primary cause of NMOSD, this drug is expected to improve (reduce recurrence of) the symptoms of these diseases as it inhibits the production of those antibodies by blocking the IL-6 signal. Chugai has licensed exclusive rights to Roche for the development and marketing of Enspryng worldwide, with the exception of Japan and Taiwan. Enspryng has received orphan drug designation in Japan, the United States, and Europe. In the United States, it received breakthrough therapy designation for the treatment of NMOSD from the U.S. FDA in December 2018 and was approved in August 2020. It has now been approved in more than 10 countries including Japan, the United States, Canada, Switzerland, and Taiwan. In Europe, the marketing application was accepted by the European Medicines Agency in 2019.

Review of 2020 Performance
Enspryng achieved sales of ¥1.3 billion. The effects of the COVID-19 pandemic delayed its uptake by hospitals following its launch in Japan on August 26. It has however been introduced for certain patients, mainly those awaiting the development of a new drug because existing therapies (oral steroids and immunosuppressants) did not prevent recurrence and those in whom the existing therapies did control recurrence but were accompanied by side effects.

Spinal Muscular Atrophy

Spinal muscular atrophy (SMA) is a lower motor neuron disease characterized by amyotrophy and progressive muscle weakness caused by degeneration of anterior horn cells in the spinal cord. The estimated number of patients in Japan is reported to be around 1,000. The disease is caused by a defect in the *SMN1* gene, and onset usually occurs in childhood. In severe cases it is fatal.

RG7916 Development project

SMN2 splicing modifier
(Generic name: risdiplam)

RG7916 is an SMN2 splicing modifier that increases generation of a protein derived from the *SMN2* gene. This protein is nearly identical to the protein made from the *SMN1* gene, which is not functional in SMA patients. RG7916 shows promise in improving neural and muscular function. Global phase II/III studies are under way, and RG7916 met its primary endpoint in the SUNFISH study in patients with Type 2 or 3 SMA and the FIREFISH study in patients with Type 1 SMA, respectively. RG7916 was granted PRIME designation by the European Medicines Agency in December 2018, and received orphan drug designation in Japan in March 2019. In October 2020, Chugai filed a regulatory application in Japan for RG7916 as the first oral therapy for SMA.

Alzheimer's Disease

Alzheimer's disease (AD) is the most common form of dementia. Pathologically, it is a progressive neurodegenerative disease that causes neuron death in the brain and brain atrophy. It leads to a general and progressive loss of memory and other cognitive functions, which can interfere with daily life. While existing AD treatments have some effect in slowing the progression of dementia symptoms, they do not slow pathological progress and are unable to stop neuron death, and a treatment for the underlying cause does not yet exist. Consequently, unmet medical needs are high, and there is strong demand for a more effective drug.

RG1450 Development project

Anti-amyloid-beta human monoclonal antibody
(Generic name: gantenerumab)

RG1450 targets aggregate amyloid beta, with a high binding affinity to plaques in particular. It is expected to reduce cognitive deterioration by removing amyloid beta in the brain. Global phase III studies of RG1450 for AD began in June and July 2018.

RG6100 Development project

Anti-tau humanized monoclonal antibody
(Generic name: semorinemab)

RG6100 binds to tau proteins found in the extracellular space of the brain, and is expected to slow the deterioration of cognitive functions in AD by halting the propagation of tau via neurons. A phase I clinical trial for AD began in April 2019.

Huntington's Disease

Huntington's disease is an intractable, progressive neurodegenerative disease that causes nerve cells in the brain to break down. Characterized mainly by involuntary movements (most commonly chorea), neuropsychiatric symptoms, and dementia, this disease profoundly affects the lives of affected individuals. As the disease progresses, people with Huntington's disease may develop walking and swallowing difficulties, personality changes and loss of cognitive functions.

The prevalence of Huntington's disease varies by ethnicity and geographical location. It is reported to affect 4 to 8 out of every 100,000 people in Western countries, but in Japan it is a rarer disease, affecting 0.7 out of every 100,000 people, about 1/10 the rate in Western countries. Existing drug therapies treat chorea and other involuntary movements, as well as neuropsychiatric symptoms, but a treatment for the underlying cause does not yet exist.

RG6042 Development project

Antisense oligonucleotide (ASO) targeting
human huntingtin messenger ribonucleic acid (*HTT* mRNA)
(Generic name: tominersen)

RG6042 is an ASO targeting human *HTT* mRNA, which is believed to be the cause of Huntington's disease. It has the potential to delay or slow disease progression in people with Huntington's disease by binding specifically to *HTT* mRNA, after which synthesis of the HTT protein is inhibited. A global phase III study began in March 2019. RG6042 has received orphan drug designation as a treatment for Huntington's disease in Japan, the United States, and Europe, and was granted PRIME designation by the European Medicines Agency in 2018.

Schizophrenia

Schizophrenia, a psychiatric disorder characterized by hallucination and delusion, occurs with high frequency, affecting just under one in 100 people. The symptoms are associated with impairment of daily life, affecting the ability to interact with others and conduct a family and social life, and impaired awareness of the illness, so that patients tend to be unable to recognize in retrospect that their perceptions, thoughts, and actions are distorted by the disease. As with many psychiatric disorders, it frequently develops chronically, with acute phases marked by more intense hallucinations and delusions. The development of new drugs and advances in psychosocial care mean that almost half of initially diagnosed patients can now be expected to make a full recovery or experience long-term remission (WHO 2001). The condition was previously sometimes referred to as "split personality disorder," but in Japan the official medical term was changed in 2002 to "schizophrenia."

RG7906 Development project
Partial TAAR1 agonist
(Generic name: ralmitaront)
RG7906 has the novel pharmacological action of working as a partial agonist of trace amino-associated receptor Type 1 (TAAR1). In August 2019, it completed a phase I clinical study in Japan in which a good safety profile was confirmed. Global phase II studies for schizophrenia began in February 2020.

Parkinson's Disease
Parkinson's disease is a progressive neurodegenerative disease characterized by aggregation of α-synuclein in the central nervous system and peripheral nervous system. A wide range of motor symptoms (tremor, muscle rigidity, akinesia, impairment of postural reflexes, etc.) and non-motor symptoms (sleep disorders, autonomic dysfunction, cognitive and mental disorders, etc.) occur. The estimated number of patients in Japan is 200,000. A progressive disease seen mainly in people age 50 or older, it can lead to becoming bedridden as the condition worsens.

RG7935 Development project
Anti-α-synuclein monoclonal antibody
(Generic name: prasinezumab)
RG7935 is a monoclonal antibody that targets α-synuclein. It slows the expansion of nerve cell death by inhibiting the cell-to-cell propagation of aggregated forms of neurotoxic α-synuclein, and is expected to reduce and delay progression of the disease. In a phase I clinical trial that began in 2018, RG7935 demonstrated good tolerability, and there were no significant racial differences in pharmacokinetics.

Neuromuscular Disease

GYM329/RG6237 Development project (In-house development)
Anti-latent myostatin sweeping antibody
GYM329, created by Chugai, is a next-generation antibody that applies Chugai's proprietary antibody engineering technologies, including its recycling antibody and sweeping antibody technologies. Latent myostatin is an inactive form that is mainly secreted from muscle cells, and is activated by BMP-1 and other protein degrading enzymes. Activated myostatin inhibits muscle growth and hypertrophy, and by inhibiting myostatin, GYM329 is expected to improve the various conditions associated with muscle atrophy and loss of muscular strength. Currently under development for neuromuscular disease, this antibody began a phase I clinical trial in October 2018. Chugai out-licensed GYM329 to Roche at an early stage before the start of clinical trials in order to accelerate global development by taking advantage of Roche's experience and expertise.

Other Diseases

COVID-19
Coronavirus Disease 2019 (COVID-19) is an infectious disease caused by the novel coronavirus SARS-CoV-2. The main symptoms of COVID-19 are fever, cough, fatigue, and breathing difficulties. Many of those infected recover after only mild symptoms, but some experience rapid deterioration and develop pneumonia. These patients may need to be hospitalized for oxygen administration and artificial ventilation and some experience a fatal outcome.

Actemra (MRA/RG1569) (In-house development)
Humanized anti-human IL-6 receptor monoclonal antibody
(Generic name: tocilizumab)
Actemra, created by Chugai and the first therapeutic antibody originating in Japan, acts to inhibit the inflammatory cytokine IL-6. Sales were launched in Japan in June 2005, with the intravenous infusion formulation approved for RA and five further indications (Castleman's disease, sJIA, pJIA, cytokine release syndrome induced by tumor-specific T-cell infusion therapy, and adult Still's disease) and the subcutaneous formulation for three indications (RA, Takayasu arteritis, and giant cell arteritis). Approval has currently been obtained in more than 110 countries worldwide.

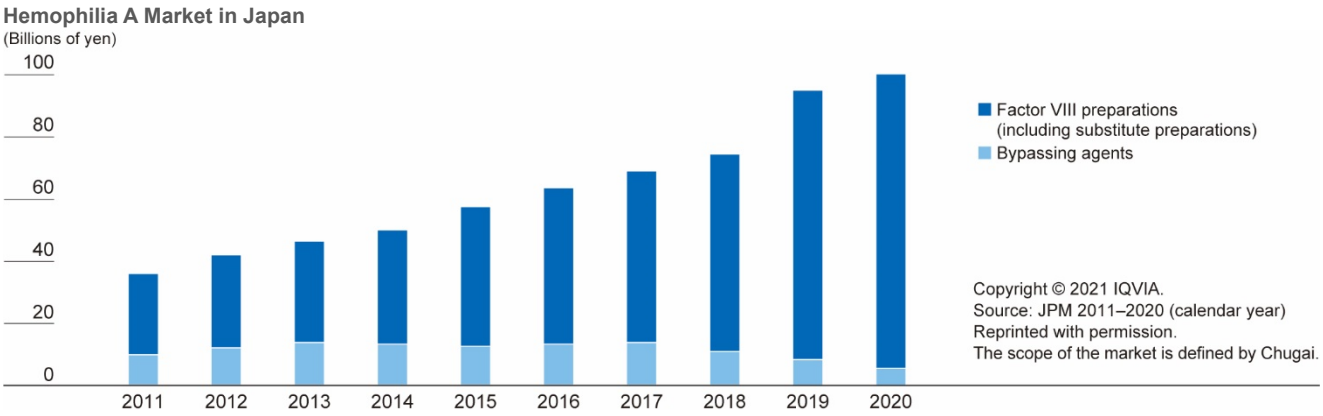
Outside of Japan, the phase III COVACTA clinical study in COVID-19-associated pneumonia led by Roche did not meet both the primary endpoint of improvement in clinical status and the key secondary endpoint of reduced mortality rate. The EMPACTA clinical study, which focused on minority patients with insufficient access to medical services, achieved its primary endpoint, with Actemra administration reducing the likelihood of mechanical ventilation being needed.

A single-arm phase III J-COVACTA clinical study was conducted in Japan. Of the 48 patients treated with Actemra, 35 (72.9 percent) had been discharged from the hospital or were ready to be discharged at 28 days after the start of Actemra administration, while 5 (10.4 percent) experienced fatal outcome.

For information on development for other indications and sales performance, including for COVID-19-associated pneumonia, please refer to the Bone and Joint Diseases/Autoimmune Diseases section above.

Hemophilia
Hemophilia is a disease that leads to bleeding in the joints, muscles, and other areas in the body due to a congenital deficiency or abnormal function of blood coagulation factors. A low level or absence of blood coagulation factor VIII is known as hemophilia A, while a low level or absence of blood coagulation factor IX is referred to as hemophilia B. Treatment of hemophilia A is centered on replacement therapy to supplement factor VIII. However, since it involves intravenous injections one to three times a week, treatment is a significant burden, particularly on children. Moreover, patients must be monitored for the development of autoantibodies, called inhibitors, to the supplemented factor. Patients with inhibitors are treated by means such as bypass therapy or immune tolerance therapy, but these therapies are limited in terms of convenience and the stability of their effects. A more useful treatment method is therefore needed.

Meanwhile, the autoimmune disease where patients develop autoantibodies to factor VIII is known as acquired hemophilia A. Acquired hemophilia A is associated with more frequent serious hemorrhage than the congenital form, and immunosuppressant therapy to eliminate the autoantibodies raises the risk of infectious diseases, making this a disease with poor prognosis.



Hemlibra (ACE910/RG6013) (In-house development)

Anti-coagulation factor IXa/X humanized bispecific monoclonal antibody
(Generic name: emicizumab)
Launched in Japan: May 2018

Hemlibra is a bispecific antibody that employs Chugai's innovative antibody engineering technologies. Like factor VIII, which is low or missing in hemophilia A, Hemlibra simultaneously binds to factor IXa and factor X, stimulating the activation of factor X by activated factor IX and promoting normal blood coagulation for hemostasis. Unaffected by inhibitors, Hemlibra can prevent bleeding with subcutaneous injections once a week, once every two weeks, or once every four weeks, and is promising as a drug that can change the existing system of treatment. Another key feature is that Chugai's proprietary technology ART-Ig is applied to Hemlibra, enabling industrial production of bispecific antibodies.

Chugai concluded an out-licensing agreement with Roche in July 2014 and in May 2017 entered into a license agreement with JW Pharmaceutical Corporation for the exclusive marketing rights in South Korea. The drug received breakthrough therapy designation from the U.S. FDA in September 2015 for its potential to prevent bleeding in hemophilia patients with inhibitors, and in April 2018 for its potential to prevent bleeding in patients without inhibitors. In the United States, Hemlibra received priority review designation in August 2017, and in November 2017 obtained approval for routine prophylaxis with once-weekly subcutaneous administration in adult and pediatric patients with hemophilia A with factor VIII inhibitors. Hemlibra was also granted accelerated assessment in Europe, and received regulatory approval from the European Commission in February 2018. In Japan, it obtained approval in March 2018 and was launched in May 2018. It also obtained approval in Taiwan in December 2018 and was launched there in November 2019.

Applications were filed in the United States, Europe, and Japan in April 2018, and in Taiwan in January 2019, for routine prophylaxis of bleeding episodes, as well as for additional dosage and administration as a biweekly or four-weekly treatment, for people with hemophilia A without inhibitors. In the United States, Hemlibra was granted priority review status in June 2018, and in October 2018, it obtained approval for prophylactic treatment by subcutaneous administration once weekly, every two weeks, or every four weeks in adults or children with hemophilia A without inhibitors, as well as additional dosing options of every two weeks or every four weeks in adults and children with hemophilia A with inhibitors. Hemlibra also obtained approval in Japan in December 2018, and in the EU in March 2019.

Chugai also began a phase III clinical study for the treatment of acquired hemophilia A in June 2020.

Review of 2020 Performance

Sales of Hemlibra increased ¥8.9 billion, or 35.3 percent, year on year to ¥34.1 billion. Due to repricing based on market expansion, the NHI drug price was reduced by 15 percent in April 2020. Hemlibra achieved good market penetration in non-inhibitor patients driven by its differentiated mode of action from factor VIII agents and longer half-life. However, as the impact of the COVID-19 pandemic slowed down the switch to Hemlibra, performance remained below expectations.

NXT007 Development project (In-house development)

Anti-coagulation factor IXa/X bispecific antibody

NXT007, created by Chugai, is a bispecific antibody that stimulates blood coagulation using the same mode of action as Hemlibra. One difference from Hemlibra is the application of Chugai's antibody engineering technologies FAST-Ig, which enhances large-scale production of the bispecific antibody and ACT-Fc, which is expected to improve antibody pharmacokinetics. NXT007 is expected to achieve the levels of hemostasis found in healthy adults and children, and is being developed to improve convenience, including the administration device. A phase I/II clinical trial for hemophilia A began in August 2019.

Influenza

Influenza is an acute infectious disease characterized by the rapid onset of high fever (38 degrees centigrade or higher) and severe systemic symptoms. It is highly infectious, and epidemics can develop quickly. In some cases, secondary infections can lead to very serious illness and death. Influenza is classified into types A, B, and C based on differences in the antigenicity of the underlying virus. Types A and B can infect humans and cause major outbreaks.

Tamiflu

Anti-influenza agent
(Generic name: oseltamivir)
Launch in Japan: February 2001

Tamiflu is an oral anti-influenza agent that is effective against both type A and type B infections. It inhibits viral replication by blocking the action of neuraminidase, an enzyme essential for the multiplication of the influenza virus. Launched in capsule form in February 2001 and dry syrup form in July 2002, dosages are available for patients one year of age and older. From March 2007, restrictions on the use of Tamiflu in teenage patients with seasonal influenza were in force in Japan. The measure was

introduced as a safety precaution following several reports of abnormal behavior in influenza patients who had taken Tamiflu. In May 2018, the Subcommittee on Drug Safety of the MHLW confirmed that abnormal behavior occurs regardless of whether anti-influenza drugs have been given, and in July 2018, the same subcommittee decided that the restrictions should be removed. Accordingly, the package insert was revised and restrictions on the use of Tamiflu in teenage patients were removed in August 2018.

The shelf life of Tamiflu capsules was extended to 10 years from seven years for capsules manufactured after July 2013, and the shelf life of Tamiflu dry syrup was extended to 10 years starting with the portion shipped in 2015. In March 2017, Chugai obtained approval for additional dosage and administration of Tamiflu dry syrup for neonates and infants younger than 12 months.

Review of 2020 Performance
Ordinary sales of Tamiflu decreased ¥6.6 billion, or 89.2 percent, to ¥0.8 billion, while sales for government stockpiles were ¥3.7 billion. Not only was the spread of influenza in the January to March period of the 2019-20 season very limited in scale, but the 2020-21 season had seen no outbreak at all as of the end of December 2020. Sales performance therefore remained far below expectations.

Others

CellCept
Immunosuppressant
(Generic name: mycophenolate mofetil)
Launch in Japan: November 1999
Sales of CellCept decreased ¥0.2 billion, or 2.2 percent, to ¥9.1 billion. CellCept is used to treat refractory rejection after kidney transplants and to prevent rejection after kidney, heart, liver, lung, and pancreas transplants. The need for transplantation medication has been rising in Japan, driven by advances in transplantation therapy. In May 2016, CellCept received approval for the indication of lupus nephritis, a refractory disease associated with the autoimmune disease systemic lupus erythematosus.

Atopic Dermatitis
A type of allergic disorder, atopic dermatitis is a chronic skin disease characterized by an itchy rash that alternately improves and worsens. Scratching the affected area exacerbates the skin symptoms and makes the itching worse, leading to an itch-scratch cycle. The basic treatment is drug therapy using topical steroid preparations and/or immunosuppressants to control the inflammation and a skin care regimen to prevent the inflammation from recurring.

Prurigo Nodularis
Prurigo nodularis is a chronic skin disorder that causes thick papules or nodules accompanied by intensive itching. Patients with prurigo nodularis worry that the severe itching will interfere with their daily lives. The cause of prurigo nodularis is not yet fully understood, and control of the symptoms is difficult, and thus an effective treatment is needed.

CIM331 Development project (In-house development)
Anti-IL-31 receptor A humanized monoclonal antibody
(Generic name: nemolizumab)
Nemolizumab (CIM331) is an anti-IL-31 receptor A humanized monoclonal antibody originating from Chugai. The drug is expected to improve itching and skin inflammation in atopic dermatitis by blocking IL-31, a proinflammatory cytokine, from binding to its receptor.

In July 2016, Chugai entered into a global license agreement granting Galderma S.A. of Switzerland exclusive rights for the development and marketing of nemolizumab worldwide, with the exception of Japan and Taiwan. In September 2016, Chugai entered into a license agreement granting Maruho Co., Ltd., the rights for the development and marketing of nemolizumab in the skin disease area for the Japanese market. In development for atopic dermatitis, Maruho, filed an approval application in Japan in the third quarter of fiscal 2020, while Galderma initiated global phase III studies in 2019. In addition, nemolizumab was granted breakthrough therapy designation by the U.S. FDA for pruritus associated with prurigo nodularis. Galderma launched a phase III clinical study for the treatment of prurigo nodularis in October 2020, while Maruho, started phase II/III clinical studies in Japan in December 2020.

Paroxysmal Nocturnal Hemoglobinuria
Paroxysmal nocturnal hemoglobinuria (PNH) is a disorder that leads to complications such as thrombosis and CKD, in addition to anemia and dark brown urine caused by hemolysis as well as infections and bleeding tendency associated with a decrease in white blood cells and platelets. It is an acquired genetic disorder that affects hematopoietic stem cells, causing the creation of red blood cells that have no complement resistance, and hemolysis occurs when complements are activated in vivo. Although the estimated number of people affected is small, with 764 in Japan (based on the number of holders of specific medical expense recipient certificates for designated intractable diseases as of the end of fiscal 2018), and around 5,000 worldwide, it is a progressive disease with a high mortality risk.

SKY59/RG6107 Development project (In-house development)
Anti-C5 recycling antibody
(Generic name: crovalimab)
SKY59 is a recycling antibody discovered by Chugai that inhibits the C5 complement component.

The onset of a number of diseases is reported to be caused by complement activation. SKY59 is expected to inhibit cleavage of C5 to C5a and C5b, thus suppressing complement activation and improving disease conditions. In PNH, SKY59 may have a suppressive effect on hemolysis by preventing the destruction of red blood cells. Application of multiple Chugai proprietary antibody engineering technologies resulted in a prolonged half-life, and the antibody is being developed as a subcutaneous self-injection. Due to the severity of the disease, regular administration is necessary, but making self-injection possible is expected to lessen the burden on patients by reducing the frequency of hospital visits. In September 2020, Chugai launched a global phase III study for the treatment of PNH in co-development with Roche. In September 2017, SKY59 received orphan drug designation in the United States for PNH.

wAMD/DME
Wet age-related macular degeneration (wAMD) is a disease in which abnormal blood vessel growth (choroidal neovascularization) caused by age-related accumulation of waste products extends into the space under the retinal pigment epithelium (RPE) or between the retina and the RPE, leading to retinal tissue damage. If the choroidal neovascularization and the associated effusion progress into the fovea centralis, which

governs vision, it may lead to deterioration of visual acuity along with the symptoms of image distortion, vision loss, and central scotoma. Left untreated, wAMD may lead to irreversible visual impairment.

Diabetic macular edema (DME) is a retinal disease associated with diabetic retinopathy. In diabetes, consistently high blood sugar causes blockage of retinal capillaries, ischemic change, and edema induced by vascular hyperpermeability. Blurred vision occurs when swelling extends to the central part of the macula, which governs vision. Left untreated, DME may lead to irreversible visual impairment.

RG7716 Development project

Anti-VEGF/Ang-2 bispecific antibody
(Generic name: faricimab)

RG7716, which Chugai in-licensed from Roche, is the first bispecific antibody for ophthalmology diseases. It selectively binds to vascular endothelial growth factor A (VEGF-A), a key mediator of angiogenesis and vascular permeability, and angiopoietin-2 (Ang-2, an antagonist of Ang-1, which contributes to the stability of mature vessels), a destabilizer of chorioretinal vessels and inducer of vascular permeability. By simultaneously neutralizing intraocular VEGF-A and Ang-2 in wAMD and DME patients, RG7716 is expected to demonstrate better treatment outcomes and a more sustained effect than the anti-VEGF drugs that are the current standard of care. Two global phase III studies for the treatment of DME achieved their primary endpoints in December 2020, as did two global phase III studies for the treatment of wAMD in January 2021.

Endometriosis

Affecting one out of 10 women in their twenties to forties, endometriosis is the repeated proliferation and shedding of endometrial tissue outside the uterus, accompanied by dysmenorrhea and chronic lower abdominal pain, and is a cause of infertility. The disease can interfere with daily life, including absences from work or school, as sufferers find it difficult to do more than lie still when symptoms are severe. The only existing medications are hormonal agents. Moreover, if the pain cannot be controlled by drugs, the only treatment is surgical removal, and many patients experience a recurrence several years after surgery, making this a disease with a high level of unmet medical needs.

AMY109 Development project (In-house development)

AMY109 is the third therapeutic antibody to apply the recycling antibody engineering technology created by Chugai. Its approach differs from hormone therapy, which is the standard treatment for endometriosis, and its anti-inflammatory action is expected to provide new value to patients. A phase I clinical trial started in February 2018.

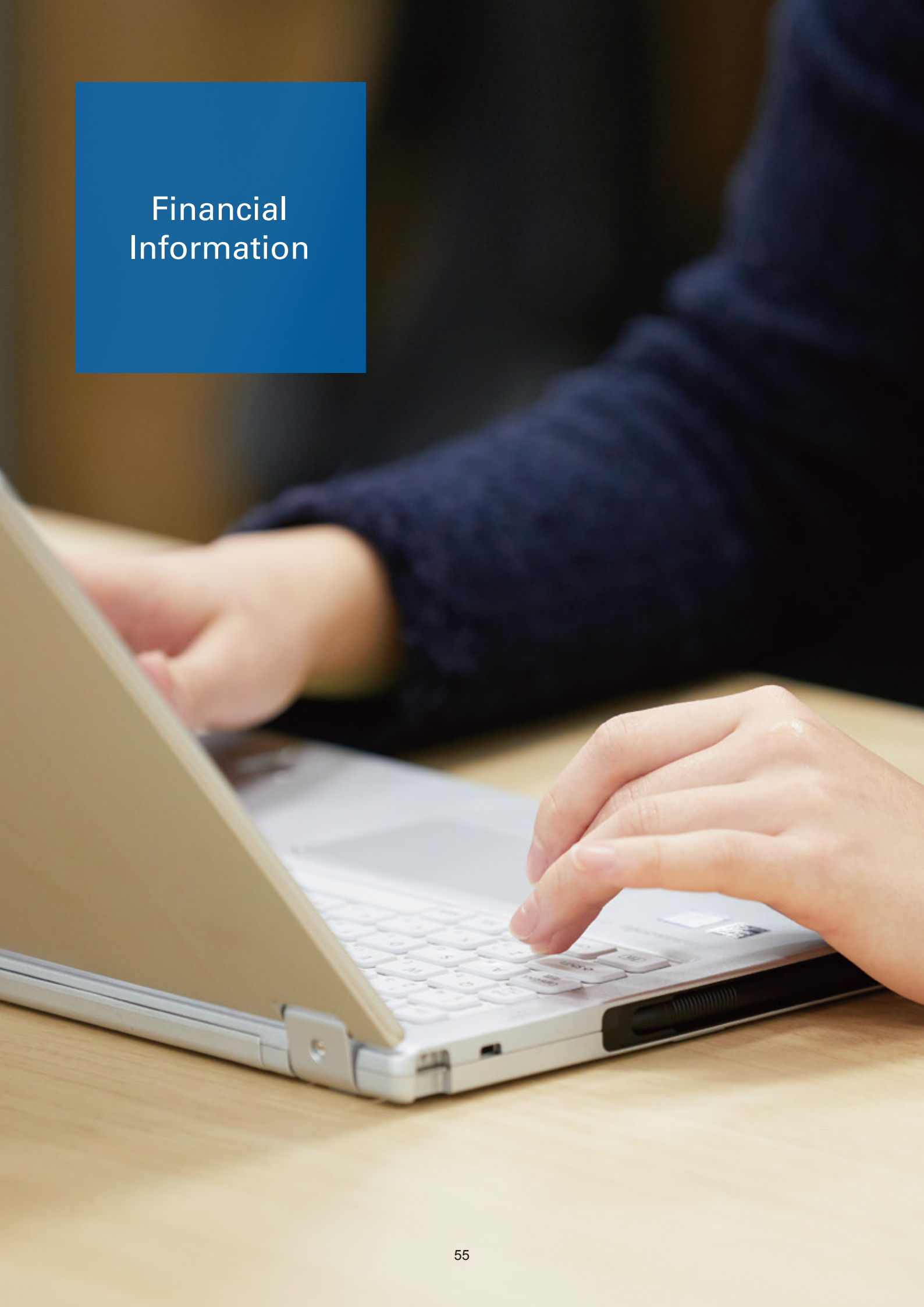
Type 2 Diabetes

Type 2 diabetes is an illness in which genetic predisposition and lifestyle cause impaired insulin secretion and resistance to insulin action, resulting in high plasma glucose concentration. There are no symptoms in the early stages, but if the condition is left untreated, the risk of cardiovascular diseases such as stroke and myocardial infarction increases. The disease can also cause complications such as retinopathy, nephropathy, and neuropathy, which lead to blindness, dialysis, and leg amputation, respectively, significantly reducing QoL. According to the International Diabetes Federation, the number of people with diabetes worldwide, including prediabetes, is 463 million in 2019, and is projected to increase to 700 million in 2045. Treatment of this condition is thus a worldwide issue.

OWL833 Development project (In-house development)

OWL833 is an oral non-peptidic GLP-1 receptor agonist created by Chugai. GLP-1 agonists have potent hypoglycemic action and induce weight loss, but convenience for patients has been an issue because they are conventionally administered in a subcutaneous injection. Because OWL833 is orally bioavailable, it is easier for patients to take, and is thus expected to contribute to the treatment of diabetes, including through improvement of drug adherence. In September 2018, Chugai licensed the worldwide development and commercialization rights for OWL833 to Eli Lilly and Company. A phase I clinical study by Eli Lilly is under way.

Financial Information



Consolidated Financial Indicators

Chugai Pharmaceutical Co., Ltd. and Consolidated Subsidiaries
Years ended December 31

(Billions of yen)

International Financial Reporting Standards (IFRS)	2020		2019		2018		2017	
	IFRS	Core[1]	IFRS	Core	IFRS	Core	IFRS	Core
Results								
Revenues[2]	**786.9**		686.2		579.8		534.2	
Sales	**633.3**		588.9		527.8		499.3	
Royalties and other operating income	**153.6**		97.3		51.9		34.9	
Cost of sales	**(273.5)**	**(272.3)**	(266.1)	(265.1)	(262.8)	(261.9)	(254.2)	(252.9)
Operating expenses	**(212.3)**	**(206.7)**	(209.5)	(196.2)	(192.6)	(187.6)	(181.1)	(178.1)
Marketing and distribution	**(72.6)**	**(71.5)**	(77.2)	(73.5)	(73.7)	(73.7)	(72.8)	(72.8)
Research and development	**(117.9)**	**(113.5)**	(107.9)	(102.1)	(99.2)	(94.2)	(92.9)	(88.9)
General and administration	**(21.8)**	**(21.7)**	(24.4)	(20.6)	(19.7)	(19.7)	(15.3)	(16.3)
Operating profit	**301.2**	**307.9**	210.6	224.9	124.3	130.3	98.9	103.2
Profit before taxes	**298.2**	**304.9**	207.9	222.2	121.4	127.5	97.0	101.3
Net income	**214.7**	**219.4**	157.6	167.6	93.1	97.3	73.5	76.7
Attributable to Chugai shareholders	**214.7**	**219.4**	157.6	167.6	92.5	96.7	72.7	75.9
Core EPS (Yen)[3]	**—**	**133.39**	—	101.93	—	58.81	—	46.23
Cash dividends per share (Yen)[3]	**55.00**		46.67		28.67		20.67	
Core payout ratio	**—**	**41.2%**	—	45.8%	—	48.7%	—	44.7%
Financial Position								
Net operating assets (NOA)	**646.0**		547.0		505.3		440.2	
Total assets	**1,235.5**		1,058.9		919.5		852.5	
Total liabilities	**(255.5)**		(204.9)		(163.0)		(159.6)	
Total net assets	**980.0**		854.0		756.5		692.9	
Investments in property, plant and equipment	**75.2**		54.0		71.8		34.3	
Depreciation	**22.0**		17.8		14.6		14.5	
Main Indicators								
Cost to sales ratio	**43.2%**	**43.0%**	45.2%	45.0%	49.8%	49.6%	50.9%	50.7%
Ratio of operating profit to revenues	**38.3%**	**39.1%**	30.7%	32.8%	21.4%	22.5%	18.5%	19.3%
Ratio of research and development expenditures to revenues	**15.0%**	**14.4%**	15.7%	14.9%	17.1%	16.2%	17.4%	16.6%
Core return on invested capital (Core ROIC)[4, 5]	**36.5%**	**37.3%**	30.1%	31.9%	20.3%	21.2%	17.3%	18.1%
Ratio of net income to equity attributable to Chugai shareholders (ROE)[6]	**23.4%**	**—**	19.6%	—	12.8%	—	10.9%	—
Ratio of profit before taxes to total assets (ROA)[7]	**26.0%**	**—**	21.0%	—	13.7%	—	11.7%	—
Equity per share attributable to Chugai shareholders (BPS) (Yen)[3]	**596.16**	**—**	519.91	—	460.42	—	421.82	—
Ratio of equity attributable to Chugai shareholders	**79.3%**	**—**	80.6%	—	82.2%	—	81.2%	—
Number of employees	**7,555**		7,394		7,432		7,372	

1. Core basis results are IFRS basis results adjusted for items recognized by Chugai as non-recurring. Core basis results are used by Chugai as internal performance indicators for representing recurring profit trends both internally and externally, and as indices for establishing profit distributions such as returns to shareholders.
2. Revenues do not include consumption tax.
3. Effective July 1, 2020, Chugai has implemented a three-for-one stock split of its common stock. Figures are calculated based on the assumption that the stock split was implemented at the beginning of 2012.
4. Core return on invested capital (Core ROIC) = Core net operating profit after taxes / Net operating assets (Core ROIC is calculated by using Core income taxes.)
5. Return on invested capital (ROIC) = Net operating profit after taxes / Net operating assets (Net operating profit after taxes = Operating profit – Income taxes)
6. Ratio of net income to equity attributable to Chugai shareholders (ROE) = Net income attributable to Chugai shareholders / Capital and reserves attributable to Chugai shareholders (average of beginning and end of fiscal year)
7. Ratio of profit before taxes to total assets (ROA) = Profit before taxes / Total assets (average of beginning and end of fiscal year)

Consolidated Financial Indicators

(Billions of yen)

International Financial Reporting Standards (IFRS)	2016		2015		2014		2013		2012	
	IFRS	Core	IFRS	Core	IFRS	Core	IFRS	Core	IFRS	Core
Results										
Revenues	491.8		498.8		461.1		423.7		386.6	
Sales	472.7		468.4		436.9		401.3		375.2	
Royalties and other operating income	19.1		30.4		24.2		22.4		11.3	
Cost of sales	(247.9)	(246.7)	(240.2)	(238.9)	(218.1)	(217.0)	(187.0)	(186.1)	(168.2)	(167.3)
Operating expenses	(167.0)	(164.5)	(171.8)	(169.3)	(167.2)	(166.8)	(157.9)	(157.7)	(143.7)	(143.7)
Marketing and distribution	(69.8)	(69.8)	(74.8)	(74.7)	(71.7)	(71.7)	(71.6)	(71.5)	(67.9)	(67.9)
Research and development	(85.0)	(82.6)	(83.8)	(81.9)	(80.8)	(80.6)	(74.3)	(74.1)	(66.6)	(66.6)
General and administration	(12.2)	(12.1)	(13.2)	(12.8)	(14.6)	(14.6)	(12.1)	(12.1)	(9.2)	(9.2)
Operating profit	76.9	80.6	86.8	90.7	75.9	77.3	78.7	79.9	74.7	75.6
Profit before taxes	74.4	78.1	87.3	91.2	76.2	77.6	76.9	78.1	72.7	73.6
Net income	54.4	56.8	62.4	64.9	52.1	53.0	51.9	52.6	46.8	47.4
Attributable to Chugai shareholders	53.6	56.1	61.1	63.7	51.0	51.9	50.9	51.6	46.1	46.6
Core EPS (Yen)	—	34.17	—	38.81	—	31.68	—	31.56	—	28.55
Cash dividends per share (Yen)	17.33		19.33		16.00		15.00		13.33	
Core payout ratio	—	50.7%	—	49.8%	—	50.5%	—	47.5%	—	46.7%
Financial Position										
Net operating assets (NOA)	431.1		380.4		357.7		325.2		307.9	
Total assets	806.3		787.4		739.5		697.2		645.3	
Total liabilities	(159.8)		(160.1)		(141.8)		(124.0)		(116.2)	
Total net assets	646.5		627.3		597.8		573.2		529.2	
Investments in property, plant and equipment	19.4		28.7		16.3		13.0		14.2	
Depreciation	14.8		14.0		13.7		13.5		13.3	
Main Indicators										
Cost to sales ratio	52.4%	52.2%	51.3%	51.0%	49.9%	49.7%	46.6%	46.4%	44.8%	44.6%
Ratio of operating profit to revenues	15.6%	16.4%	17.4%	18.2%	16.5%	16.8%	18.6%	18.9%	19.3%	19.6%
Ratio of research and development expenditures to revenues	17.3%	16.8%	16.8%	16.4%	17.5%	17.5%	17.5%	17.5%	17.2%	17.2%
Return on invested capital (ROIC)	—	14.6%	—	—	—	—	—	—	—	—
Ratio of net income to equity attributable to Chugai shareholders (ROE)	8.4%	—	10.0%	—	8.7%	—	9.3%	—	9.0%	—
Ratio of profit before taxes to total assets (ROA)	9.3%	—	11.4%	—	10.6%	—	11.5%	—	11.8%	—
Equity per share attributable to Chugai shareholders (BPS) (Yen)	393.89	—	382.06	—	364.30	—	349.82	—	323.36	—
Ratio of equity attributable to Chugai shareholders	80.1%	—	79.5%	—	80.6%	—	82.0%	—	81.8%	—
Number of employees	7,245		7,169		7,023		6,872		6,836	

Management Policy

Chugai's Mission is to dedicate itself to adding value by creating and delivering innovative products and services for the medical community and human health around the world based on its strategic alliance with Roche. Aiming at becoming a top innovator for advanced and sustainable patient-centric healthcare, we set up our fundamental management policy of growing together with society.

In our mid-term business plan IBI 21, launched in 2019, we laid the foundation for further growth by exceeding its goals in both quantitative and qualitative terms ahead of the target date of 2021, the final year of the plan. We have therefore concluded IBI 21 one year ahead of schedule and formulated a new growth strategy, TOP I 2030, to give concrete substance to our target profile as a top innovator in the healthcare industry, which the new plan aims to realize by 2030.

In recent years, all aspects of our business environment, from the evolution of science and technology to government healthcare policy and market trends, have been drastically changing, which has made it all the more important to review and implement strategy in a more flexible manner. In response, our new growth strategy, instead of adopting a management plan with the conventional three-year format, sets out an interim milestone for each strategy to serve as a shorter-term goal, enabling more agile adjustment of these milestones as conditions change and the strategy progresses. In parallel, we will formulate a series of single-year plans focused on the 2030 goals and the interim milestones.

The new growth strategy rests on two pillars: realizing global first-class drug discovery and building a futuristic business model. To firmly implant these pillars, in addition to concentrating company-wide management resources on research and early development, which is the source of our value creation, Chugai will utilize AI-based drug discovery and other digital technologies to energetically drive open innovation. Additionally, as specific initiatives within the new growth strategy, we have announced five areas of reform: drug discovery, development, pharmaceutical technology, value delivery through our various value chains, and the growth foundation supporting each of these areas.

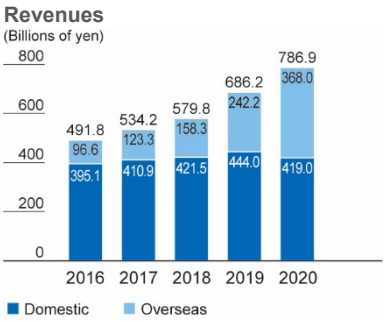
In the area of shareholder returns, Chugai's aim is to offer shareholders a continuous stable dividend after taking into account projected business results and evolving needs in strategic investment funding. In line with this approach, our target payout ratio is 45% on average based on Core EPS. Internal reserves will be used to increase corporate value through investments for further growth in existing strategic areas and to explore future business opportunities.

Overview of Results

Revenues

(Billions of yen)

	2018	2019	2020	2019/2020 Change
Revenues	579.8	686.2	786.9	+14.7%
Sales	527.8	588.9	633.3	+7.5%
Royalties and other operating income (ROOI)	51.9	97.3	153.6	+57.9%

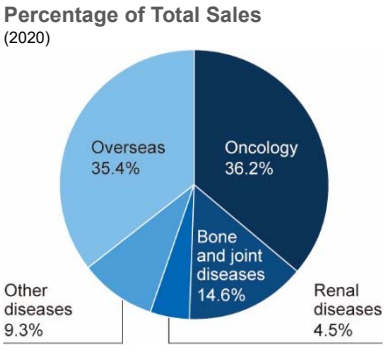


- In 2020, revenues were impacted by the NHI drug price revision and the market penetration of generics, resulting in a decrease in sales in Japan. However, overall sales increased year on year due to growth in exports of Chugai products to Roche and a rise in ROOI.
- Overseas revenues increased steadily with the growth of global products from Chugai research.
- ROOI increased year on year due to a significant increase in royalty and profit-sharing income associated with Hemlibra.

Domestic Sales by Area

(Billions of yen)

	2018	2019	2020	2019/2020 Change
Domestic sales	399.9	437.6	409.1	–6.5%
Oncology	225.7	240.5	229.5	–4.6%
Bone and joint diseases	100.5	108.4	92.4	–14.8%
Renal diseases	36.3	34.6	28.6	–17.3%
Other diseases	37.5	54.1	58.7	+8.5%



- Domestic sales decreased 6.5% in 2020, mainly due to a decline in sales of mainstay products in the oncology, bone and joint diseases, and renal diseases areas affected by the NHI drug price revision in April and the market penetration of generics.
- In the oncology area, the new product Tecentriq and the mainstay products Alecensa and Perjeta saw sales growth, but sales decreased overall due to the impact on Avastin, Herceptin, and other products of the NHI drug price revision and market penetration by generics.

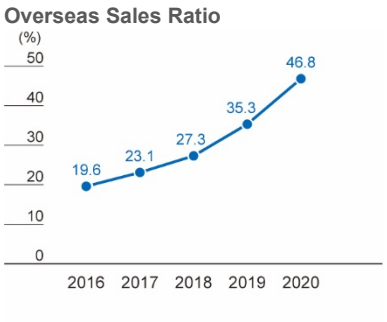
- The bone and joint diseases area saw a substantial sales decrease due to the impact of the NHI drug price revision on Actemra and the sales launch of generics in competition with Edirol.
- In the other diseases area, sales grew as the new product Hemlibra made steady progress.

Overseas Sales

(Billions of yen)

	2018	2019	2020	2019/2020 Change
Overseas sales	127.9	151.3	224.2	+48.2%
Actemra (exports to Roche)	78.7	86.5	132.0	+52.6%
Alecensa (exports to Roche)	28.9	44.6	43.0	–3.6%
Hemlibra (exports to Roche)	2.3	3.3	24.6	+645.5%
Enspryng (exports to Roche)	—	—	5.6	—%

- Overseas sales increased year on year in 2020. The main reasons for the increase were that exports to Roche of Actemra grew substantially in the context of the COVID-19 pandemic, that exports to Roche of Hemlibra switched to the regular shipment price, and that exports to Roche of Enspryng began in 2020.

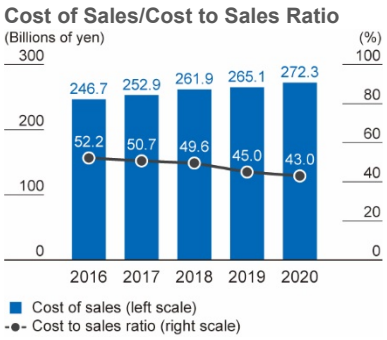


Cost of Sales (Core Basis)

(Billions of yen)

	2018	2019	2020	2019/2020 Change
Cost of sales	(261.9)	(265.1)	(272.3)	+2.7%
Cost to sales ratio	49.6%	45.0%	43.0%	–2.0% pts

- The cost to sales ratio decreased year on year in 2020, mainly because of Chugai products, which have a lower cost to sales ratio than products in-licensed from Roche, accounting for a higher percentage of the sales mix, and because of the switch to the regular shipment price for Hemlibra exports to Roche.

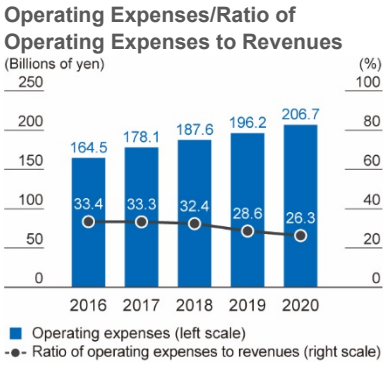


Operating Expenses (Marketing and Distribution Expenses, R&D Expenditures, and General and Administration Expenses) (Core Basis)

(Billions of yen)

	2018	2019	2020	2019/2020 Change
Total operating expenses	(187.6)	(196.2)	(206.7)	+5.4%
Marketing and distribution expenses	(73.7)	(73.5)	(71.5)	–2.7%
R&D expenditures	(94.2)	(102.1)	(113.5)	+11.2%
General and administration expenses	(19.7)	(20.6)	(21.7)	+5.3%

- Marketing and distribution expenses decreased as a result of the reduction in business activities caused by the COVID-19 pandemic.
- R&D expenditures increased year on year as development projects progressed and were the main factor in an overall increase in operating expenses.

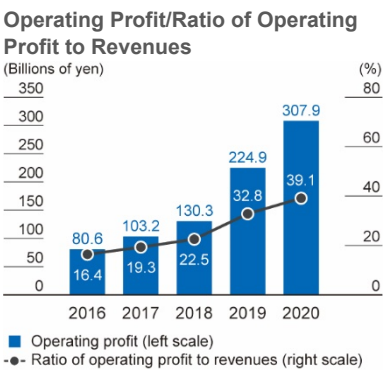


Operating Profit and Net Income (Core Basis)

(Billions of yen)

	2018	2019	2020	2019/2020 Change
Operating profit	130.3	224.9	307.9	+36.9%
Ratio of operating profit to revenues	22.5%	32.8%	39.1%	+6.3% pts
Net income	97.3	167.6	219.4	+30.9%

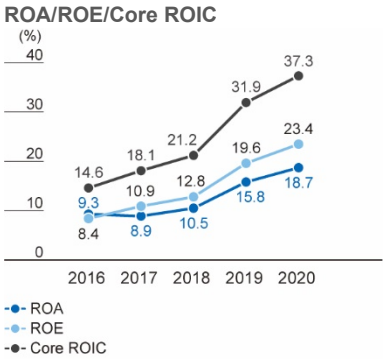
- Both operating profit and net income increased significantly in 2020, mainly due to the substantial growth in exports to Roche of Actemra and Hemlibra, an increase in ROOI from Hemlibra, and the decrease in cost to sales ratio accompanying the increased share of Chugai products in total sales.



Profitability Indicators

	2018	2019	2020	2019/2020 Change
Gross profit to revenues (%) (Core)	54.8	61.4	65.4	+4.0% pts
Operating profit to revenues (%) (Core)	22.5	32.8	39.1	+6.3% pts
Ratio of profit before taxes to total assets (ROA) (%) (IFRS)	10.5	15.8	18.7	+2.9% pts
Ratio of net income to equity attributable to Chugai shareholders (ROE) (%) (IFRS)	12.8	19.6	23.4	+3.8% pts
Core return on invested capital (Core ROIC) (%)	21.2	31.9	37.3	+5.4% pts

Notes: 1. ROA = Net income attributable to Chugai shareholders / Total assets
2. ROE = Net income attributable to Chugai shareholders / Capital and reserves attributable to Chugai shareholders
3. Core ROIC = Core net operating profit after taxes / Net operating assets (Core ROIC is calculated by using Core income taxes.)



- Net operating assets (NOA) increased significantly due to aggressive strategic investments such as Chugai Life Science Park Yokohama. Core ROIC also grew year on year in 2020 due to growth in Core net operating profit after taxes.

Financial Position

Assets, Liabilities, and Net Assets

In conjunction with its decision to apply IFRS from 2013, Chugai has reorganized the consolidated balance sheets and discloses assets and liabilities including net operating assets for use as internal performance indicators (Roche discloses the same indicators). No items have been excluded from the IFRS balance sheet, as the Core basis results concept only applies to the income statement.

Net Operating Assets (NOA)

(Billions of yen)

	2018	2019	2020	2019/2020 Change
Net working capital	235.1	237.2	300.0	+26.5%
Long-term net operating assets	270.1	309.8	346.0	+11.7%
Net operating assets (NOA)	505.3	547.0	646.0	+18.1%

- Net working capital increased from the end of the previous year due mainly to increase in accounts receivable. Long-term net operating assets grew, notably due to the increase in property, plant and equipment resulting from the investment in Chugai Life Science Park Yokohama.

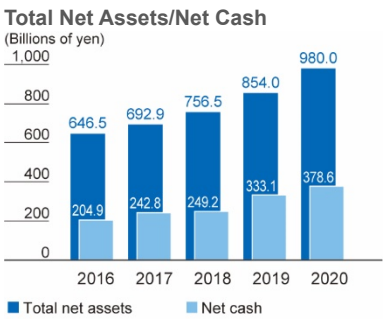
NOA are the total of net working capital and long-term net operating assets. Net working capital is composed of accounts receivable, inventories, accounts payable, and other payables and receivables. Long-term net operating assets are composed of property, plant and equipment, intangible assets, and other items.

Total Net Assets

(Billions of yen)

	2018	2019	2020	2019/2020 Change
Net operating assets (NOA)	505.3	547.0	646.0	+18.1%
Net cash	249.2	333.1	378.6	+13.7%
Other non-operating assets – net	2.1	(26.1)	(44.6)	+70.9%
Total net assets	756.5	854.0	980.0	+14.8%

- Total net assets at December 31, 2020 increased from a year earlier due to factors including an increase in property, plant and equipment resulting from investment in Chugai Life Science Park Yokohama and an increase in net cash.
- Despite the rapid evolution of life science and digital technology, operating conditions for pharmaceutical companies are becoming more challenging due to the increasing fiscal pressure at a global level. In response, we will work to further increase corporate value through continuous innovation supported by strategically targeted investment.



Total Assets and Total Liabilities

(Billions of yen)

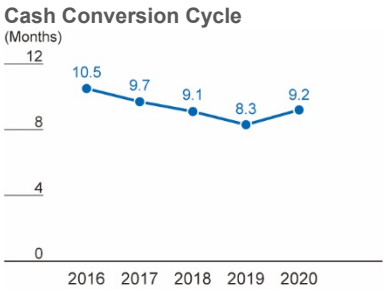
	2018	2019	2020	2019/2020 Change
Total assets	919.5	1,058.9	1,235.5	+16.7%
Total liabilities	(163.0)	(204.9)	(255.5)	+24.7%

- Calculated under the headings of assets, liabilities, and net assets, there has been an increasing tendency in total assets, total liabilities, and total net assets.

Financial Position Indicators

	2018	2019	2020	2019/2020 Change
Ratio of equity attributable to Chugai shareholders (%)	82.2	80.6	79.3	–1.3% pts
Cash conversion cycle (Months)	9.1	8.3	9.2	+0.9 months
Net cash turnover period (Months)	5.2	5.8	5.8	0.0 months
Current ratio (%)	443.8	390.3	353.7	–36.6% pts
Debt-to-equity ratio (%)	0.0	0.0	0.0	—

Notes: 1. Ratio of equity attributable to Chugai shareholders = Capital and reserves attributable to Chugai shareholders (fiscal year-end) / Total assets (fiscal year-end)
2. Cash conversion cycle = [Trade accounts receivable / Sales + (Inventories – Trade accounts payable) / Cost of sales] x Months passed
3. Net cash turnover period = Net cash / Revenues x Months passed
4. Current ratio = Current assets (fiscal year-end) / Current liabilities (fiscal year-end)
5. Debt-to-equity ratio = Interest-bearing debt (fiscal year-end) / Capital and reserves attributable to Chugai shareholders (fiscal year-end)

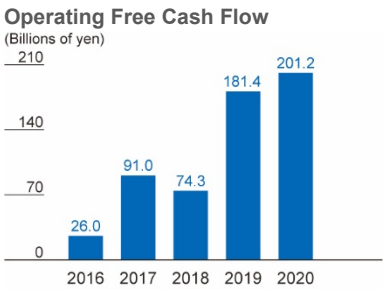


Cash Flows

In conjunction with its decision to apply IFRS from 2013, Chugai has reorganized the consolidated statements of cash flows and uses free cash flows as internal performance indicators (Roche discloses the same indicators). No items have been excluded from cash flows, as the Core basis results concept only applies to the income statement.

(Billions of yen)

	2018	2019	2020	2019/2020 Change
Movement of Free Cash Flow				
Operating profit	124.3	210.6	301.2	+43.0%
Operating profit, net of operating cash adjustment	147.4	245.2	335.5	+36.8%
Operating free cash flow	74.3	181.4	201.2	+10.9%
Free cash flow	43.7	142.6	135.4	–5.0%
Net increase/decrease in cash	6.4	83.9	45.5	–45.8%
Consolidated Statement of Cash Flows				
Cash flows from operating activities	119.1	206.6	205.0	–0.8%
Cash flows from investing activities	(74.1)	(81.7)	(98.3)	+20.3%
Cash flows from financing activities	(35.0)	(66.9)	(99.5)	+48.7%
Net increase in cash and cash equivalents	7.8	57.1	8.4	–85.3%
Cash and cash equivalents at end of year	146.9	203.9	212.3	+4.1%



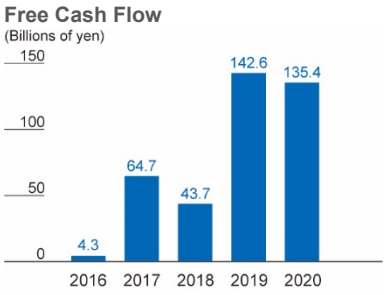
Operating free cash flow

- Operating profit, net of operating cash adjustment, is calculated by adjusting for depreciation and other items that are included in operating profit but are not accompanied by cash inflows or outflows and all inflows and outflows related to NOA that are not accompanied by profit or loss.
- Operating free cash flow for the fiscal year under review amounted to a net inflow of ¥201.2 billion due to a significant increase in operating profit and other factors, despite an increase in net working capital and other related items of ¥64.4 billion, as well as expenditures of ¥57.0 billion for the purchase of property, plant and equipment. The purchase of property, plant and equipment included investment and other expenditures for Chugai Life Science Park Yokohama.

- With the application of IFRS 16 "Leases," operating free cash flow includes expenditures of ¥8.4 billion for lease liabilities paid.

Free cash flow

- Free cash flow was a net cash inflow of ¥135.4 billion due mainly to income taxes paid of ¥66.8 billion.
- Net cash as of December 31, 2020, after subtracting dividends paid of ¥91.4 billion and other expenditures, showed an increase of ¥45.5 billion from the previous year end to ¥378.6 billion.

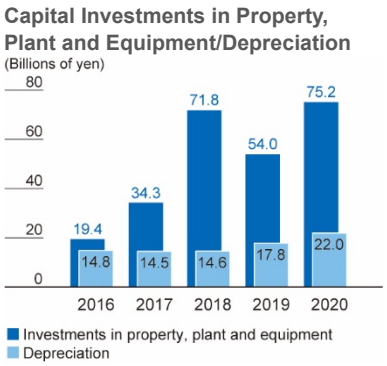


Capital Investments

(Billions of yen)

	2018	2019	2020	2019/2020 Change
Investments in property, plant and equipment	71.8	54.0	75.2	+39.3%
Depreciation	14.6	17.8	22.0	+23.6%

- Capital investments in 2020 included investment in Chugai Life Science Park Yokohama and investments in manufacturing facilities at the Fujieda Plant.
- Chugai plans to make capital investments of ¥79.5 billion during 2021, consisting primarily of new investment in the main facilities below, and expects depreciation to total ¥21.0 billion.



Major Capital Investments—Current and Planned
(Chugai Pharmaceutical Co., Ltd.)

Facilities (Location)	Description	Planned investment (Billions of yen)		Fund-raising method	Start of construction	Planned transfer/completion date
		Total amount	Investment to date			
Chugai Life Science Park Yokohama (Totsuka-ku, Yokohama City, Kanagawa)	Pharmaceutical research	128.5	65.2	Self-financing	June 2019	August 2022
Fujieda Plant (Fujieda City, Shizuoka)	Small and mid-size molecule API manufacturing	19.1	12.7	Self-financing	May 2019	October 2022

Outlook for 2021

Forecast Assumptions

For 2021, Chugai assumes exchange rates of ¥116/CHF, ¥126/EUR, ¥105/USD, and ¥78/SGD.

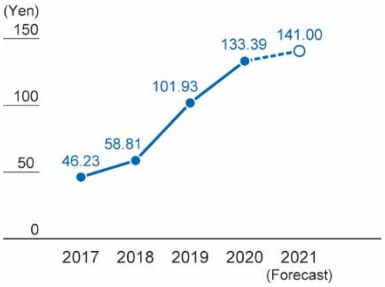
Results Forecast (Core Basis)

(Billions of yen)

	2019	2020	2021 Forecast	2020/2021 Change
Revenues	686.2	786.9	800.0	+1.7%
Sales	588.9	633.3	631.0	–0.4%
Domestic	437.6	409.1	393.7	–3.8%
Overseas	151.3	224.2	237.3	+5.8%
Royalties and other operating income (ROOI)	97.3	153.6	169.0	+10.0%
Royalty and profit-sharing income	76.5	129.6	163.0	+25.8%
Other operating income	20.8	24.1	6.0	–75.1%
Core operating profit	224.9	307.9	320.0	+3.9%
Core EPS (Yen)[1]	101.93	133.39	141.00	+5.7%

- Although sales growth is expected from new products including Hemlibra and Tecentriq, domestic sales are forecast to decrease overall compared with 2020 due to the impact of generics and other competitor products and the first interim NHI drug price revision.
- Overseas sales are forecast to increase mainly on large growth in exports of Hemlibra, whose exports to Roche switched to the regular shipment price in 2020. For Actemra, whose exports increased in 2020 due to COVID-19, the effect of the pandemic in 2021 is projected to be limited.
- ROOI is forecast to increase substantially because royalties and profit-sharing income are expected to increase, primarily in connection with Hemlibra. Other operating income is also expected to decrease due to factors including a decrease in one-time income.
- The cost to sales ratio is forecast to decrease year on year due to a change in the product mix based on the continued growth of Chugai product sales in and outside Japan.
- We expect operating expenses to increase overall due mainly to an increase in R&D activity, including the progress of development projects and related expenses to produce investigational drugs.
- We forecast that Core operating profit and Core EPS will increase despite the expected decrease in domestic sales, mainly as a result of growth in exports of Hemlibra to Roche, increased royalty income, and the lower cost of sales.

Core EPS[1, 2]



1. Effective July 1, 2020, Chugai has implemented a three-for-one stock split of its common stock. Figures are calculated based on the assumption that the stock split was implemented at the beginning of 2017.
2. Core EPS = Core net income attributable to Chugai shareholders / Diluted weighted average shares outstanding

Fundamental Profit Distribution Policy and Dividends

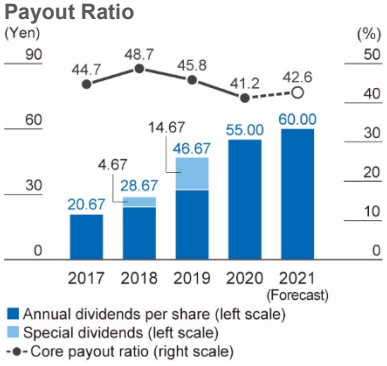
After taking into account projected business results and evolving needs in strategic investment funding, Chugai aims to offer shareholders a stable dividend, with a target payout ratio of 45 percent on average based on Core EPS. Internal reserves will be used to increase corporate value through investments for further growth in existing strategic areas and to explore future business opportunities.

(Yen)

	2018	2019	2020	2021 Forecast
Basic net income per share (EPS)[3]	56.36	95.95	130.66	—
Core EPS[3]	58.81	101.93	133.39	141.00
Equity per share attributable to Chugai shareholders (BPS[3])	460.42	519.91	596.16	—
Cash dividends per share[3]	28.67	46.67	55.00	60.00
Core payout ratio	48.7%	45.8%	41.2%	42.6%
Core payout ratio (five-year average)	48.6%	47.4%	44.9%	43.8%

- Cash dividends per share for 2020 totaled ¥55, and the five-year average Core EPS payout ratio was 44.9 percent.
- The dividend forecast for 2021 calls for an interim dividend of ¥30 and a year-end dividend of ¥30.

Cash Dividends per Share[1]/Core Payout Ratio



3. Effective July 1, 2020, Chugai implemented a three-for-one stock split of its common stock. Figures are calculated based on the assumption that the stock split was implemented at the beginning of 2018.

Business Risks

Principal Risks

Chugai's corporate performance is subject to material impact from a range of possible future events. Below, we list what we consider the principal sources of risk to our business operations.

We recognize the possibility of these risk events actually occurring, and have prepared policies to forestall such events and take appropriate measures when they do occur.

Please note that this does not constitute a comprehensive listing of all risks facing the Chugai Group and that there are other risks, which may affect investment decisions. The categories of future risks identified in this section are based on assessments made by Chugai as of December 31, 2020.

1. Potential Risks in Management Strategy (Strategic Risk)

1) Technology and Innovation

Under its strategic alliance with Roche, the Chugai Group works to enhance its strengths in science and technology for the creation of innovative drugs. The Group is focused specifically on developing drug discovery technology for mid-size molecules to address unmet medical needs for which solutions have so far not been found using small molecules and therapeutic antibodies. Chugai is also actively progressing with the use of digital technology to boost efficiency in the research process.

However, in the constantly advancing fields of science, drug discovery technology, and digital technology, delayed development of in-house technology, the emergence of solutions with strong competitive advantage, and similar eventualities carry the risk of decline in the value of in-house technology and products, revision of development plans, and other negative outcomes. The Chugai Group applies a range of intellectual property (IP) rights in its business activities, which it understands to either be its own proprietary rights or rights that it is licensed to use under relevant laws. Nevertheless, there remains the possibility, based on a different understanding, that the Group might suffer an infringement of its IP rights by a third party or itself infringe on those of a third party. Major disputes involving IP rights associated with the Group's business activities could have a material impact on its strategy execution through outcomes such as reduction in projected profits, suspension of production and sale, loss of access to use of technologies, and payment of usage fees.

To respond to these risks, Chugai works through selection and concentration of management resources to increase the superiority of its proprietary technology, securing appropriate access to cutting-edge science and technology. At the same time, we seek to increase diversification by enhancing external collaborations. For the development of mid-size molecule drugs, we are taking measures for stronger collaboration between the relevant internal organizations (drug discovery, development, and pharmaceutical technology and production) and to address IP rights issues with an enhanced IP strategy.

Based on the risk appetite of the Group, Chugai takes risks to aggressively pursue opportunities to create innovation. In parallel, we seek to reinforce factors that encourage innovation in such areas as workplace environment, organizational culture, and human resource development and to reduce risks that hinder innovation.

2) Healthcare System and Pharmaceutical Regulation

In order to address unmet medical needs, the Chugai Group is focused on the successive creation of innovative new drugs that can achieve the status of first-in-class (an original drug of that is highly novel and useful, and will significantly change the therapeutic system) and best-in-class (a drug that offers clear advantages over other existing drugs in the same category such as those with the same molecular target).

Meanwhile, Japan and other countries are strengthening measures to reduce drug prices as issues such as aging populations and surging healthcare costs put strains on their finances. The great fiscal mobilization associated with the COVID-19 pandemic is expected to further accelerate efforts by each country to curb healthcare costs. In Japan specifically, in addition to the National Health Insurance (NHI) drug price revision that takes place every two years, a revision in interim years has been introduced from 2021, with approximately 70 percent of all products designated as potential candidates for price reduction. If the policy of drug price reduction and promotion of generics is expanded, the result will be a still greater reduction in revenues than so far experienced, which would risk impairing investment in research and development.

Moreover, we believe that this policy will lead to the continued advance of value-based healthcare (VBHC), adding further momentum to the trend to pursue only solutions that offer true value for patients. Chugai will continue efforts to deliver new value through innovation and to strengthen its earnings structure. At the same time, we will work to upgrade overseas intelligence functions to remain current with reforms to the systems and pharmaceutical regulation of different countries and trends in overseas markets.

3) Markets and Customers

As well as the increasing market penetration of competing products, generics, and biosimilars, recent years have seen the development of new therapeutic modalities including regenerative medicine, cellular and genomic therapies, and therapeutic nucleic acids. Accompanying this, there have been increased calls for integrated value delivery from prevention, diagnosis, and treatment through to post-treatment. Meanwhile, the emergence of a digital oligopoly brought on by the entry of IT platform providers into the healthcare industry is engendering new technologies and threats in life science and digital markets. The competitive environment in the healthcare industry is therefore changing rapidly. Moreover, the COVID-19 pandemic has impacted pharmaceutical companies' systems for information provision, so that the nature of customer contact points is undergoing significant alteration.

These conditions carry the potential risk of decline in market position and product competitiveness and could result in pressure to carry out a fundamental revision of such systems due to the rapid change in customer contact points.

In order to address these risks, the Chugai Group works to

successively create new drugs and to diversify its product range. The Group is simultaneously engaged in efforts to advance personalized healthcare (PHC), which realizes optimal diagnosis for the individual patient through gene panel testing. We are also progressing with building a new system for value delivery to customers via a new customer engagement model with an approach that brings together physical, remote, and digital elements to match customer needs.

4) Business Foundation

i. Strategic alliance with Roche

Under its strategic alliance with Roche, Chugai is the only pharmaceutical partner of Roche in the Japanese market and has granted Roche first refusal rights with respect to Chugai's products in global markets outside Japan, excluding South Korea and Taiwan. Consequently, Chugai has in-licensed and out-licensed many products and projects from and to Roche. Changes in Chugai's strategic alliance with Roche for any reason could have a material impact on business performance. There is the additional risk that underperformance by Roche's global drug discovery network could lead to a decline in the stable revenue source provided by products in-licensed from Roche and cause delay in the global market penetration of Chugai products out-licensed to Roche, resulting in a decline in revenues and other negative outcomes. The Chugai Group is committed to pursuing innovation for the successive creation of new drugs, and will work in this way to continue contributing to the value creation of the Roche Group as a whole.

ii. Personnel and organization

In 2020, Chugai introduced a new personnel system designed to assign the right people to the right positions, establish an advanced system of talent management, and foster an organizational culture that encourages a bold spirit of challenge. In addition, we will focus on acquiring, developing, and fulfilling highly specialized talent, such as data scientists and other digital talent, that are key to the execution of our strategy. Certain risks are nevertheless envisioned. Delay in the securing and development of human resources or a drastic change in the business environment causing a change in the nature of the required work operations could result in mismatch, shortage, surplus, or other human resource issues, while innovation could be hindered by failure to create the envisaged organizational culture.

To address these risks, we have established clearly defined requirements for the human resources that are key to strategy execution, working thus to enhance the plan-based securing and development of human resources. With stronger investment in organizations and human resources, we will put in place an organizational structure and strategic recruitment plans that take careful account of trends in the business environment.

iii. Digital platforms

Despite accelerated digital investment to achieve significant increases in productivity in all value chains, there is the possibility that digital technology will fail to advance and that digital transformation (DX) will stagnate and technical issues arise due to insufficient in-house digital capability, a lack of understanding of digital compliance, and other factors. We will undertake timely revision of our DX strategy and work to strengthen capabilities. At the same time, we will make active use of specialist external human resources.

iv. Earnings structure

With rapid technological advances in the manufacturing industry and fierce competition from pharmaceutical companies in Japan and overseas, the earnings structure could be impacted by increased investment and costs required for R&D expenditures. We will therefore seek to minimize operating costs by applying digital technology to improve processes and raise productivity, and will emphasize careful scrutiny of investment projects.

2. Risks in the Execution of Business Operations (Operational Risks)

1) Quality and Side Effects

For stable delivery to patients of high-value products and services, we believe that prime importance attaches to product efficacy and safety, and the quality to guarantee these. The Chugai Group evaluates and confirms the validity of business processes during the product lifecycle and carries out corresponding improvement, and ensures the reliability of data through introduction and operation of a global IT system. For consistent quality assurance, we also emphasize enhanced collaboration with internal and external partners and hold regular meetings for considering and discussing quality together. However, if for some reason concerns were raised over product quality, a material impact on business performance could result through termination of sales, product recall, loss of public trust, and other consequences.

Pharmaceutical products and medical devices are approved by regulatory authorities in each country after strict review. Following approval, the Chugai Group continues with comprehensive activities to monitor drug safety, and uses its post-marketing surveillance and safety information database tools (PMS and SAFETY DB tools) to carry out swift provision of information matched to patient characteristics. We also operate an app to support patient adherence to medication that promotes smooth communication between patients and healthcare professionals, and helps alleviate the anxiety of patients undergoing treatment. Furthermore, we have established a safety consulting and networking system for healthcare professionals consisting mainly of our Safety Experts, who are professional safety staff. Through these and other initiatives, we are working to strengthen activities for the provision of safety information and thereby promote the proper use of pharmaceuticals. However, because of the characteristics of the products, it is difficult to completely prevent adverse outcomes, such as side effects from their use even if all possible safety measures are taken. In cases where side effects occur, particularly newly discovered serious side effects, in addition to revising the precautions listed in the package insert, the Group may have to terminate sales, recall products, or take other measures with a material impact on business performance.

2) IT Security and Information Control

Chugai makes full use of a wide range of IT systems in its business activities. If negligence or willful misconduct by employees or service providers, or external factors such as cyberattacks, were to cause a system malfunction, the suspension of external service delivery, interference with the content of information provided, or other issues, this could result in suspension or delay of business activities, revision of plans, and costs for urgent response and related measures. In the event of the leakage of trade secrets relating to research and development or other activities, or of personal information or other confidential material, Chugai could experience loss of

competitive advantage, loss of public trust, liability for damages, or other outcomes with a material impact on business performance.

To address these risks, the Chugai Group has established related rules and conducts regular education and drills for employees. We additionally work to strengthen system robustness and availability, take measures to reinforce cyberattack and virus detection functions, and upgrade monitoring systems and systems for response to information security incidents. We have moreover put in place a security management system to evaluate and enhance these countermeasures Group-wide, which operates to constantly reduce risk.

3) Impact from Large-Scale Disasters and Other Events
In the event of severe damage to Chugai Group business sites or sales locations, or to the buildings, facilities, or other property of business partners being caused by a natural disaster such as an earthquake, typhoon, or flood, or an accident such as a fire, or in the event of business activities being restricted due to a pandemic caused by a novel influenza virus or other pathogen, this could result in the suspension of drug supplies, facility repair costs and other expenditures, delay in the market penetration of new products, associated reduction of revenues, and other outcomes with a material impact on business performance.

The Group has prepared for these risks and works to reduce them with measures to protect employees and ensure an uninterrupted supply of pharmaceuticals. Measures include the use of property and casualty insurance, the implementation of business continuity plans (BCPs) and drills, the use of aseismic construction, and the maintenance of safety stock.

4) Human Rights
Delays in addressing workplace harassment or human rights issues including occupational health and safety could weaken the Chugai Group's human resources in ways such as negatively affecting the physical and mental health of employees and increasing employee turnover, and damaging public trust in the Group, which could have a material impact on business performance.

The Group addresses these human rights issues with continuous training for executives and employees, as well as with harassment hotlines. It also conducts health and safety programs as part of its health and productivity management.

In addition, the Group asks suppliers to respect human rights and works with them to resolve issues related to human rights.

5) Supply Chains
Raw material suppliers, contract manufacturers, or other business partners could be affected by damage to facilities or by restriction of business activities due to natural disasters, accidents, pandemics, etc. Delays in addressing compliance infringements or environmental issues in the supply chain could also cause problems in procuring raw materials and maintaining production. This might result in loss of public trust, decline in revenues and market share, and consequent material impact on business performance.

The Chugai Group has prepared for these supply chain risks. Measures for the uninterrupted supply of pharmaceuticals include the use of property and casualty insurance, the formulation of BCPs, maintenance of safety stock, and the establishment of systems for sharing information with suppliers.

We also work with suppliers to resolve issues such as supply chain compliance and environmental issues that the Group cannot resolve on its own.

6) Global Environmental Issues
The Chugai Group complies with environment-related laws and regulations and has established a set of even higher voluntary standards that it is committed to achieving and will continue to strengthen and enhance. However, the Group may have to bear expenses for countermeasures or liability for damages should unexpected contamination by harmful substances or collateral damage occur, which could have a material impact on business performance.

We consider climate change to be a key challenge in protecting the global environment, and are therefore committed to reducing greenhouse gas (GHG) emissions. As part of this commitment, in addition to reducing energy consumption, we have set 2025 as the target date for reaching a rate of 100 percent use of sustainable electricity that does not emit GHG. However, if there is a delay in responding to climate change in terms of technologies and facilities, this may result in the revision of capital investment plans and additional costs.

In addition, more stringent environmental regulations in the future may increase expenditures for response measures and limit Group business activities including research, development, and manufacturing.

To disclose environmental information with a high level of transparency and reliability, the Group receives third-party assurance of its environmental performance data annually. Additionally, based on the framework set out in the recommendations of the Task Force on Climate-related Financial Disclosures (TCFD), we carried out a qualitative evaluation and scenario analysis taking into account the risks and opportunities that climate change presents for Chugai, which did not identify any major climate-related risk requiring large-scale business conversion or investment in the long term. Chugai will conduct continuous analysis and evaluation going forward and seek proactive solutions to environmental issues.

7) Impact of COVID-19
The Chugai Group responded to the COVID-19 pandemic with initiatives to introduce highly flexible workstyles such as teleworking and to establish new workstyles that maintain and improve productivity. In view of its social responsibility for ensuring a stable supply of drugs to patients, Chugai's basic policy following the declaration of a state of emergency was to maintain the ability to continue the required drug supply.

Going forward, we will continue working to maintain a stable supply of drugs, while at the same time taking measures to prevent infection among employees and related business personnel. If business activities are restricted in the future by further spread of the infection or similar reasons, the resulting suspensions or delays in the supply chain could have a material impact on product supply. Moreover, there might be delays in the progress of research and clinical studies, and in the market penetration of new products and other items due to restrictions on the activities of our medical representatives (MRs).

Consolidated income statement

(Millions of yen)

	2020 Year ended December 31	2019 Year ended December 31	2018 Year ended December 31
Revenues	**786,946**	**686,184**	**579,787**
Sales	633,314	588,896	527,844
Royalties and other operating income	153,631	97,288	51,943
Cost of sales	(273,465)	(266,071)	(262,847)
Gross profit	**513,481**	**420,113**	**316,940**
Marketing and distribution	(72,585)	(77,183)	(73,706)
Research and development	(117,850)	(107,942)	(99,202)
General and administration	(21,816)	(24,391)	(19,710)
Operating profit	**301,230**	**210,597**	**124,323**
Financing costs	(62)	(125)	(111)
Other financial income (expense)	(1,477)	545	449
Other expense	(1,504)	(3,124)	(3,212)
Profit before taxes	**298,188**	**207,893**	**121,449**
Income taxes	(83,455)	(50,333)	(28,370)
Net income	**214,733**	**157,560**	**93,079**
Attributable to:			
Chugai shareholders	214,733	157,560	92,488
Non-controlling interests	—	—	591
Earnings per share:			
Basic (Yen)*	130.66	95.95	56.36
Diluted (Yen)*	130.53	95.81	56.27

* Effective July 1, 2020, Chugai has implemented a three-for-one stock split of its common stock. Figures are calculated based on the assumption that the stock split was implemented at the beginning of 2018.

Consolidated statement of comprehensive income

(Millions of yen)

	2020 Year ended December 31	2019 Year ended December 31	2018 Year ended December 31
Net income recognized in income statement	**214,733**	**157,560**	**93,079**
Other comprehensive income (OCI):			
Remeasurements of defined benefit plans	3,630	329	(2,472)
Financial assets measured at fair value through OCI	(22)	(255)	363
Items that will never be reclassified to the income statement	**3,608**	**74**	**(2,109)**
Financial assets measured at fair value through OCI	12	(17)	0
Cash flow hedges	(3,072)	(1,317)	(225)
Currency translation of foreign operations	1,467	(1,172)	(3,158)
Items that are or may be reclassified to the income statement	**(1,593)**	**(2,506)**	**(3,383)**
Other comprehensive income, net of tax	**2,015**	**(2,433)**	**(5,492)**
Total comprehensive income	**216,748**	**155,127**	**87,587**
Attributable to:			
Chugai shareholders	216,748	155,127	87,078
Non-controlling interests	—	—	509

Consolidated balance sheet

(Millions of yen)

	2020 December 31, 2020	2019 December 31, 2019	2018 December 31, 2018
Assets			
Non-current assets:			
Property, plant and equipment	289,218	255,559	222,388
Right-of-use assets	8,272	9,749	—
Intangible assets	23,880	23,540	22,699
Financial non-current assets	2,841	2,958	9,723
Deferred tax assets	47,934	42,680	35,568
Defined benefit plan assets	492	—	—
Other non-current assets	27,954	24,750	29,077
Total non-current assets	**400,592**	**359,235**	**319,455**
Current assets:			
Inventories	183,893	168,122	159,360
Accounts receivable	253,342	181,641	179,556
Current income tax assets	12	0	3
Marketable securities	166,287	129,117	102,533
Cash and cash equivalents	212,333	203,941	146,860
Other current assets	19,039	16,858	11,781
Total current assets	**834,906**	**699,680**	**600,093**
Total assets	**1,235,498**	**1,058,915**	**919,548**
Liabilities			
Non-current liabilities:			
Long-term debt	—	—	(82)
Deferred tax liabilities	(9,166)	(9,304)	(9,031)
Defined benefit plan liabilities	(2,282)	(7,094)	(14,671)
Long-term provisions	(2,142)	(2,348)	(2,072)
Other non-current liabilities	(5,835)	(6,914)	(1,946)
Total non-current liabilities	**(19,425)**	**(25,662)**	**(27,802)**
Current liabilities:			
Short-term debt	—	—	(133)
Current income tax liabilities	(63,171)	(41,047)	(19,567)
Short-term provisions	(358)	(4)	(1)
Accounts payable	(100,396)	(77,635)	(71,706)
Other current liabilities	(72,146)	(60,582)	(43,810)
Total current liabilities	**(236,070)**	**(179,268)**	**(135,218)**
Total liabilities	**(255,495)**	**(204,930)**	**(163,019)**
Total net assets	**980,003**	**853,985**	**756,529**
Equity:			
Capital and reserves attributable to Chugai shareholders	980,003	853,985	755,864
Equity attributable to non-controlling interests	—	—	664
Total equity	**980,003**	**853,985**	**756,529**
Total liabilities and equity	**1,235,498**	**1,058,915**	**919,548**

Consolidated statement of cash flows

(Millions of yen)

	2020 Year ended December 31	2019 Year ended December 31	2018 Year ended December 31
Cash flows from operating activities			
Cash generated from operations	340,228	249,500	151,857
(Increase) decrease in working capital	(64,421)	6,205	4,486
Payments made for defined benefit plans	(4,656)	(11,540)	(2,652)
Utilization of provisions	(26)	(2)	(29)
Other operating cash flows	694	(2,741)	(3,022)
Cash flows from operating activities, before income taxes paid	**271,820**	**241,423**	**150,639**
Income taxes paid	(66,785)	(34,782)	(31,565)
Total cash flows from operating activities	**205,035**	**206,641**	**119,074**
Cash flows from investing activities			
Purchase of property, plant and equipment	(57,040)	(53,009)	(71,785)
Purchase of intangible assets	(4,349)	(8,168)	(5,886)
Disposal of property, plant and equipment	(22)	119	49
Interest and dividends received	100	197	200
Purchases of marketable securities	(248,143)	(256,768)	(263,503)
Sales of marketable securities	211,000	230,158	264,711
Purchases of investment securities	(177)	(1,013)	(709)
Sales of investment securities	319	6,743	2,863
Other investing cash flows	—	0	(0)
Total cash flows from investing activities	**(98,312)**	**(81,741)**	**(74,060)**
Cash flows from financing activities			
Purchase of non-controlling interests	—	(2,307)	—
Interest paid	(34)	(27)	(5)
Lease liabilities paid	(8,432)	(8,861)	—
Dividends paid to Chugai shareholders	(91,442)	(56,370)	(35,010)
Dividends paid to non-controlling shareholders	—	—	(791)
Exercise as part of equity compensation plans	440	735	996
(Increase) decrease in own equity instruments	(30)	(25)	(19)
Other financing cash flows	—	(16)	(187)
Total cash flows from financing activities	**(99,497)**	**(66,872)**	**(35,014)**
Net effect of currency translation on cash and cash equivalents	1,166	(947)	(2,215)
Increase (decrease) in cash and cash equivalents	**8,393**	**57,081**	**7,785**
Cash and cash equivalents at January 1	203,941	146,860	139,074
Cash and cash equivalents at December 31	**212,333**	**203,941**	**146,860**

Consolidated statement of changes in equity

(Millions of yen)

	Attributable to Chugai shareholders						
	Share capital	Capital surplus	Retained earnings	Other reserves	Subtotal	Non-controlling interests	Total equity
Year ended December 31, 2019							
At January 1, 2019	**73,000**	**66,043**	**618,091**	**(1,270)**	**755,864**	**664**	**756,529**
Net income	—	—	157,560	—	157,560	—	157,560
Financial assets measured at fair value through OCI	—	—	—	(272)	(272)	—	(272)
Cash flow hedges	—	—	—	(1,317)	(1,317)	—	(1,317)
Currency translation of foreign operations	—	—	—	(1,172)	(1,172)	—	(1,172)
Remeasurements of defined benefit plans	—	—	329	—	329	—	329
Total comprehensive income	**—**	**—**	**157,889**	**(2,761)**	**155,127**	**—**	**155,127**
Dividends	—	—	(56,373)	—	(56,373)	—	(56,373)
Equity compensation plans	16	52	—	—	68	—	68
Own equity instruments	—	941	—	—	941	—	941
Changes in non-controlling interests	—	—	(1,662)	19	(1,643)	(664)	(2,307)
Transfer from other reserves to retained earnings	—	—	4,131	(4,131)	—	—	—
At December 31, 2019	**73,016**	**67,037**	**722,076**	**(8,143)**	**853,985**	**—**	**853,985**
Year ended December 31, 2020							
At January 1, 2020	**73,016**	**67,037**	**722,076**	**(8,143)**	**853,985**	**—**	**853,985**
Net income	—	—	214,733	—	214,733	—	214,733
Financial assets measured at fair value through OCI	—	—	—	(9)	(9)	—	(9)
Cash flow hedges	—	—	—	(3,072)	(3,072)	—	(3,072)
Currency translation of foreign operations	—	—	—	1,467	1,467	—	1,467
Remeasurements of defined benefit plans	—	—	3,630	—	3,630	—	3,630
Total comprehensive income	**—**	**—**	**218,363**	**(1,615)**	**216,748**	**—**	**216,748**
Dividends	—	—	(91,467)	—	(91,467)	—	(91,467)
Equity compensation plans	186	(774)	—	—	(588)	—	(588)
Own equity instruments	—	1,324	—	—	1,324	—	1,324
Transfer from other reserves to retained earnings	—	—	121	(121)	—	—	—
At December 31, 2020	**73,202**	**67,586**	**849,093**	**(9,879)**	**980,003**	**—**	**980,003**