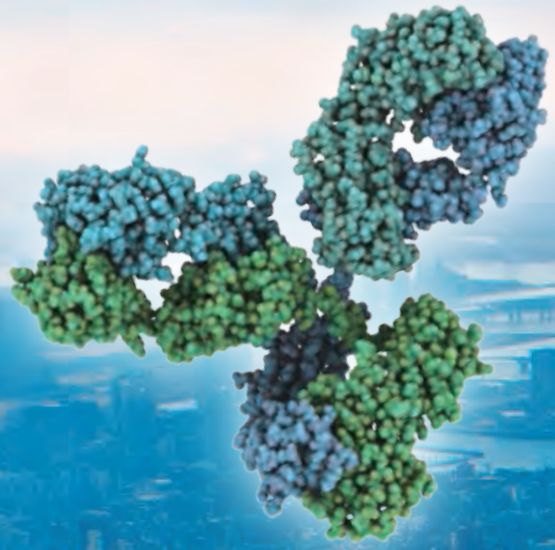
CHUGAI

Roche Group

Annual Report 2014

Fiscal year ended December 31, 2014



INNOVATION BEYOND IMAGINATION

Innovation all for the patients

CHUGAI PHARMACEUTICAL CO., LTD.

25 Categories of Chugai's Strengths

アンメットメディカルニーズを満たす革新的な新薬

ドラッグラグ解消につながる国際共同治験

国産初の抗体医薬品アクテムラ

国内No.1シェアを誇るがん領域の製品力

骨・腎領域における国内トップクラスの製品力

がん領域の充実したパイプライン

アンメットメディカルニーズに対応した開発品

ロシュからの集約的・効率的な新薬導入

バイオ医薬でトップレベルのジェネンテック社とのネットワーク

ロシュ・グループで230万の化合物ライブラリー

国内トップレベルのバイオ技術力

中外独自の抗体技術

がん領域におけるグローバルレベルの創薬力

中分子医薬の創薬技術

バイオ医薬品承認までの豊富な経験

バイオマーカー測定技術と医薬品との同時開発体制

個別化医療のパイオニアであるロシュ診断薬事業との協業

エビデンスに基づいた安全性情報の提供

安全性情報の収集・分析・対策立案力

グローバル水準の安全性評価・分析体制の確立

メディカルスタッフからの高い支持

地域医療連携の推進

高い専門性を備えたがんMR

チーム医療推進への充実したサポート

誠実な人財

Business Philosophy

Innovation all for the patients

Innovation all for the patients

Chugai will become a top pharmaceutical company by constantly innovating to carve out its own path to value creation.

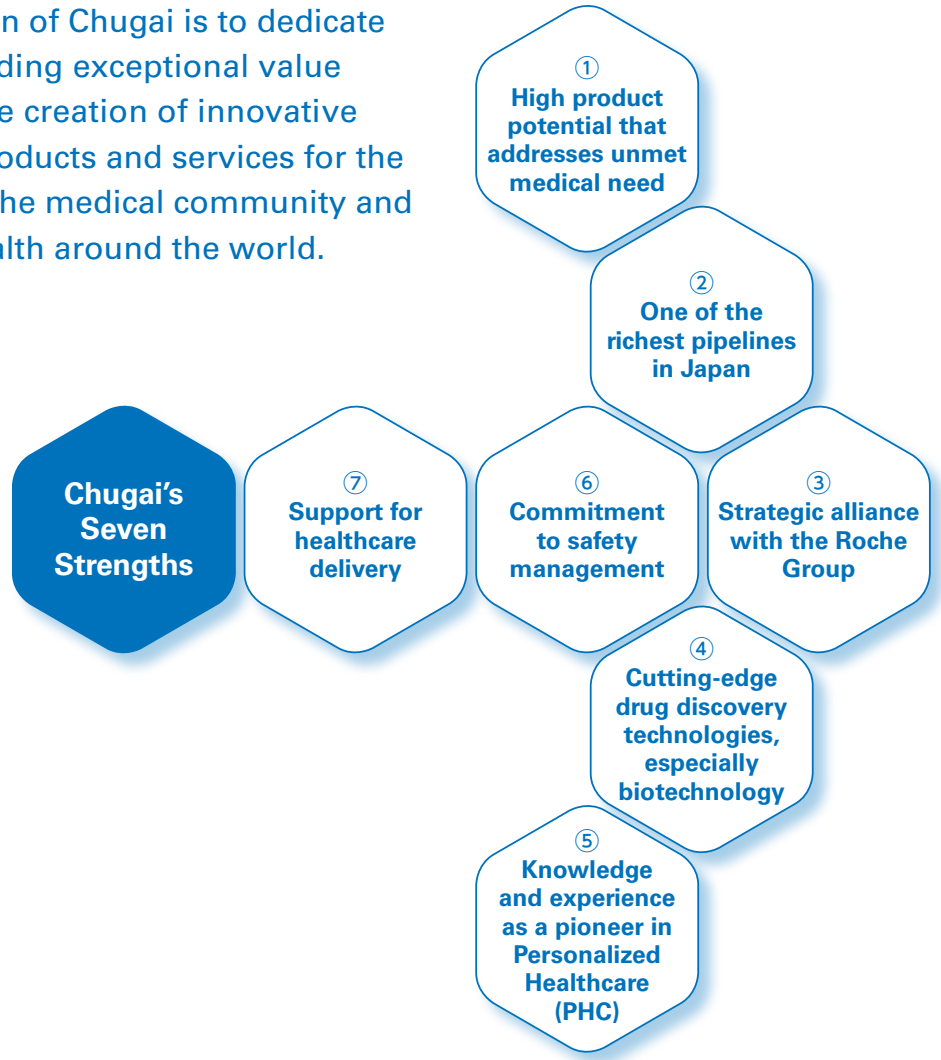
Osamu Nagayama
Representative Director, Chairman & CEO

PROFILE

The mission of Chugai Pharmaceutical Co., Ltd. and its consolidated subsidiaries (“Chugai”) is to dedicate itself to adding exceptional value through the creation of innovative medical products and services for the benefit of the medical community and human health around the world. We at Chugai believe that achieving this mission will result in the creation and improvement of corporate value, and we continue to take on new challenges based on the business philosophy of “Innovation all for the patients.” Our aim to become a top pharmaceutical company is reflected in our new slogan, “INNOVATION BEYOND IMAGINATION,” which embodies our commitment to being a company that consistently exceeds expectations with innovative ideas.

Mission

The mission of Chugai is to dedicate itself to adding exceptional value through the creation of innovative medical products and services for the benefit of the medical community and human health around the world.



Contents

4 Message from the CEO/ Introduction

Message from the CEO 4
Chugai's Strengths..... 6
Chugai's Business Model 12
Financial and Non-Financial Highlights 16

20 Strategy

Overview and Progress of ACCEL 15..... 22
Message from the President..... 23
Message from the Deputy Chairman..... 28
Discussion on Chugai's Value Creation..... 30

34 Feature:
Leadership and Increased Value Driven by Chugai's Unique Strengths
Our Approach to Three Key Issues in the Pharmaceutical Industry

Adoption of Personalized Healthcare 36
Healthcare Compliance 39
Enhancing Safety Management Systems 41
Chugai's Seven Unique Strengths..... 43

44 Performance Report and Future Initiatives

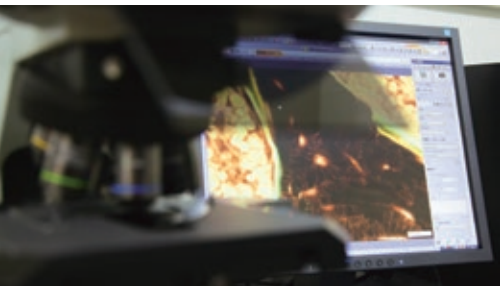
Overview of Activities in 2014..... 46
Review of Operations 50
Marketing 52
Development..... 62
Production and Procurement..... 66
Research 68
Medical Affairs 72
Drug Safety 73
Intellectual Property..... 75
Environmental Protection and Occupational Safety 77
Social Contribution Activities 80
Human Resources..... 82
Corporate Governance 85
Corporate Communication 92
Board of Directors/ Audit & Supervisory Board..... 94
Executive Officers..... 96

97 Data Section

Development Pipeline 98
Basic Information..... 100
Glossary..... 114

115 Financial Section

Message from the CFO..... 116
11-Year Financial Summary..... 118
Management's Discussion and Analysis..... 120
Consolidated Financial Statements 128
Independent Auditor's Report..... 173
Network 174
Organization..... 176
Shareholder Information..... 177
Corporate Data..... 178



Editorial Policy

Chugai has adopted integrated reporting to communicate both the financial and non-financial aspects of its corporate value by combining the traditional annual report with the print version of the corporate social responsibility (CSR) report.

For CSR information, we are focusing on the main initiatives of 2014 in this annual report and providing our action policies and more detailed information on the Chugai website.

Scope of This Report

This report presents information on Chugai Pharmaceutical Co., Ltd. and its consolidated subsidiaries. In some places, however, it gives data specifically pertaining to Chugai Pharmaceutical Co., Ltd.

Timeframe

The basic timeframe for this report is the financial reporting period of January to December 2014. However, in view of the importance of providing the latest information available, some information relating to activities that occurred in 2015 is included, mainly in research and clinical development data.

Information in This Report

The information presented in this report is information that Chugai believes to be of high importance given its significance in building Chugai's corporate value over the short, medium and long term, and its degree of impact on stakeholders. More detailed CSR information is reported on the Chugai website.

Reference Guidelines

Since Annual Report 2013, content has focused on value creation, using as reference The International Integrated Reporting Framework issued by the International Integrated Reporting Council (IIRC).* This framework is designed to promote reporting on a company's short-, medium- and long-term value creation, underpinned by the seven guiding principles below, and is consistent with Chugai's integrated reporting objectives and fundamental thinking.

A) Strategic focus and future orientation, B) Connectivity of information, C) Stakeholder relationships, D) Materiality, E) Conciseness, F) Reliability and completeness, G) Consistency and comparability

CSR information was prepared with reference to the Environmental Reporting Guidelines (Fiscal Year 2012 Edition) of the Ministry of the Environment of Japan and the 2013 Sustainability Reporting Guidelines of the Global Reporting Initiative (GRI).

* Established in 2010 to provide an international corporate reporting framework, the IIRC is a global coalition of private corporations, investors, the accounting profession, government agencies, NGOs and others. The framework was released in December 2013.

Forward-Looking Statements

This annual report includes forward-looking statements pertaining to the business and prospects of Chugai Pharmaceutical Co., Ltd. and its consolidated subsidiaries ("Chugai" or "the Company"). These statements reflect the Company's current analysis of existing information and trends. Actual results may differ from expectations due to risks and uncertainties that may affect the Company's businesses.

Note

The information regarding pharmaceuticals (including products under development) is not intended for advertising, promotion or medical advice. All trademarks are the property of their respective holders.

Click on items in the table of contents to jump to the relevant pages.

About the Cover

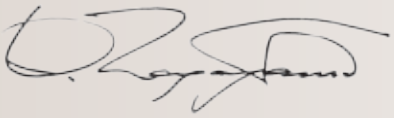
All of Chugai's activities are based on its business philosophy of "Innovation all for the patients" and its unique strengths. To express this idea, we have used a gatefold design for the cover. The fold-out flap can be inserted at section gate pages or elsewhere in this report as a bookmark.

Message from the CEO

Innovation all for the patients——

Chugai will become a top pharmaceutical company by constantly innovating to carve out its own path to value creation.

Osamu Nagayama
Representative Director, Chairman and CEO



Chugai is aiming to achieve its goal of becoming a "top pharmaceutical company" in the second half of this decade. We are currently executing our mid-term business plan ACCEL 15 as a preliminary step toward reaching that goal as early as possible.

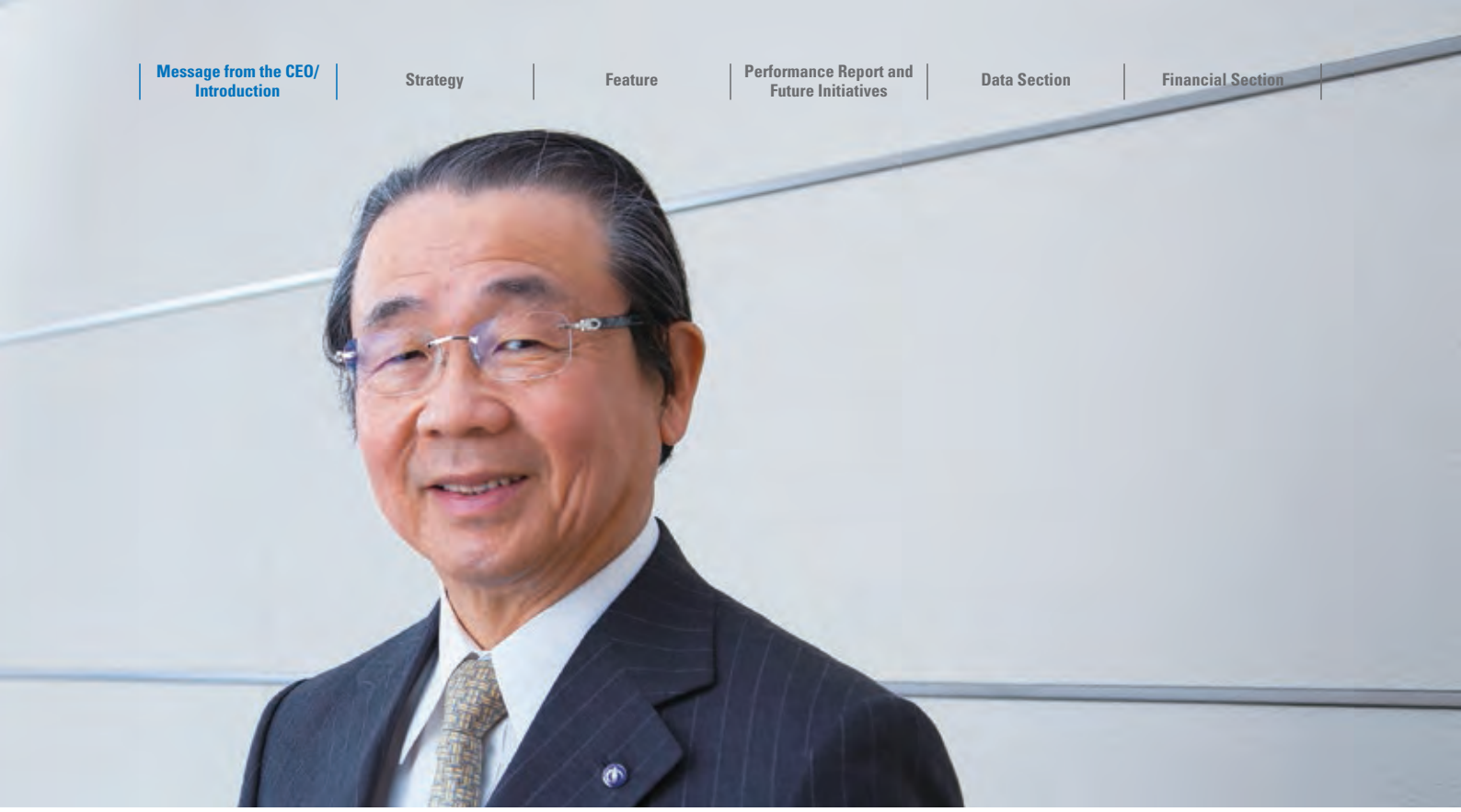
In 2014, successful initiatives that took advantage of Chugai's unique strengths moved us steadily closer to becoming a top pharmaceutical company. Strong sales in Japan helped to solidify our presence in oncology and other main therapeutic fields. Alecensa, a treatment for *ALK* fusion gene-positive non-small cell lung cancer, was launched in September, just seven years after the project was conceived. Outside Japan, we are co-developing this drug with our alliance partner Roche, and it has been granted Breakthrough Therapy designation by the U.S. Food and Drug Administration (FDA). In research and development, ACE910, an in-house project that employs Chugai's next-generation antibody engineering technologies for the potential treatment of hemophilia A, has attracted significant attention after showing promise in clinical studies. Co-development with Roche started in 2014. We also made steady progress in building the foundation and making the necessary investments for future growth. We reinforced our research and development bases and production facilities, increased marketing productivity, and enhanced our overseas sales operations.

Around the world, though, the pharmaceutical industry is facing a number of challenges and growing competitive pressure, including a focus on cost controls and health technology assessment (HTA)[1] in many countries due to worsening fiscal conditions, as well as soaring research and development costs, stricter safety and quality regulations, and the transformation of marketing activities.

On the other hand, the healthcare sector is positioned as a growth industry in the Japanese government's growth strategy. A set of measures designed to promote the practical application of innovative drugs, medical devices and medical technologies is expected to provide a boost to industry overall. Regardless of past successes, only companies that respond quickly to these changes and offer new value through continuous innovation will survive and grow.

For us, a "top pharmaceutical company" is a company that provides a high level of satisfaction to stakeholders while receiving their active support and trust. To be such a company, we must lead the way in creating value through seamless innovation achieved by taking risks.

Chugai is celebrating its 90th anniversary in 2015. Over the years, the Company has faced some tough times, but has always found a way forward by boldly taking a different path than others in pursuit of true value for patients. Chugai's founder Juzo Ueno, alarmed at the severe shortage of medicine after the Great Kanto Earthquake of 1923, decided to start the Company in 1925. Later, about 30 years ago, Chugai began to develop biopharmaceuticals. In the 1990s, Chugai decided to make a large investment in the development of Actemra, the first therapeutic antibody originating in Japan. Then, in 2002, an unprecedented strategic alliance with Roche ushered in the Company's new incarnation and transformed its management strategy. Each of these major decisions included unknowns. Nonetheless, these decisions all shaped the foundation of our present business model.



Today, revenues have nearly doubled and operating profit has grown about 2.5 times compared with levels before the alliance. We have world-leading antibody technologies and are conducting research employing next-generation technologies at Chugai Pharmabody Research Pte. Ltd., a subsidiary we established in Singapore in 2012. Just as past innovations led to the successes of today, we must continue to move forward and innovate in order to achieve lasting value creation. There are still many diseases in the world that have no effective treatments, and many countries are facing rapidly aging populations. Chugai's mission is to contribute to human health around the world by accelerating the pace of innovation to create new drugs with first-in-class[2] or best-in-class[3] potential, thus enabling more people to actively participate in society for a longer time.

Based on this idea, we made "acceleration" the keyword of ACCEL 15, our mid-term business plan, and are building a strong foundation to realize our goal of becoming a top pharmaceutical company as early as possible. In 2015, the final year of ACCEL 15, we will focus on reforms aimed at raising our quality and speed to a world-class level.

Discovery research is the key to our growth. To address unmet medical need,[4] we will further develop our proprietary antibody engineering technologies and expand our open innovation[5] initiatives with academia, biotech companies and other institutions. We are also reinforcing our early-stage clinical development functions and collaborating with Roche from earlier stages to accelerate global development. This will enable us to quickly bring the projects generated by our in-house research to market as new medicines, thus maximizing the value of each project earlier. In marketing, we will accurately respond to the needs of patients and healthcare providers by supporting regional healthcare and promoting the adoption of Personalized Healthcare.[6]

The success of these innovations will depend on each of our employees. We are stepping up our efforts to promote diversity in gender, nationality, age and other characteristics to establish our desired corporate culture, one in which our people find solutions through discussions informed by a global perspective and diverse values, and pursue innovation autonomously.

Chugai recently unveiled its new slogan, "INNOVATION BEYOND IMAGINATION." I want Chugai to remain driven by innovation and to pursue its own path.

We will continue innovating for the benefit of patients as we seek to contribute further to healthcare worldwide.

1. A multidisciplinary process of transparently summarizing information on the clinical efficacy, cost effectiveness, social impact and other issues related to new health technologies. HTA provides information to assist in the formulation of safe and effective healthcare policies centered on patients.
2. An original drug that is highly novel and useful, and will significantly change the therapeutic system
3. A drug that offers clear advantages over other existing drugs
4. Medical need that is not adequately met due to a lack of effective treatments
5. Generating innovative, new value by utilizing the technologies and development capabilities of external research networks with universities, research institutions and other organizations, in addition to in-house capabilities
6. A treatment approach designed and implemented according to each patient's unique molecular and genetic profile

Continuously creating and delivering

To address unmet medical need, Chugai applies its proprietary research technologies to create innovative drugs, while making full use of its network with Roche, one of the world's leading pharmaceutical companies. Steadily evolving these strengths is the key to our ability to continue benefitting patients. It is also our responsibility as a leader in therapeutic antibodies and Personalized Healthcare.

Chugai's Seven Strengths

innovative drugs

① High product potential that addresses unmet medical need

② One of the richest pipelines in Japan

③ Strategic alliance with the Roche Group

④ Cutting-edge drug discovery technologies, especially biotechnology

⑤ Knowledge and experience as a pioneer in Personalized Healthcare (PHC)

This part of the feature explains how Chugai is applying its proprietary technologies and knowledge to promote Personalized Healthcare, one of three issues in the pharmaceutical industry that the Company is focusing on.

➡Page 36

Evolving safety essentials to a higher

Ensuring safety is a responsibility of every pharmaceutical company. We believe that we can maximize the value of our products by helping patients and healthcare providers use them more effectively through greater transparency and higher quality in our communication of safety information. We are leveraging our extensive experience to enhance our safety management system – one of the strongest in the Japanese pharmaceutical industry – from the non-clinical stage to clinical and post-marketing phases, and contribute to raising the level of drug safety in Japan.

Chugai's Seven Strengths

level

⑥
Commitment to safety management

This part of the feature explains Chugai's industry leadership in enhancing safety management systems, a second issue in the pharmaceutical industry that the Company is focusing on.

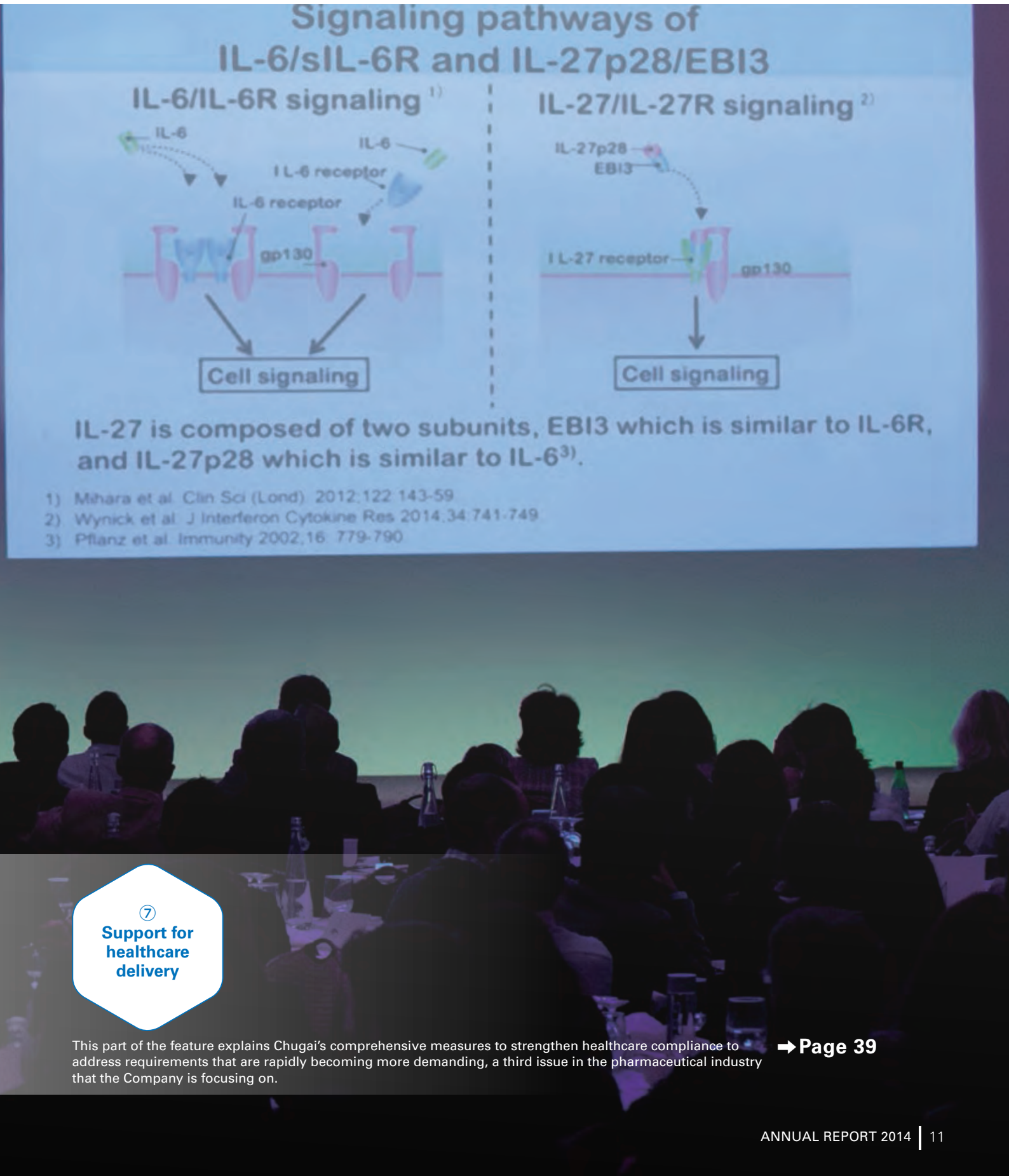
➡**Page 41**

Contributing to the advancement of

Chugai has been applying its expertise and information provision capabilities to contribute to advances in healthcare delivery, with initiatives including the promotion of multidisciplinary team care and regional healthcare coordination. Given expectations that the healthcare environment will continue to change dramatically, we still have many roles to play in raising the level of treatment and care for patients. We aim to increase our corporate value by further enhancing our unique strengths to benefit the medical community and human health around the world.

Chugai's Seven Strengths

healthcare in Japan and worldwide



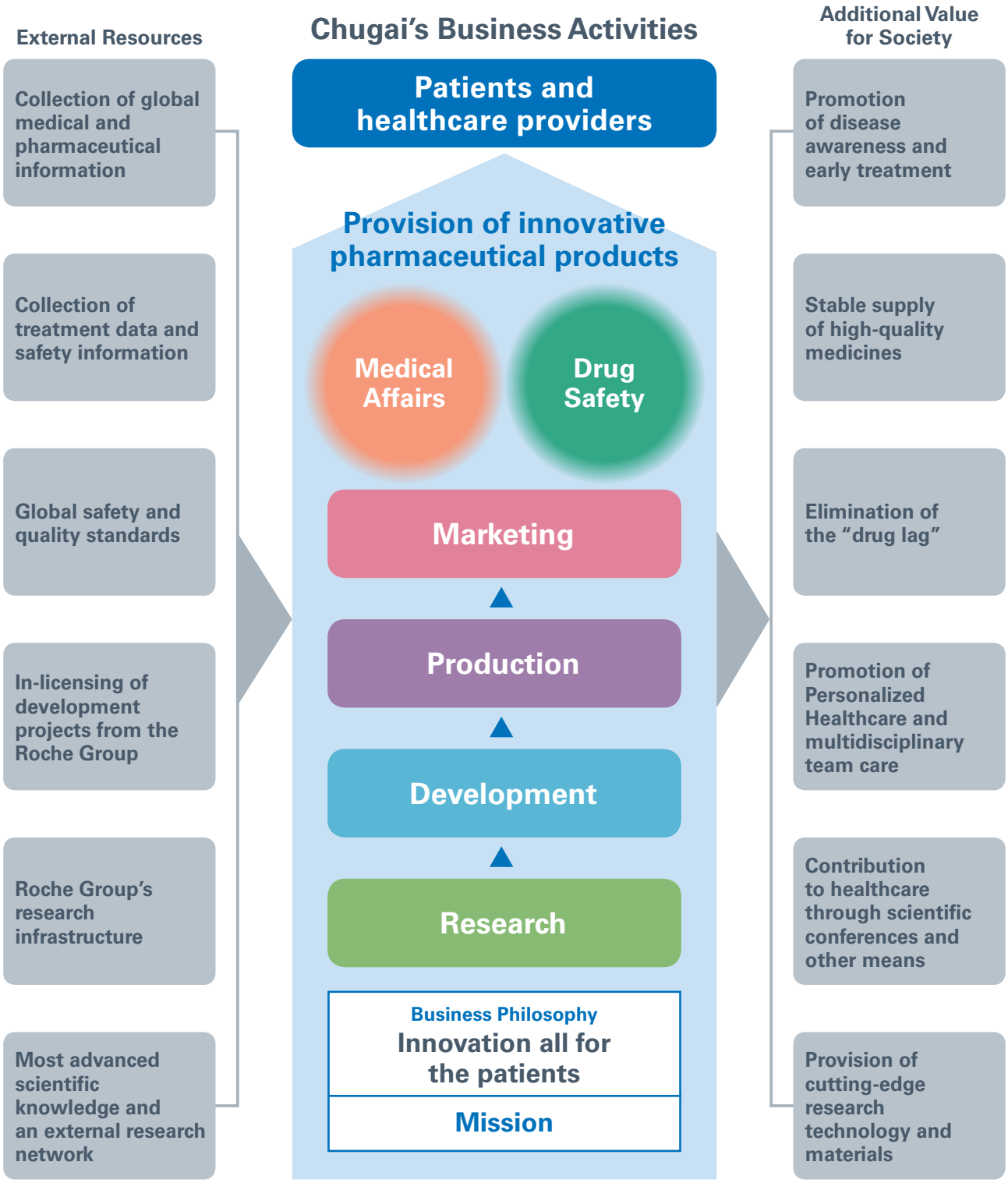
⑦ **Support for healthcare delivery**

This part of the feature explains Chugai's comprehensive measures to strengthen healthcare compliance to address requirements that are rapidly becoming more demanding, a third issue in the pharmaceutical industry that the Company is focusing on.

➡**Page 39**

Chugai's Business Model

Chugai's mission and business philosophy are the foundation of its business. Provision of innovative pharmaceutical products is a source of value creation, and by making maximum use of external resources in our business activities to deliver new value for society we are working to expand our corporate value.



Marketing

Patients' needs are placed at the center of Chugai's marketing functions, which are conducted by medical representatives (MRs) with a high level of expertise. The foundation of our marketing activities is what we call consulting-based promotion, in which our MRs propose treatment options and side-effect management strategies tailored to each individual patient. We also contribute to the advancement of healthcare overall by actively promoting the use of multidisciplinary team care; supporting the coordination of regional healthcare; holding lectures and study sessions; and conducting disease awareness activities. Through these and other proactive initiatives, we will fulfill our mission as a leader in oncology and therapeutic antibodies in Japan.

Production

The most important task of Chugai's production functions is to ensure thorough safety and quality management and stable supply so that patients and healthcare professionals can use our products with confidence. We have built a global-standard safety and quality management system for pharmaceutical products sold in Japan, the United States and Europe, and have established one of Japan's leading pharmaceutical supply platforms in terms of both quality and quantity. In addition, we in- and out-license production technologies with the Roche Group to help ensure stable supply of our global products. To reduce our environmental footprint, our production operations are managed in accordance with stringent voluntary standards based on the Chugai Environmental Policy.

Development

In its development functions, Chugai seeks to deliver innovative medicines to patients as quickly as possible. To accomplish that end, we have established a lifecycle management system for integrated management of all functions at the project level to conduct clinical development with exceptional speed, efficiency and science, supported by the cooperation of many medical institutions and clinical trial facilities. Moreover, through our alliance with the Roche Group, we are implementing many multinational studies and strengthening the process to enable simultaneous development of therapies and corresponding diagnostic agents suitable for Personalized Healthcare. Through these initiatives, we are creating best practices in development and filing in Japan, which may contribute to the advancement of the industry.

Research

In its research functions, Chugai works to continuously create new compounds with first-in-class or best-in-class potential to address unmet medical need. We have industry-leading research and technology capabilities, backed by access to the Roche Group's world-class research infrastructure and a strong external network with academia and other research institutions, in addition to our pioneering advances in antibody engineering technologies. These advantages allow us to contribute to healthcare overall through our own drug discovery projects, scientific conference presentations of our research findings, and application of advanced technologies.

Marketing

35.4[1] **percent**
Top share in the Japanese therapeutic antibody market
(2014)

22.0[1] **percent**
Top share in the Japanese oncology market
(2014)

190
MRs with a high level of expertise[2]
(As of December 31, 2014)

+10.9 percent
Increase in productivity per MR
(Compared with 2013)

1. Copyright 2015 IMS Health Source: JPM 2014. Reprinted with permission. The scope of the market is defined by Chugai.
2. According to Chugai's internal certification system

Production

10,000-liter × 8
2,500-liter × 4
bioreactor capacity
Biological active pharmaceutical ingredient (API) production facilities
(Utsunomiya and Ukima plants)

12
Biopharmaceutical products produced

Over 90
Countries in which Chugai's biopharmaceutical Actemra is sold

2 percent decrease
CO_2 emissions
(Compared with 2013)

Development

29
New products launched and new indications
(2008-2014)

22
Products in-licensed from Roche
(2008-2014)

27
Projects co-developed with the Roche Group
(As of January 28, 2015)

50 percent
Ratio of PHC projects to total development projects
(As of January 28, 2015)

Research

8
In-house projects in pipeline
(As of January 28, 2015)

SMART-Ig
ART-Ig
Chugai's proprietary antibody technologies

34
Publications in academic papers and presentations at scientific conferences regarding Chugai's innovative proprietary technologies
(2010-2014)

122
Published articles regarding Chugai research findings
(2010-2014)

Medical Affairs

Chugai focuses on properly delivering the value of medicines to patients. We have achieved global-level compliance standards, including separation of marketing and medical affairs[3] and funding transparency. At the same time, we are creating internal systems and reinforcing functions to help raise the quality and scientific level of clinical studies in Japan.

15

Contract-based post-marketing studies
(As of December 31, 2014)

10

Fields in which Chugai is conducting contract-based post-marketing studies
(As of December 31, 2014)

60

Staff with the GCP Passport certification of the Japan Society of Clinical Trials and Research
(As of January 31, 2015)

Drug Safety

To ensure that our products can be used with peace of mind, Chugai has established one of the strongest safety management systems in Japan, with expert safety evaluation as well as rapid and timely reporting and disclosure. An industry leader in safety management, Chugai was ahead of its competitors in introducing and applying risk management plans (RMPs) for its products, and communicates safety information globally in collaboration with Roche.

More than 20,000 cases

Safety measures taken (cumulative)

Total number of evaluable patients in all-case registration surveillance for Avastin, Tarceva and Actemra since 2007

Approx. 170,000

Cases for which safety information was collected in clinical trials and post-marketing studies
(January-December 2014)

211

Specialist staff in Drug Safety Division
(As of December 31, 2014)

3. Activities to generate data useful for patient treatment based on knowledge gained in clinical studies, and to optimize patient access to drugs based on that data

Financial and Non-Financial Highlights

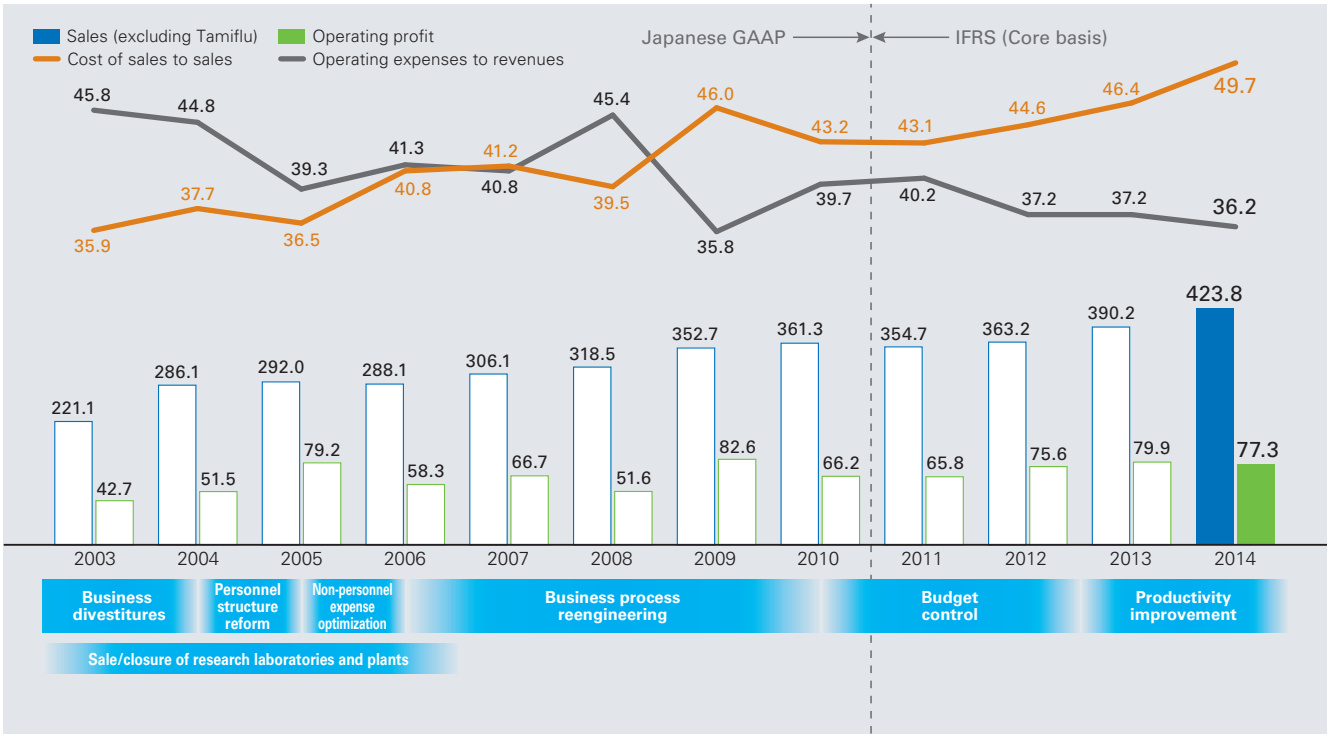
International Financial Reporting Standards (IFRS)

Chugai Pharmaceutical Co., Ltd. and Consolidated Subsidiaries/Years ended December 31
(Figures for 2003 are for the nine months ended December 31, 2003)

Financial Indicators (Core Basis)

Results

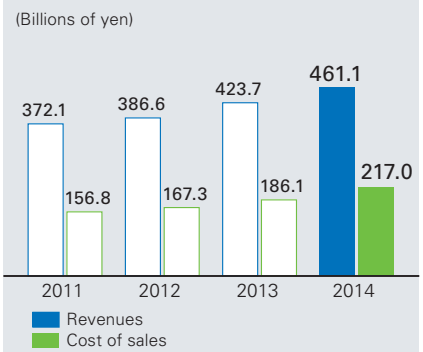
(Billions of yen/%)



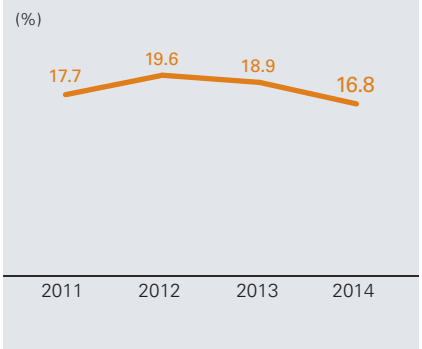
Since the alliance with Roche, Chugai has transformed its earnings structure while expanding sales. Given the higher cost of sales to sales ratio resulting from the increase in in-licensing products from Roche, we implemented continuous business structure reforms and cost reduction measures. As a result, we have reduced the ratio of operating expenses to revenues to a level comparable with the world's leading pharmaceutical companies. In ACCEL 15, we set the Core EPS CAGR and the Core EPS payout ratio as quantitative guidance, and are using them as key performance indicators both internally and externally.

(See page 19 for an explanation of Core basis results and page 22 for details on quantitative guidance in ACCEL 15.)

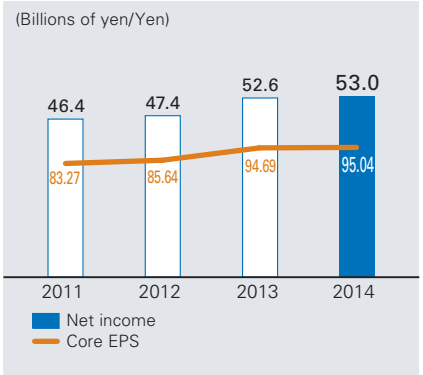
Revenues/Cost of Sales



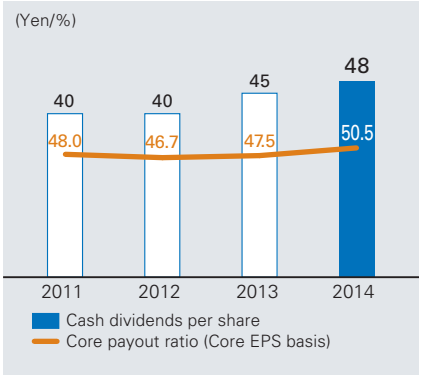
Operating Profit to Revenues



Net Income/Core EPS



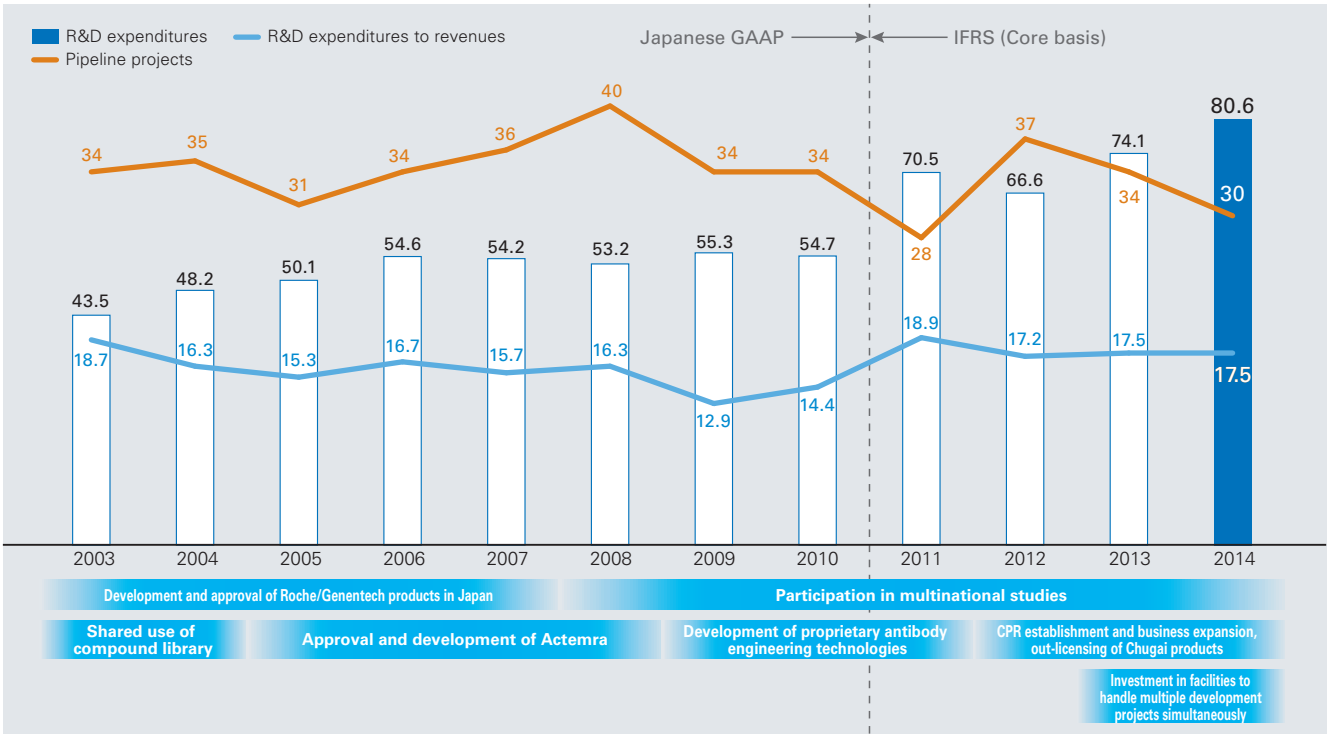
Cash Dividends/Core Payout Ratio



Research, Clinical Development and Production

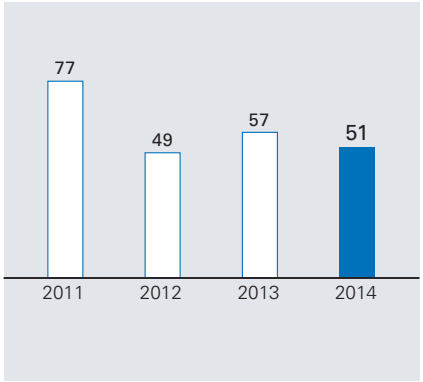
R&D Expenditures/R&D Expenditures to Revenues/Pipeline Projects

(Billions of yen/%/Projects)

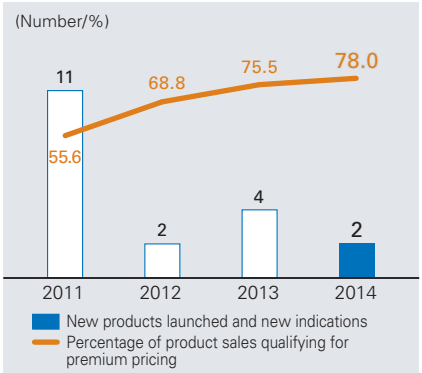


As revenues grow, Chugai increases investment in research and development to steadily create innovative drugs. These investments have also led to the creation of research technologies and findings that may contribute to the advancement of healthcare and the pharmaceutical industry worldwide. Development of Roche Group products in Japan has proceeded smoothly since our alliance began, and we currently have a development system capable of simultaneous filings in Japan, the United States and Europe. We have also maintained a robust pipeline by enhancing our development infrastructure, with numerous products from Chugai's research having moved into the clinical phase and reached the stage where they can be out-licensed to Roche. While continuing to make investments to handle multiple development projects simultaneously, we are taking steps to avoid significant increase of our CO_2 emissions in consideration of the environment.

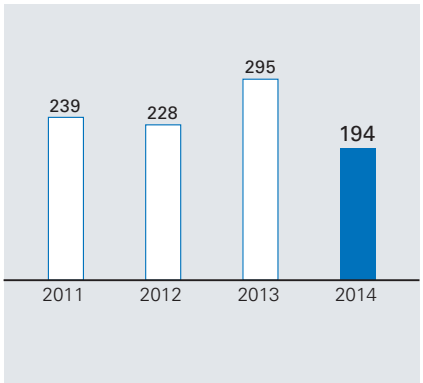
Publications in Academic Papers and Presentations at Scientific Conferences regarding Chugai Research Findings



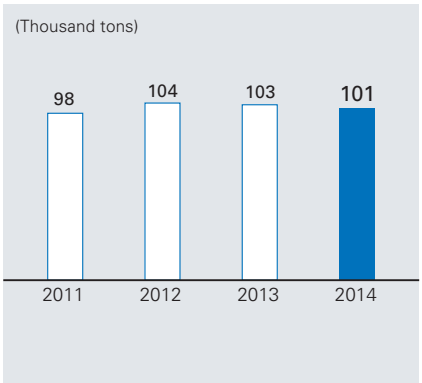
New Products Launched and New Indications/Percentage of Product Sales Qualifying for Premium Pricing



New Patents Granted



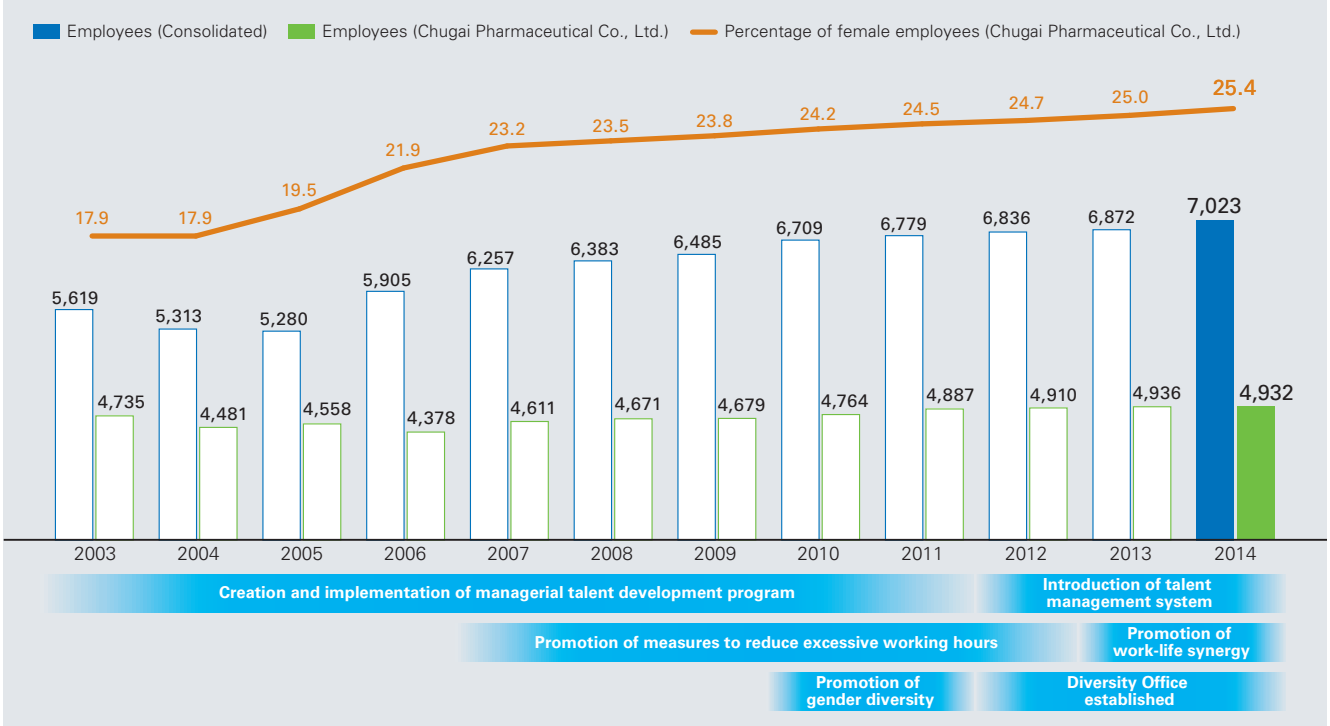
CO_2 Emissions



Human Resource Management

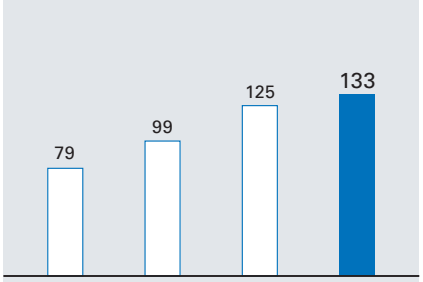
Employees/Percentage of Female Employees

(Number of employees/%)

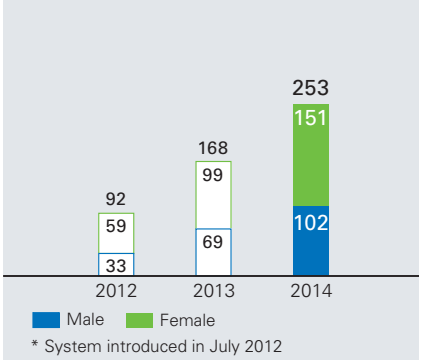


Chugai is working to enhance its management of human resources based on the belief that they are the source of its contribution to patients in terms of expanding the value it provides. To train or secure the leaders and core personnel who are the key to becoming a top pharmaceutical company, we have introduced a talent management system, devise individualized growth plans and upgrade our training programs. We also promote diversity and work-life synergy so our diverse human resources can create new value. As a result, the percentages of female employees and female managers are steadily rising, and our measures are leading to the creation of working arrangements that fit employees' individual lifestyles.

Employees Taking Childcare Leave

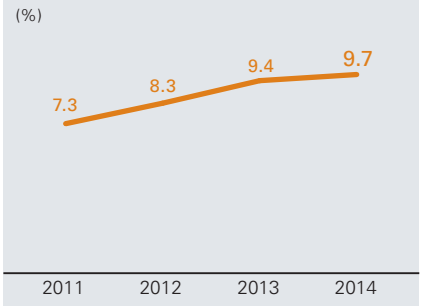


Employees Approved for Telecommuting*



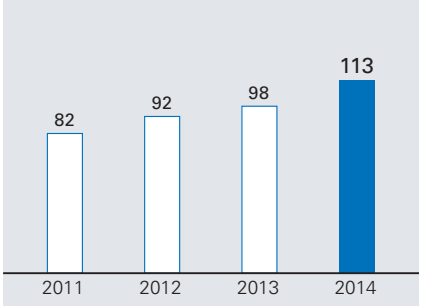
* System introduced in July 2012

Percentage of Female Managers*



* Chugai Pharmaceutical Co., Ltd.

Employees Posted through the Roche Human Resource Exchange Program*



* Cumulative total since 2004

Financial Summary (Core Basis)

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

	Billions of yen (Except as otherwise specified)			Percent change	Millions of U.S. dollars[1] (Except as otherwise specified)
	2014	2013	2012	2014/2013	2014
Results for the year:					
Revenues	¥ 461.1	¥ 423.7	¥386.6	+8.8%	$3,875
Operating profit	77.3	79.9	75.6	–3.3	650
Net income	53.0	52.6	47.4	+0.8	445
R&D expenditures	(80.6)	(74.1)	(66.6)	+8.8	(677)
Sales	¥ 436.9	¥ 401.3	¥375.2	+8.9%	$3,671
Oncology	188.9	172.4	156.1	+9.6	1,587
Bone and joint diseases	69.6	60.6	66.3	+14.9	585
Renal diseases	44.7	48.9	48.1	–8.6	376
Transplant, immunology and infectious diseases	20.8	18.8	20.3	+10.6	175
Others	25.6	28.6	30.1	–10.5	215
Overseas	74.3	61.1	42.3	+21.6	624
Royalties and other operating income	24.2	22.4	11.3	+8.0	203
Financial position at year-end:					
Total assets	¥ 739.5	¥ 697.2	¥645.3	+6.1%	$6,214
Interest-bearing debt	(0.2)	(0.2)	(0.3)	0.0	(2)
Total net assets	597.8	573.2	529.2	+4.3	5,024
Cash flows during the year:					
Cash flows from operating activities	¥ 37.0	¥ 53.5	¥ 77.5	–30.8%	$ 311
Operating free cash flows	43.9	63.0	91.0	–30.3	369
Amounts per share (Yen and U.S. dollars):					
Net income	¥ 95.04	¥ 94.69	¥ 85.64	+0.4%	$0.799
Equity per share attributable to Chugai shareholders (BPS)	1,092.90	1,049.47	970.08	+4.1	9.184
Dividends	48	45	40	+6.7	0.403
Number of shares outstanding	559,685,889	559,685,889	559,685,889		
Number of employees	7,023	6,872	6,836		
Ratios:					
Operating profit to revenues (%)	16.8	18.9	19.6		
Ratio of net income to equity attributable to Chugai shareholders (ROE) (%)[2]	8.7	9.3	9.0		
Ratio of equity attributable to Chugai shareholders (%)	80.6	82.0	81.8		
R&D expenditures to revenues (%)	17.5	17.5	17.2		
Payout ratio (%)[3]	50.5	47.5	46.7		

Notes: 1. The U.S. dollar amounts have been converted from Japanese yen amounts at the rate of ¥119 to U.S.$1.00, the approximate exchange rate prevailing on December 31, 2014.
2. 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)
3. Equivalent to the Total return ratio because Chugai did not implement a share repurchase.

About Core Basis Results

Chugai reports its results on a Core basis from 2013 in conjunction with its decision to adopt IFRS. Core basis results are the IFRS basis results adjusted to exclude non-Core items, and are consistent with the concept of Core basis results disclosed by Roche. 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. No items have been excluded from the IFRS balance sheet and cash flows, as the Core basis results concept only applies to the income statement.

Realization of "A Top Pharmaceutical Company"
Late 2010s
ACCEL 15
2013 -15
Chugai Business Conduct Guidelines
Mission Statement
Mission
Core Values
Envisioned Future

Strategy

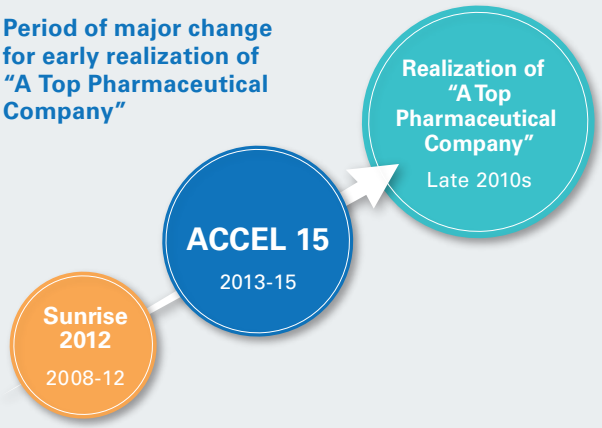
In our mid-term business plan ACCEL 15, we are executing four strategic policies designed to further increase corporate value by evolving and linking Chugai's current strengths and accelerating innovation. We will continue our drive to make Chugai a top pharmaceutical company that creates new value and meets the expectations of stakeholders.

Overview and Progress of ACCEL 15..... 22
Message from the President..... 23
Message from the Deputy Chairman 28
Discussion on Chugai's Value Creation 30

Overview and Progress of ACCEL 15

Positioning of ACCEL 15 Mid-Term Business Plan

Period of major change for early realization of "A Top Pharmaceutical Company"



Strategic Policies

1. **Increase of Marketing Productivity**
2. **Acceleration of Global Development**
3. **Continuous Generation of Innovative Projects**
4. **Further Strengthening of Management Infrastructure**

Quantitative Guidance

- **Core EPS CAGR[1] (2012-15)**
  Mid-to-high single-digit growth[2]
- **Core EPS payout ratio**
  Approx. 50% on average

Notes: 1. CAGR: Compound Annual Growth Rate
2. Average constant exchange rate for 2012

Strategic Policies	Achievements
1 **Increase of Marketing Productivity**	• Fast penetration of new products HER2 franchise, Alecensa • Enhancement of area promotion strategy • Utilization of e-promotion
2 **Acceleration of Global Development**	• Started phase III multinational study of Alecensa (NSCLC) • Progress of in-house antibody projects ACE910, CIM331, SA237 • Amendment of Chugai – Roche out-licensing arrangements
3 **Continuous Generation of Innovative Projects**	• Progress of research at Chugai Pharmabody Research (CPR) • Enrichment of preclinical projects • Initiated development of seven new projects
4 **Further Strengthening of Management Infrastructure**	• Capital investment Expansion of CPR and production facilities of investigational drugs • In-licensing of products in E.U. PharmaMar, Helsinn Group • Acceleration of diversity

Definition of "A Top Pharmaceutical Company" (Chugai's Goal for the Second Half of This Decade)

Quantitative Aspects

1. **One of the Top Three Pharmaceutical Companies in Japan in Each of the Following Categories**
   - ◆ Domestic share
   - ◆ Consolidated operating income margin
   - ◆ Consolidated operating income per employee
   - ◆ Domestic sales per medical representative
2. **Top Domestic Market Share in Each of Our Strategic Fields**
3. **Increase in Proportion of Sales from Overseas Business**
   - ◆ RoACTEMRA/Actemra
   - ◆ New drugs following the above

Qualitative Aspects

1. **A Company That Satisfies All Its Stakeholders and Receives Their Active Support and Trust**
2. **A Company That Works Proactively on a Global Level**
   - ◆ Continuous creation/development/domestic and overseas launches of products with a competitive advantage in clinical results
   - ◆ Contribution to the Roche Group's results through product-appropriate fostering and sales
   - ◆ Leadership in pharmaceutical industry activities
   - ◆ Activities in which all employees have an awareness, sense of responsibility and pride as part of a top pharmaceutical company

Message from the President

Tatsuro Kosaka
Representative Director,
President and COO

Under our mid-term business plan ACCEL 15, we are making steady progress toward becoming a top pharmaceutical company. We need to further improve our ability to provide value to patients in order to compete globally over the long term. We will accelerate innovation to increase our corporate value by pursuing world-class levels of quality and speed as a key to success.

Progress of ACCEL 15

Steady progress in our four strategic policies in 2014

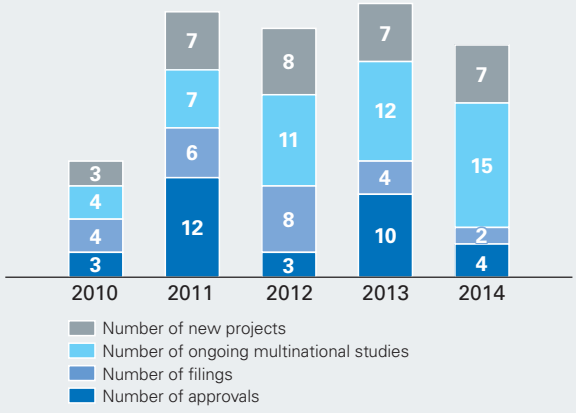
The mid-term business plan ACCEL 15 is aimed at further increasing Chugai's corporate value through evolution of its unique strengths and acceleration of innovation. To support our goal of becoming a top pharmaceutical company as early as possible, we are working on various innovations that address the four strategic policies in the plan: "increase of marketing productivity," "acceleration of global development," "continuous generation of innovative projects," and "further strengthening of management infrastructure."

In 2014, year two of ACCEL 15, we continued to make steady progress in each of these areas, and I believe we clearly demonstrated the power of our acceleration to our stakeholders.

For the first strategic policy, "increase of marketing productivity," Alecensa, a new product from Chugai research, penetrated the market more quickly than expected. With the addition of Kadcyla to existing products Herceptin and Perjeta, our HER2 franchise also grew impressively and is making a greater contribution to the treatment of HER2-positive cancer. In marketing, we responded to the emphasis on regional healthcare by making changes to our organization and enhancing our promotion strategy in each regional healthcare area, where cooperation among institutions is increasing.

In "acceleration of global development," our pipeline is well balanced and projects generally showed solid progress, including in-house antibody projects ACE910, CIM331 and SA237. In particular, we have increased our participation in multinational clinical studies year by year, and conducted such studies for 15 projects in 2014. Chugai-managed multinational studies for CIM331 and SA237 are

R&D Performance



currently under way as part of our effort to establish a new model for global development.

A visible result of "continuous generation of innovative projects" was the launch of seven new projects in 2014. In addition, antibody discovery research at Chugai Pharmabody Research Pte. Ltd. (CPR), a subsidiary we established in Singapore in 2012, advanced steadily and is beginning to yield new therapeutic antibody candidates. Moreover, we are further evolving our proprietary next-generation antibody technologies such as the recycling antibody, and new antibody engineering technologies are being developed.

We are also steadily moving forward in "further strengthening of management infrastructure," which supports the other strategic policies. To prepare for further growth at CPR and the continuous creation of new drug candidates, we began to expand production facilities for investigational drugs. In addition, we are in-licensing products at our sales subsidiaries in Europe.

Quantitative Results in 2014 and Current Position

Increased presence with strong top-line growth

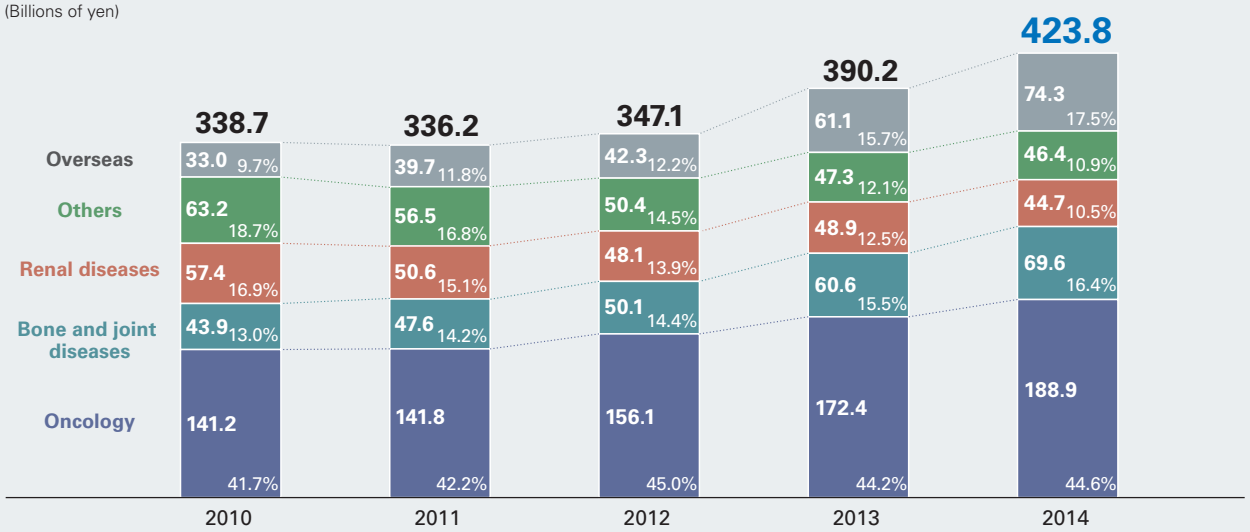
In 2014, we achieved double-digit sales growth in our strategic therapeutic areas of oncology and bone and joint diseases. Sales outside Japan grew by more than 20 percent year on year, led by the subcutaneous formulation of Actemra. With worldwide Roche Group sales surpassing 1 billion Swiss francs, Actemra has become a global drug that is contributing significantly to the Group's growth.

Core earnings per share (EPS), which we set as quantitative guidance in ACCEL 15, increased 0.4 percent to ¥95.04 with solid growth in revenues, despite the impact of higher cost of sales due to the weak yen. This exceeded our original forecast. Core operating profit was well above our original forecast owing to higher sales volume, despite a slight year-on-year decline mainly due to the impact of exchange rates on cost of sales.

The table (bottom of page 25) shows our progress toward our medium-to-long-term goal of becoming a

Breakdown of Changes in Sales (Excluding Tamiflu)

(Billions of yen)



Note: Figures for years prior to 2013 have been restated to exclude sales of Evista.
Japanese GAAP is applied to the figures prior to 2011.

top pharmaceutical company. We are still only halfway to our targets for market share in Japan and for market share in our strategic therapeutic areas other than oncology. For other items, though, we already reached our targets by the end of 2014. Compared with 2013, our market share in Japan rose from fifth to fourth place, and sales per medical representative (MR) in Japan improved from third to second place. I feel that our strategic policies are progressing steadily, and that Chugai's presence in the market is expanding further.

Note: Core indicators were introduced with the application of International Financial Reporting Standards (IFRS) in 2013 to represent Chugai's profit trends internally and externally. Core results are IFRS results adjusted to exclude the impact of non-Core items such as acquisition of intangible assets (managed as investments) and other nonrecurring items (including major restructuring expenses, litigation expenses and any other extraordinary items arising outside of the Company's core pharmaceutical business).

ACCEL 15 and Future Initiatives

Focusing on world-class quality and speed

As I said, we are making very good progress in ACCEL 15, and our functions and employee talent levels are steadily approaching the highest in Japan. In 2015, the final year of ACCEL 15, we will make changes aimed at bringing Chugai's quality and speed to a world-class level as we move closer to becoming a top pharmaceutical company.

Creating markets by providing solutions

Our efforts for the "increase of marketing productivity" will focus on providing differentiated solutions as part of our commitment to bringing the maximum value of our high-potential products to patients and healthcare providers. Under the new marketing system we introduced in 2013 to respond to local market characteristics, our 11 branches are carrying out area-based promotion strategies that coordinate customer, product and distribution policies in their respective areas. In addition, with regulations for MR visits to physicians becoming stricter, we will

Progress toward Quantitative Targets for Becoming a Top Pharmaceutical Company

1. Gain a position among the top three major Japanese pharmaceutical companies[1]

○ = Achieved △ = Partly achieved

		2014	(2013)
◆Domestic sales share	△	**Ranked 4th**	(5th) ↗
◆Consolidated operating profit to revenue	○	**Ranked 2nd**	(2nd) →
◆Consolidated operating profit to revenue per employee	○	**Ranked 1st**	(1st) →
◆Domestic sales per MR[2]	○	**Ranked 2nd**	(3rd) ↗

2. Gain the top share in our strategic therapeutic fields in Japan

◆Oncology	○	**Ranked 1st[3]** (1st) →

3. Increase overseas sales ratio

Other main fields in 2014
Renal (ESA): 2nd[3], Osteoporosis: 3rd[3], Rheumatoid arthritis: 3rd[3]

◆Overseas sales ratio	○	**19.1%** (17.2%) ↗

1. Financial results: Chugai: 2014/(2013), other companies: Years ended December 31, 2013 or March 31, 2014
2. Calculated by Chugai, based on data from Fuji-Keizai Co., Ltd.
3. Copyright 2015 IMS Health Source: JPM 2014. Reprinted with permission. The scope of the market is defined by Chugai.

deepen our use of information and communication technology, with initiatives such as providing support for virtual study meetings among physicians, and will link this e-promotion with MR marketing activities.

Upgrading our organization for achievement of early PoC and PoC[1]

Among the four strategic policies, "acceleration of global development" is where we must first establish world-class quality and speed. In August 2014, we amended our out-licensing arrangements with Roche to create a more efficient global development structure. Under the revised arrangements, we will offer Roche first refusal rights to develop Chugai products upon achievement of early proof-of-concept (PoC). Making this decision early on will allow us to concentrate our resources to obtain PoC as we pursue a level of quality and speed in our development operations comparable to the top global pharmaceutical companies. Based on this new business framework, we moved to strengthen our early clinical development functions with the establishment of the Translational Clinical Research Division in April 2015, which will facilitate faster global development.

1. Proof-of-concept (PoC) is a demonstration 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.

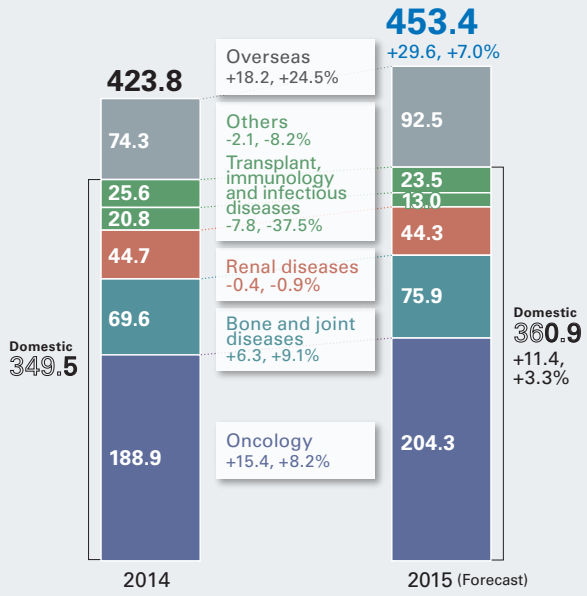
Expanding use of proprietary technologies and evolving our research process

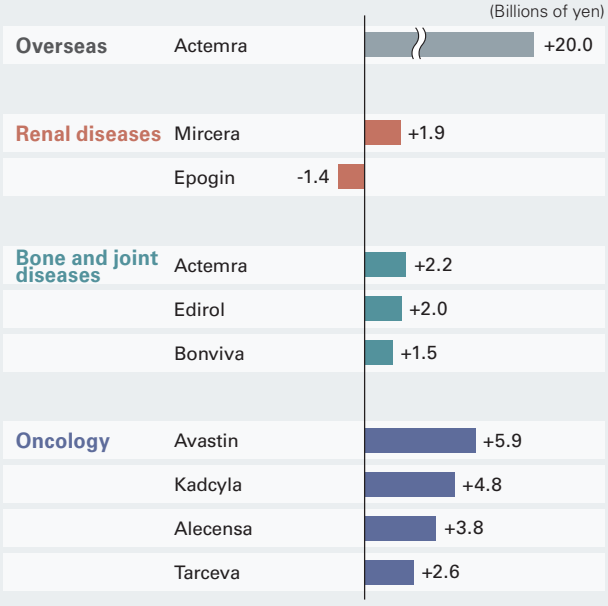
In "continuous generation of innovative projects," Chugai will create high-quality projects by maximizing use of its proprietary next-generation antibody technologies. We will also further strengthen and utilize CPR, which is steadily generating results, and accelerate open innovation with academia and research institutions. Up to now, Chugai has excelled in research that approaches diseases from target discovery. Going forward, we will also approach diseases on the basis of issues in the social environment and changes in those issues.

Expanding investment and enhancing human resource management

In "strengthening of management infrastructure," Chugai will focus in particular on strengthening investment and human resource management. For the expansion of CPR, our original plan was to invest ¥12.5 billion from 2012 to 2016, but we extended and expanded that plan to roughly ¥40.0 billion from 2012 to 2021, including about ¥5.0 billion[2] for capital investments. We will also make capital investments at the Ukima and Utsunomiya plants to expand production capacity for investigational biologics and

2015 Sales Forecast (Excluding Tamiflu)





biological drug substances and upgrade production functions to handle high-mix, low-volume production. In addition, we will enhance the three pillars of our human resource management – promotion of diversity, pursuit of work-life synergy and promotion of talent management – to strengthen global competitiveness and raise productivity.

2. Based on an exchange rate of ¥90/SGD for 2015 and later

Moving toward the targets of ACCEL 15 with strong growth

In 2015, we expect further penetration of core products and new products to expand sales in the fields of oncology and bone and joint diseases, as well as overseas sales. As a result, we forecast a 5.5 percent increase in revenues compared with 2014. We also forecast a 10.0 percent increase in Core operating profit as strong revenue growth outpaces the increase in operating expenses.

Core EPS is projected to increase 9.9 percent to ¥104.42. At that level, we are also eyeing double-digit Core EPS compound annual growth based on the average exchange rate in 2012, which was assumed in the numerical targets of ACCEL 15.

Capital Strategy and Shareholder Returns

Commitment to delivering strong returns to shareholders

I believe that constant innovation to become a top pharmaceutical company will lead directly to higher corporate and shareholder value, but I also recognize the importance of our capital strategy to effectively manage our ample net cash. We intend to increase returns to shareholders while making strategic investments to explore future business opportunities and lay the foundations for new growth based on the medium-to-long-term outlook for the operating environment. In ACCEL 15, we are targeting a Core EPS basis payout ratio of 50 percent on average while maintaining stable dividends. Based on that policy, cash dividends per share for 2014 were ¥48, higher than our original plan. For 2015, we plan to pay cash dividends per share of ¥52, a projected Core basis payout ratio of 49.8 percent. We remain committed to generating steady profit growth to become a top pharmaceutical company while maintaining appropriate returns to shareholders.

Chugai's Value Creation

Continuing to take on challenges to improve our ability to deliver value to patients

Chugai's unique business model has been the basis for our rapid growth in recent years, but no business model is effective forever. Changes in healthcare delivery systems, technological innovation, intensifying global competition in drug development and other factors are changing our operating environment faster than ever, and the value of the solutions we provide for patients are being scrutinized ever more closely. By responding flexibly to changes in the environment while continuing to innovate with a focus on speed, we will improve our ability to provide new value that benefits the medical community and human health worldwide.

As I have said, our focus is on achieving world-class quality and speed. With our next mid-term business plan, which is now being formulated, we intend to make Chugai a top pharmaceutical company with world-class competitiveness.

We look forward to the ongoing support of our shareholders and investors as we continue to take on new challenges to deliver value for all stakeholders.

Message from the Deputy Chairman

A company's processes and quality are vital to its development. Chugai will increase its corporate value through the simultaneous pursuit of economic performance, social awareness and human development.

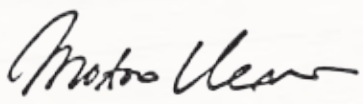
Chugai is celebrating its 90th anniversary in 2015. I believe that our ability to maintain our business operations for so many years, overcoming several difficult periods along the way, is the result of our history of continuously creating products that meet the needs and expectations of patients and markets, and that make a positive contribution to society. Our raison d'etre is to provide innovative products and services that address unmet medical need and resolve the social issues of disease treatment. Fulfilling that role is precisely what will allow us to continue in the future.

From the standpoint of corporate value, profit growth alone is no longer sufficient for a company to develop; today, its processes and quality are also scrutinized. Under these circumstances, I feel strongly that harmonizing and simultaneously realizing economic performance, social awareness and human development are important, and I communicate that message at every opportunity to people in the Company. To be more specific, achieving sustained development through growth in profits – or economic performance – and demonstrating social awareness by consistently meeting the needs of society as a pharmaceutical company are both important. And both ultimately depend on the pursuit of human development that creates job satisfaction by motivating employees and enables them to continuously improve their abilities.

In becoming a top pharmaceutical company, Chugai's fundamental management goal, we are likewise focusing on simultaneously achieving numerical targets and qualitatively evolving the process for achieving them. In 2014, under our mid-term business plan ACCEL 15, we delivered solid results for the benefit of patients. We launched new products, supplied products for patients in an appropriate manner and promoted their appropriate use, and accelerated global development of innovative drug candidates. Going forward, we will continue to lead the industry with innovations that include advancing the adoption of Personalized Healthcare while focusing particularly on promoting diversity, strengthening compliance and other measures to further enhance the management infrastructure that forms the backbone of value creation and innovation.

We are committed to meeting the expectations of all our stakeholders by increasing Chugai's corporate value through the simultaneous pursuit of economic performance, social awareness and human development.

Motoo Ueno
Representative Director and Deputy Chairman
In Charge of Promoting Corporate Social Responsibility, Audit



Our View of CSR

To realize its mission, Chugai has established a Mission Statement that includes seven Core Values to be shared as individuals and as a company in order to ensure sound business activities as we work toward our Envisioned Future. The Core Values also form the basis of the Chugai Business Conduct Guidelines (Chugai BCG), a code of behavior for management decision-making and employees. The Chugai BCG is reflected in the activities of each business unit and serve as a foundation to support the execution of our mid-term business plan, ACCEL 15. We believe that corporate activities consistent with our Mission Statement and the Chugai BCG are the essence of our CSR.

Mission Statement

Mission

Chugai's mission is to dedicate itself to adding exceptional value through the creation of innovative medical products and services for the benefit of the medical community and human health around the world.

Core Values

1. The primary focus of all our activities is patients and consumers.
2. In all our activities we are committed to the highest ethical and moral standards.
3. We value employees who develop profound expertise and broad perspectives and pursue innovation and challenges without fear of failure.
4. Wherever we operate around the world we seek to understand and respect people and cultures and to behave as good corporate citizens.
5. We promote an open and active corporate culture that respects individuality, ability and teamwork.
6. We care about the global environment.
7. We aim to achieve a fair return for our shareholders and to disclose information appropriately and in a timely manner.

Envisioned Future

As a most important member of the Roche Group, we aim to become a top Japanese pharmaceutical company by providing a continuous flow of innovative new medicines domestically and internationally.

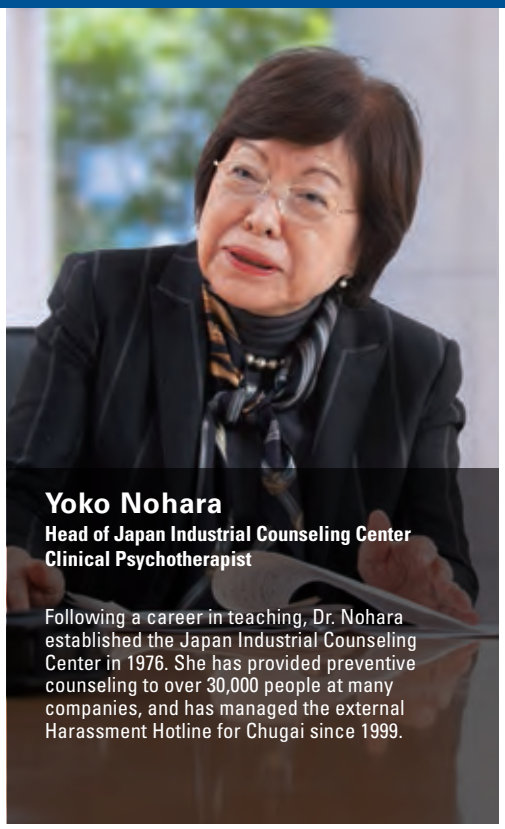
Chugai Business Conduct Guidelines

- **Responsibility to Patients and Consumers**
  We will always put the patient and the consumer first, and provide high-quality products and services of superior safety and efficacy.
- **Strict Adherence to the Law**
  In all our business activities, we will strictly adhere to all laws and their underlying principles.
- **Respect for Human Rights**
  We will respect human rights in every aspect of our business activities.
- **Fair Trade**
  We will engage in fair and transparent transactions with medical institutions and organizations, suppliers and customers.
- **Management of Corporate Assets**
  We will achieve our management objectives through the optimal and appropriate management and use of corporate assets.
- **Disclosure of Information**
  We will actively and fairly disclose corporate information in accordance with both legal requirements and the principles of social justice.
- **Social Contribution**
  We will remain aware of our responsibility as a good corporate citizen and actively continue with our social action programs.
- **Protection of the Global Environment**
  We believe the supreme value to the future of "one and only Earth" and, therefore, we continue our efforts to reconcile our business activity with nature and environments.
- **Relations with Governmental and Administrative Bodies**
  We will maintain fair and transparent relations with policymakers and administrative bodies.
- **Relations with External Bodies**
  We will maintain fair and transparent relations, within reason, with external bodies.

Discussion on Chugai's Value Creation

Daisuke Okamoto
Professor, Faculty of Business and Commerce, Keio University

Dr. Okamoto's fields of interest are managemetrics and corporate appraisal. He focuses on empirical studies designed to quantitatively analyze the relationship between various factors and results. He earned his doctorate in business and commerce from Keio University in 2004.



Yoko Nohara
Head of Japan Industrial Counseling Center
Clinical Psychotherapist

Following a career in teaching, Dr. Nohara established the Japan Industrial Counseling Center in 1976. She has provided preventive counseling to over 30,000 people at many companies, and has managed the external Harassment Hotline for Chugai since 1999.

Motoo Ueno
Representative Director, Deputy Chairman Corporate Social Responsibility, Audit Chugai Pharmaceutical Co., Ltd.

After joining Chugai in 1984, Mr. Ueno served in positions including General Manager of London Representative Office, Director and General Manager of Medical Information Division, General Manager of Clinical Research & Development Division, and Deputy General Manager of Research and Development Division. He has been Representative Director and Deputy Chairman since 2012.

To examine Chugai's future value creation, it is important to bring in outside stakeholder perspectives and incorporate them into management. We invited two outside experts who are also members of Chugai's CSR Advisory Committee – Dr. Daisuke Okamoto and Dr. Yoko Nohara – to engage in a dialogue with Chugai Deputy Chairman Motoo Ueno.

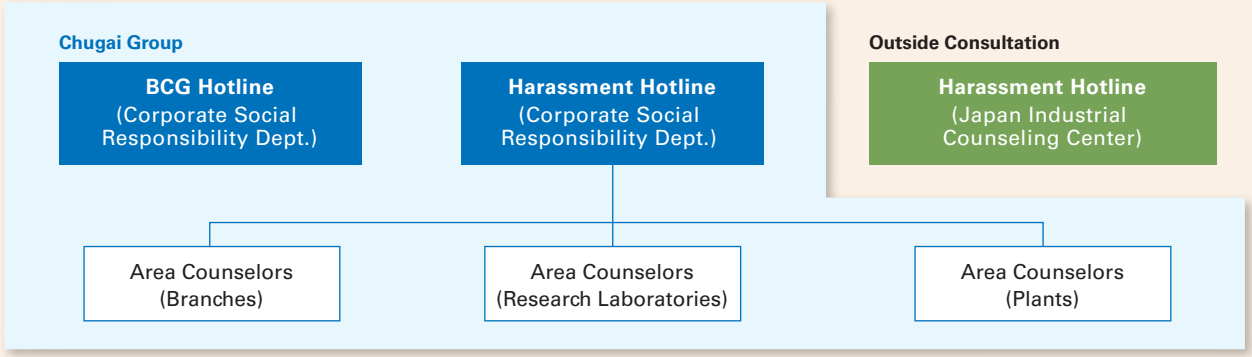
Simultaneous Pursuit of Economic, Social and Human Value

Ueno: I would like to open this discussion on value creation by talking about Chugai's approach. I've spoken with both of you about this before, but we at Chugai believe corporate value should be determined by a comprehensive assessment of the company's economic performance, social awareness and human development. To pursue and realize all of these aspects simultaneously, we need to think of them as integrated parts of a whole rather than as separate elements.

Okamoto: I strongly agree with that view. The way you express and define your approach is different but very similar to the idea of corporate appraisal that I have been advocating for nearly 20 years. I look at companies in terms of three criteria – profitability, growth potential and social relationship – and the relative importance of each factor changes depending on the time frame. In other words, profitability is emphasized in the short term, growth potential in the medium to long term, and social awareness over the ultra-long term. Discussing corporate value from a longer-term viewpoint has become essential, so companies need to consider how to include social awareness as part of their overall strategy.

Nohara: Social relationship as you define it includes Mr. Ueno's perspective of human development, doesn't it? As a specialist in this component at the front line, I think Chugai is a commendable company in terms of human development. I handle outside hotlines for various companies, including Chugai, and Chugai has been sincere in responding to my suggestion, based on

Chugai Group Hotline System
(Consultation on compliance and harassment)



hotline consultations, that human rights should be given the highest priority. The response of staff at Chugai's internal hotline has also been very conscientious. These are good examples of how Chugai's initiatives in this area are working effectively.

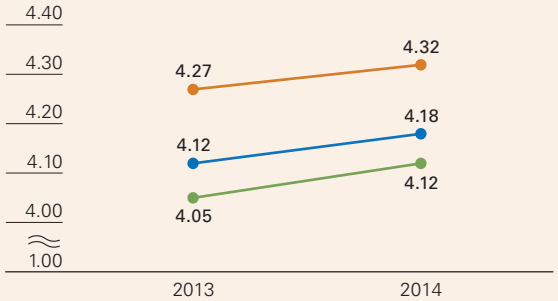
Okamoto: From the aspect of human value, I am researching the close connection between corporate ethics and corporate growth. Ethics change with the times, and it is important to keep up with and anticipate social change. For example, healthcare compliance seems to be a much discussed issue in the pharmaceutical industry recently. It is worth noting that Chugai took steps in this area, such as structural reform, earlier than its industry peers.

Ueno: At Chugai, our idea of compliance is achieving our goals while meeting the needs of society. The needs of society and stakeholders are very important to us, and I think they should be our yardstick for measuring compliance. Therefore, we have continued to enhance healthcare compliance with initiatives such as the structural changes we implemented in 2012, followed by the launch of the Healthcare Compliance Committee in 2014. (For details, see the "Healthcare Compliance" section of the feature on page 39.)

Value Created by the Strategic Alliance with Roche

Ueno: The alliance with Roche was unquestionably a major turning point in producing visible results from our value creation efforts. At Chugai, we have always thought it was important. At the time the alliance was formed, we drew up our Mission Statement and the Chugai Business Conduct Guidelines to integrate the different cultures of Chugai and Nippon Roche. We have undertaken various measures to instill these principles in the more than 10 years since then, and I think we are

Degree of Penetration of Chugai BCG*
(5-level 5-point evaluation)



Evaluation Items
- The Chugai Group is practicing CSR appropriate for a top pharmaceutical company through decisions and actions based on the Chugai BCG
- In doing your job, you make judgments based on the Chugai BCG, laws, regulations and other rules
- In your workplace, human rights are respected and there is no discrimination or harassment

* Chugai Employee Survey 2013/2014
Copyright Recruit Management Solutions Co., Ltd.

finally at a point where they are permeating the Company and taking concrete form. We still have a long way to go, though, and we should strive for a higher level of adoption.

Okamoto: Many companies have created management philosophies and codes of conduct, but as you said, the important point is how well these principles are understood and put into practice. What impresses me about Chugai is that you conduct Company-wide awareness surveys to gauge the degree of employees' understanding and use the survey results as the basis for improvement measures. Another outcome of the alliance is the management system. The alliance has made it easier for Chugai's management to take a long-term perspective. While maintaining Japan's traditional lifetime employment system, Chugai has abolished the seniority system and evaluates employees individually. A considerable number of Japanese companies have done this, but not many are managing it as well as Chugai.

Nohara: I agree. I have watched many companies that merged, but Chugai's alliance with Roche is truly a case of a major integration that brings out the best in both companies. Today, many companies consist of employees of various ages and nationalities, including new parents taking care of young children, employees caring for elderly relatives, employees with disabilities, and so on. Perhaps this inclusive approach stems from the acceptance of diversity that also enabled the successful integration of Chugai and Roche.

Promoting Diversity

Ueno: We are focusing on promoting diversity because we believe it is essential for innovation. That is why we made it one of the strategic policies of ACCEL 15. Since we are trying to create innovative drugs globally, it is vital that we heighten performance with teams that include women and non-Japanese employees.

Okamoto: Government policies promote gender diversity, and about half of patients are women in the first place, so male-dominated corporate management doesn't make sense. I understand that Chugai started addressing diversity in earnest around 2010. Just from looking at the employees, I sense that Chugai has made considerable progress, but what are your thoughts? Aren't there still few women at the executive level?

Nohara: From my perspective, I expect a higher level of diversity at Chugai. The percentage of women in management positions has been rising, but the Company needs to provide a wider range of opportunities to women and support for their professional growth. I feel that front-line male managers in some workplaces are somewhat reluctant to engage with female employees. They need to manage them more stringently while maintaining proper communication, which includes sharing relevant information and background. Even with strict management, women can achieve professional growth if they are given hope that allows them to envision their future. Having employees with diverse life experience and values will also become increasingly important. I think Chugai should keep this diversity of backgrounds in mind in front-line management and communication.

Ueno: We need to seriously reflect on the issues you have pointed out and take steps to address problems. I personally believe it is important to see things from the other person's perspective, and to do so, one should take an interest in that person. We implement systems and measures, of course, but I view raising the level of front-line management skills as a priority issue. The employees who consulted Dr. Nohara are only the ones who had enough courage to knock on her door, so we need to make efforts to address issues across the

Company. I want to create workplace environments in which diversity spreads naturally, rather than consciously focusing on differences such as gender or nationality.

Becoming a Top Pharmaceutical Company

Ueno: You raised issues related to promotion of diversity, but what other kinds of innovation do you expect as we move toward our goal of becoming a top pharmaceutical company?

Okamoto: When you talk about a top pharmaceutical company, in what aspects will you be a top company? That's a critical point. I believe it is imperative to strategically incorporate a long-term perspective of asking what your company will contribute to society as it develops. In that sense, initiatives such as the promotion of Personalized Healthcare that are currently under way are extremely important. Tailoring treatment to each patient rather than taking a one-size-fits-all approach is a truly innovative idea. Promoting the adoption of this novel approach to treatment is an important role for Chugai, and I look forward to seeing how things develop. The truth is, as a layman I first learned about Personalized Healthcare and its future potential from Chugai's website dedicated to the subject.* The concept was explained in plain language and videos, so it was easy to understand. However, most people still do not know about it, so I hope Chugai will conduct more initiatives like this to broaden awareness.

* "Personalized Healthcare: Enabling Future Treatment Tailored to Each Patient" at http://chugai-pharm.info/phc/ (Japanese only)

Nohara: These days, the emphasis is on not simply extending life but increasing the quality of life. Perhaps you could instill more confidence in all employees that Chugai is enhancing that quality as it works to become a top pharmaceutical company. In particular, employees in research and manufacturing, who have no direct contact with patients, may find it harder than medical representatives to get a sense of this.

Ueno: Chugai employees understand our philosophy, "Innovation all for the patients," and I think our patient-oriented approach extends across the

Company. But it is true that some employees find it more difficult to sense what this really means. Currently, comments we have received from patients and stories from healthcare professionals are shared within Chugai, with permission. We plan to conduct more initiatives like this to help give all our employees greater confidence that they are contributing to the benefit of patients, and therefore to society as a whole.

We've covered a lot of ground today, but our discussion has reminded me that both of you have high expectations for Chugai.

Creating value over the medium to long term requires a foundation of consistently sound, highly ethical business activities. In other words, I believe it is important to maintain a virtuous cycle in which we earn the trust of society by contributing to patients, and then contribute to society based on that trust. That is the kind of organization I want Chugai to be, and I am committed to creating workplace environments where trust is earned by all employees. I look forward to receiving guidance from both of you and from all our stakeholders in the future. Thank you for participating in this discussion.

Nohara, Okamoto: Thank you.

Chugai's Seven Strengths
① High product potential that addresses unmet medical need
② One of the richest pipelines in Japan
③ Strategic alliance with the Roche Group
④ Cutting-edge drug discovery technologies, especially biotechnology
⑤ Knowledge and experience as a pioneer in Personalized Healthcare (PHC)
⑥ Commitment to safety management
⑦ Support for healthcare delivery

Feature: Leadership and Increased Value Driven by Chugai's Unique Strengths

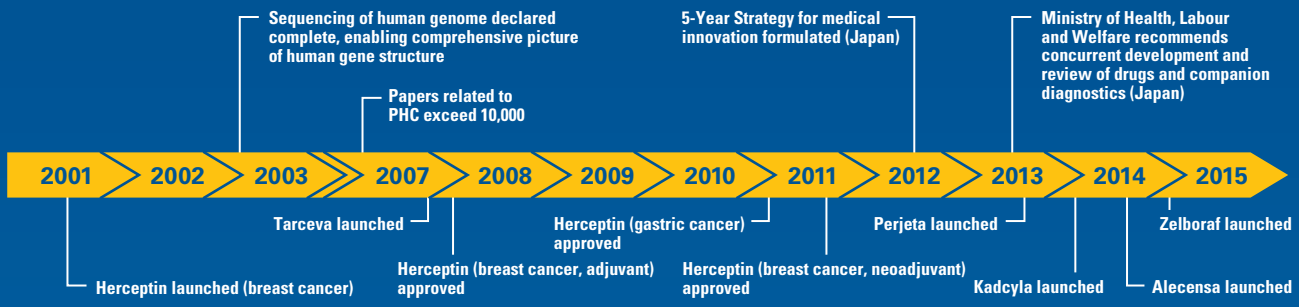
Our Approach to Three Key Issues in the Pharmaceutical Industry

The Japanese pharmaceutical industry is undergoing major change centered on Personalized Healthcare, healthcare compliance and safety management. This feature presents Chugai's approach and initiatives to address each of these issues in a rapidly shifting business landscape, along with the unique strengths that Chugai has cultivated to date.

Adoption of Personalized Healthcare 36
Healthcare Compliance 39
Enhancing Safety Management Systems 41

Chugai's Seven Unique Strengths 43

Adoption of Personalized Healthcare



Chugai's Unique Strengths

- PHC-based discovery and development

15 projects in our pipeline
(As of January 28, 2015)

- Rich antibody and oncology pipeline

Projects for oncology in our pipeline: 16
(As of January 28, 2015)

- Dominant presence in the oncology field

Market share in Japan: 22.0%* (No. 1)
(2014)

- Oncology MRs with a high level of expertise

Approx. 500 oncology MRs
(As of December 31, 2014)

* Copyright 2015 IMS Health
Source: JPM 2014. Reprinted with permission.
The scope of the market is defined by Chugai.

What is Personalized Healthcare?

Response to treatment and the type and severity of side effects may vary greatly among patients treated with the same medicine for the same disease. These variations were long attributed to innate individual differences. In recent years, however, a scientific explanation has emerged. By testing for biomarkers[1] – specific molecules in the blood and tissue, and in the proteins and genes of patients' cells – before beginning treatment, researchers discovered that what were once thought to be single diseases can actually be separated into several disease subgroups. This knowledge has enabled pharmaceutical companies to develop drugs, known as molecular targeted therapies,[2] that act only on the molecules behind the disease. Testing a patient's disease at the molecular level and then tailoring treatment with a drug designed to fit the patient's disease profile is called Personalized Healthcare, or PHC.

PHC has the potential to maximize the therapeutic effect, while minimizing side effects by categorizing patients through testing and administering medicines only to those who are likely to show a significant response. Avoiding treatment where it is unlikely to be effective also makes PHC very economical not only for patients, but for healthcare providers regulators and policymakers, as well as supporting the management of national healthcare costs.

The Roche Group is a PHC pioneer all over the world, including Japan, where PHC really began in 2001 when Chugai (the former Nippon Roche) launched Herceptin, an anti-HER2 humanized monoclonal antibody for the treatment of breast cancer.

1. A characteristic (biological substance in the body) that can be objectively measured and evaluated as an indicator of a normal biological process, a pathogenic process, or a response to a therapeutic intervention. Biomarkers may also serve as the basis for the development of diagnostic tests.
2. A drug designed to specifically inhibit the action of a molecular target that is implicated in a disease process. Molecular targeted therapies play a central role in PHC, which uses advance testing for biomarkers.

PHC in Breast Cancer

In the field of oncology, where treatment commonly involves the use of drugs whose therapeutic effects are accompanied by strong side effects, PHC is particularly important. For example, it has become apparent that a protein called HER2 is overexpressed in the tumor cells of about one in five breast cancer patients. It has also become apparent that breast cancer with HER2 overexpression (HER2-positive breast cancer) progresses more rapidly and has a higher risk of recurrence than HER2-negative breast cancer. Treatment guidelines now state that when breast cancer is diagnosed, patients should be categorized by type through testing for HER2 expression and hormone sensitivity together with the determination of operability.

Chugai's Herceptin is a molecular targeted therapy for HER2. It is administered only to patients diagnosed as HER2-positive through HER2 testing,[3] and helps to improve their prognosis. Since the debut of Herceptin, patients with inoperable or recurrent breast cancer can be expected to have a prognosis similar to that of HER2-negative patients. Herceptin is also used in operable, early-stage breast cancer as a neoadjuvant (before surgery) to shrink the tumor and then as an adjuvant (after surgery) to reduce the possibility of recurrence.

Herceptin is thus a representative PHC drug that has brought about a transformation in the diagnosis and treatment of breast cancer.

3. Testing for the expression of the HER2 biomarker using an immunohistochemical (IHC) test and a genetic test called fluorescence in situ hybridization (FISH)

Progress in the Adoption of PHC

For PHC to work, testing must be done correctly. When Herceptin came onto the market, however, there was no established standard testing method for HER2. At Chugai, we considered the promotion of PHC to be our responsibility, and worked to create algorithms for testing and diagnosis. By collaborating with the Japanese Society of Pathology, we were able to establish uniform standard procedures and pathological assessment criteria right down to the formalin level to be used when fixing samples collected from patients.

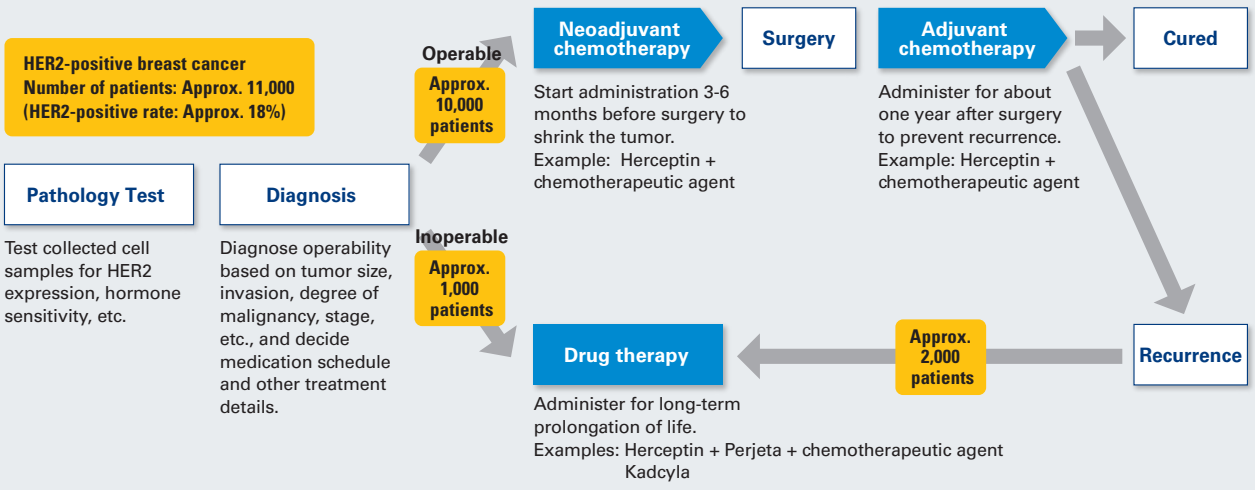
In informing medical practitioners nationwide about standard testing methods, Chugai provided information to promote their understanding and improve skills in using them, and also focused on serving as a liaison between clinicians and pathologists.

After Herceptin obtained approval for advanced or recurrent gastric cancer in 2011, we followed the same approach used for breast cancer: establishing diagnostic algorithms and familiarizing healthcare providers with HER2 testing. In 2014, the HER2 testing rate in gastric cancer reached 90 percent in Japan, indicating that PHC is taking root in the treatment of this disease.

Dynamism in the Treatment of HER2-positive Breast Cancer

PHC targeting HER2 continues to undergo innovation. In 2013, we launched Perjeta, a HER2 dimerization

Therapeutic System for HER2-positive Breast Cancer and Number of New Patients Affected Annually in Japan
(Chugai's estimate)



Note: Hormone-receptor-positive patients may be treated with a combination of hormone therapy and molecular targeted therapy.

inhibitory humanized monoclonal antibody, and in April 2014 we launched Kadcyla, an anti-HER2 antibody-tubulin polymerization inhibitor conjugate. Used in combination with Herceptin, Perjeta provides a more comprehensive blockade of HER signaling pathways. Kadcyla is a conjugate of the anti-HER2 humanized monoclonal antibody trastuzumab (the active ingredient of Herceptin) and the potent chemotherapeutic agent DM1. As a single agent, Kadcyla exerts a strong antitumor effect while preventing impact on normal cells because DM1 is delivered directly into HER2-positive cancer cells via trastuzumab. Market uptake of these two drugs in 2014 was exceptionally fast.

Currently, multinational studies are under way to expand the indications of these drugs to gastric cancer and adjuvant chemotherapy in HER2-positive breast cancer. If these indications are added, our HER2 franchise comprised of three products – Herceptin, Perjeta and Kadcyla – will help to realize highly effective and safe treatment and drive further innovation in the therapeutic system for HER2-positive cancer.

The Future of PHC

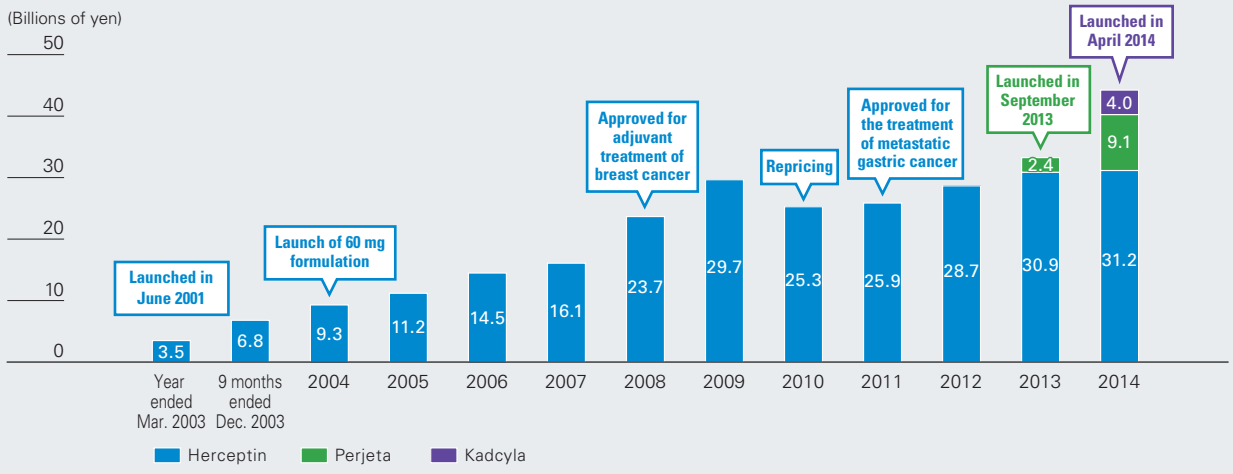
In addition to its HER2 franchise, Chugai has a number of other drugs that contribute to PHC. These include Tarceva and Alecensa for lung cancer and the BRAF inhibitor Zelboraf for melanoma.

In research and clinical development, 15 of the 30 projects in our current pipeline are PHC-based agents. (For details, see "Development Pipeline" on page 98.) We possess some of the industry's leading technologies, including our biomarker discovery and antibody engineering technologies. By advancing the identification of targets and development of new technologies, and conducting research on disease and pathologies, we will accelerate the creation of new drugs in PHC.

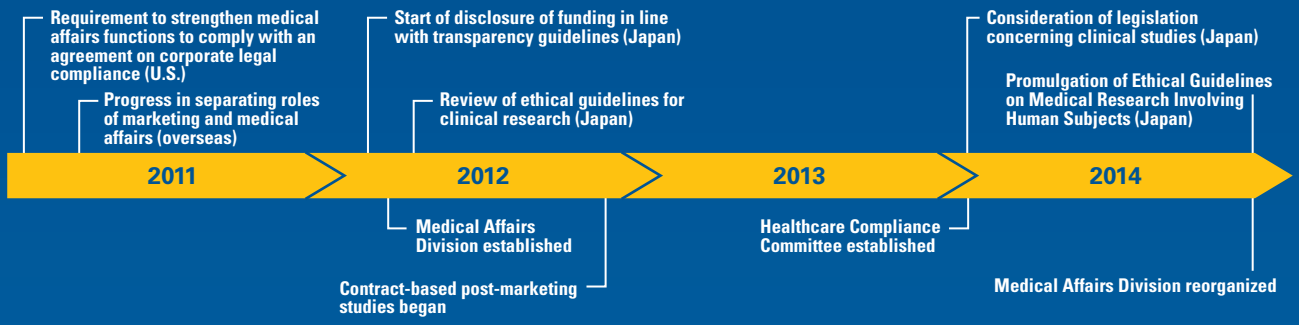
One key to facilitating the adoption of PHC will be simultaneous development of therapies and companion diagnostics for measuring biomarkers. Guidelines were released in Japan in 2013, but Chugai was already taking steps for simultaneous review and approval with companion diagnostics. We have established a system of collaboration with the Roche Group's Diagnostics Division, the global market leader in diagnostics, and actively cooperate from the early stages of research and development. Our attention is currently focused on diagnostics called multiplex testing, which test for multiple genetic conditions at the same time. We are considering their use due to the difficulty of collecting pathology specimens in large amounts, as well as the significant potential benefits that widespread use of multiplex testing would offer for patients from a cost perspective.

Going forward, PHC will be an integral part of medical care. As the PHC leader in Japan, Chugai will draw on its knowledge, accomplishments in various fields, and strengths in marketing, research and clinical development to continue to innovate and contribute to medical care through the establishment of PHC.

Sales of HER2 Franchise in Japan



Healthcare Compliance



Chugai's Unique Strengths

- Ability to validate and disseminate high-quality scientific data

Contract-based post-marketing studies commissioned: 15
(As of December 31, 2014)

Fields in which Chugai is conducting contract-based post-marketing studies: 10
(As of December 31, 2014)

- Network with regional medical institutions

Staff handling regional medical affairs: 111
(As of December 31, 2014)

- Full range of human resource development and education programs

Staff with the GCP Passport certification of the Japan Society of Clinical Trials and Research: 60
(As of January 31, 2015)

Compliance in Medical Affairs[1]

The pharmaceutical industry in the United States and Europe has faced closer scrutiny of its relationships with healthcare providers since the latter half of the previous decade, and disclosure of payments to healthcare providers became mandatory around 2011. The industry has also separated the roles of marketing and medical affairs. In Japan, falsification of data from post-marketing studies at pharmaceutical companies has prompted a rapid tightening of compliance rules for medical affairs since the latter half of 2013. The Japanese pharmaceutical industry recognizes that it must quickly bring its compliance level up to global standards and make concerted efforts to regain trust.

At the same time, post-marketing drug development, which proposes new treatment options using currently available drugs and explains the scientific basis for treatments, is vital in helping to improve patient care. It is also important that pharmaceutical companies contribute to raising the level of science in post-marketing clinical studies in Japan. Clinical trials for obtaining manufacturing and marketing approval are limited in duration and number of subjects, whereas post-marketing studies investigate efficacy and safety with the cooperation of the large number of patients who are actually taking the drug. Pharmaceutical companies are responsible for explaining the true value of their products appropriately by validating and disseminating this valuable data based on ICH-GCP[2] guidelines to ensure scientific integrity and quality. Moreover, the Japanese Ministry of Health, Labour and Welfare (MHLW) announced a new five-year plan to stimulate clinical research and trials in Japan in 2012, and the MHLW's Ethical Guidelines on Medical Research Involving Human Subjects

will be enforced starting in April 2015. Therefore, carrying out initiatives in collaboration with the government, medical institutions and various groups and organizations is an urgent task for pharmaceutical companies.

1. Activities to generate data useful for patient treatment based on knowledge gained in clinical studies, and to optimize patient access to drugs based on that data
2. Guidelines for the conduct of clinical trials issued by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)

Chugai's Healthcare Compliance[3] Structure

Chugai is responsible for marketing numerous innovative drugs, and as such it has been studying the optimal role and structure for medical affairs. In 2012, we established the Medical Affairs Division as an independent unit to separate medical affairs and marketing functions, and our contract-based post-marketing study scheme to ensure the independence and transparency of post-marketing studies. (For details, see "Contract-Based Post-Marketing Studies" on page 72.) Under this scheme, we do not simply outsource the study. We enter into a contract with a third-party research institution or foundation, not with individual hospitals or researchers (physicians), and that third party serves as the study operations office. This guarantees transparency as well as independence, because we do not intervene in the study process or results. It also helps to raise the quality of post-marketing studies because the operations office performs clinical study management at a high scientific level in accordance with ICH-GCP guidelines.

3. Chugai defines healthcare compliance as compliance in general business operations related to conducting clinical testing, clinical research and non-clinical research, support operations, collecting medical information and providing drug information.

Initiatives to Further Strengthen Healthcare Compliance

Chugai recognizes the importance of further enhancing medical affairs functions and strengthening its compliance structure to continue fulfilling its duty to patients.

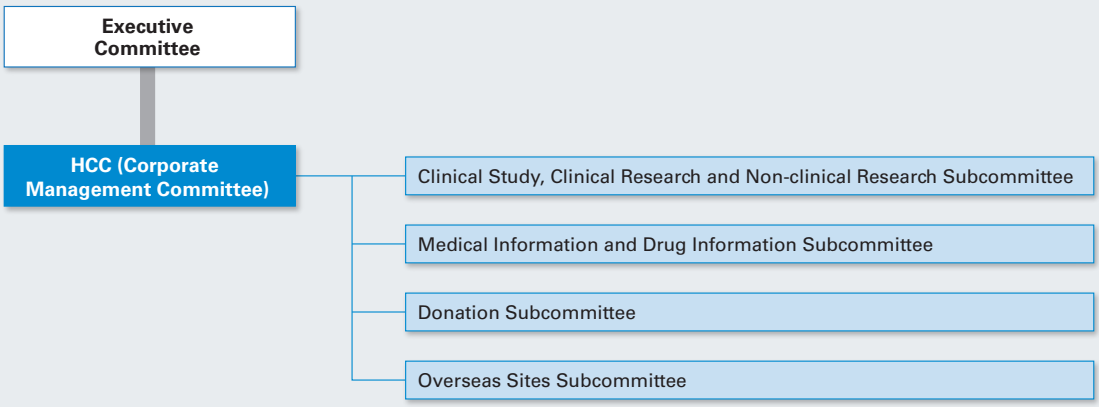
In October 2014, we established a management and training system for compliance in medical affairs and reorganized the Medical Affairs Division to strengthen its activities and enhance governance in each area.

We are confident that evolving our medical affairs functions so that they serve as a liaison between healthcare and pharmaceutical manufacturing while maintaining thorough compliance will help to elevate the level of science in healthcare and research, and thus increase the value we can contribute to patients.

In July 2014, we established the Healthcare Compliance Committee as corporate management committee.

At Chugai, we will continue to innovate because we believe that a top pharmaceutical company must carve out its own path.

Outline of Healthcare Compliance Committee (HCC)



Note: Subcommittees are formed as needed, and can be formed at the discretion of the committee chair.

Enhancing Safety Management Systems

Chugai's Unique Strengths

- Extensive experience in safety measures in oncology field and biopharmaceuticals

Safety measures taken (cumulative):

More than 20,000 cases

Total number of evaluable patients in all-case registration surveillance for Avastin, Tarceva and Actemra since 2007

- Ability to collect, analyze and respond to large quantities of safety data

Safety information collected: Approx. 170,000 cases

(January – December 2014)

- Strong support from medical staff

Assessment of quality of information provided:

No. 1 in Japan (Oncology)

Based on survey of medical staff involved in cancer treatment (Ipsos Healthcare Japan Ltd., 2014)

- World-class safety evaluation and analysis capabilities

Specialist staff in Drug Safety Division: 211

In-house pharmacists: 75

In-house medical staff with abundant clinical experience:

9 (5 full-time)

(As of December 31, 2014)

Industry Leadership

Awareness of the importance of pharmacovigilance is rapidly rising around the world, reflecting a need for more extensive collection of individual case safety reports and safety monitoring from the clinical stage. Pharmaceutical companies are also stepping up their safety measures in response to much stricter requirements for drug safety management systems in Europe and revisions to Japan's Pharmaceutical Affairs Law in November 2014.

Chugai has established one of the strongest safety management systems in Japan. Our extensive experience in this area includes all-case registration surveillance and global-standard drug safety measures. As an industry leader, we consider it our duty to help raise the level of drug safety in Japan. (For details, see "Drug Safety" on pages 73-74.)

For example, risk management plans (RMPs) became mandatory for Japanese pharmaceutical companies in April 2013, but Chugai began implementing RMP measures in 2012, ahead of legislation and our competitors. We also hold information meetings and prepared guidance for the industry on drawing up and submitting RMPs. We believe our efforts should now focus on ensuring that more transparent, high-quality information is used effectively by patients and healthcare professionals.

One of the revisions to the Pharmaceutical Affairs Law that marks a significant departure from conventional thinking is a new clause (Article 1-6) stating that the Japanese people must make efforts to use drug products appropriately and deepen their knowledge and understanding about drug efficacy and safety. Because this clause stipulates that the people are obligated to make efforts, it presents an opportunity to increase the public's drug literacy. At the same

time pharmaceutical companies are required to provide more appropriate information in a timely manner, and are expected to communicate it in a way that is easy for patients to understand. Chugai is therefore focusing on three priority issues for the reform of drug safety activities in Japan: enhancing scientific approaches to safety, meeting global compliance requirements, and establishing a communication framework. To address these issues, we are reinforcing our own safety functions – information collection and analysis, planning of safety measures, public dissemination, and information storage – and making efforts toward evolution of the industry as a whole.

Addressing Priority Issues

To enhance scientific approaches to safety, Chugai is concentrating efforts on strengthening signal detection analysis (analysis of the signs of adverse drug reactions) and epidemiology functions. We collect safety information on approximately 170,000 cases each year. The scientific evaluation and testing of this information by medical doctors with abundant clinical experience and the establishment of signal analysis management have enabled us to quickly provide information However, this safety information only applies to patients receiving a drug. Scientific comparative analysis cannot be performed without information on patients who did not receive the drug. Therefore, we are collaborating with various institutions on the establishment and use of a domestic epidemiology database for such evaluations.

To meet global compliance requirements, we have set up a review committee exclusively for verifying matters such as our compliance with domestic and overseas regulations, and for analyzing the causes of any problems found, studying measures to prevent their recurrence and closely monitoring implementation of those measures. In addition, we have modified our pharmacovigilance-related agreements with Roche and other partner companies to make our safety information consistent worldwide and conform to global safety standards, and are also taking steps to enable rapid sharing of safety information. Moreover, we have introduced an electronic system for unified management of numerous documents such as procedure manuals and reports to be submitted to regulatory agencies so that the necessary documents can be accessed from anywhere in the world.

In establishing a communication framework, we believe that the creation of a network involving all stakeholders is essential. With the rise of the Internet, more patients today are gathering drug information on their own, and patient groups and others are calling for further improvements in provision of information. In addition to direct communication through safety management staff to physicians and pharmacists, we must strengthen coordination with university and other research institutions, industry groups and the media. Recognizing that there were many resources we had not used in our communication activities, we launched the Communications Group in the Drug Safety Division in October 2013. We lead the industry in making recommendations to various organizations, and hold events such as briefings and media seminars. Going forward, we aim to be more proactive in providing drug safety information that results in the best treatment choices for patients.

Through these efforts, Chugai will continue to contribute to the reform of drug safety in Japan as an industry leader Pharmaceuticals are a balance of benefits and side effects. Accurately understanding the risk of side effects and managing that risk allows us to deliver the maximum value of our products to patients. At Chugai, creating essential safety standards is part of our commitment to uncompromising reform.

Enhancement of In-House Safety Functions at the Global Level

Collection	Data analysis	Safety planning	Implement safety measures Disseminate information	Storage
• Expanded scope of data collection (to meet new E.U. regulations) • Share global safety information with Roche and others	• Signal detection • Individual case evaluations by medical doctors	• Established epidemiology functions • Established planning process that is consistent worldwide	• Established safety communication functions • Improved content from stakeholders' perspective • Held medical seminars • Extensive experience in all-case registration surveillance, etc.	• Introduced an electronic system for RMP and other documents that can be accessed anywhere in the world

Thorough Global Compliance
Share safety information and decisions made regarding pharmacovigilance with a compliance review committee and overseas affiliates

Chugai's Seven Unique Strengths

We have identified the following seven strengths as the source of our value to help stakeholders recognize and understand Chugai as it works to realize its goal of becoming a top pharmaceutical company.

① High product potential that addresses unmet medical need

In Japan, Chugai maintains the number-one market share* in the oncology field and in the therapeutic antibody market, as the creator of the country's first therapeutic antibody. We also have market-leading products for bone and joint and renal diseases and lead our industry peers in participation in multinational studies, which helps to reduce Japan's drug lag.

② One of the richest pipelines in Japan

Chugai's oncology pipeline is one of the richest in Japan, and includes many clinical candidates targeting diseases with significant unmet medical need. This pipeline provides a foundation to continually create top-class products in Japan.

③ Strategic alliance with the Roche Group

Chugai's powerful network with Roche and Genentech, two of the world's leading pharmaceutical companies, allows it to conduct discovery research using research infrastructure that is among the most extensive in the world. We also efficiently in-license many products and development projects from Roche for the Japanese market.

④ Cutting-edge drug discovery technologies, especially biotechnology

With more than three decades of experience in biopharmaceutical research and development, Chugai has developed a series of innovative antibody engineering technologies over the last several years. We have also established a discovery research platform that allows us to continually create global drugs in-house.

⑤ Knowledge and experience as a pioneer in Personalized Healthcare (PHC)

Chugai's pipeline includes many projects based on PHC, which tailors treatment to each individual patient. In collaboration with the Roche Group's Diagnostics Division, we are also focusing on the simultaneous development and approval of drugs and companion diagnostics.

⑥ Commitment to safety management

Chugai has conducted all-case registration surveillance and managed safety of over 20,000 cases. From this experience, we have established a global-standard, industry-leading system for collection, assessment and analysis of safety information, and our safety measures have a solid reputation among healthcare providers.

⑦ Support for healthcare delivery

With a high level of expertise in oncology and other therapeutic fields, Chugai provides full support for multidisciplinary team care and promotes regional healthcare coordination. As a result of these activities, Chugai is supported and regarded highly by the medical community.

* Copyright 2015 IMS Health
Source: JPM 2014. Reprinted with permission.
The scope of the market is defined by Chugai.

The Process of Identifying Our Seven Strengths

Visualization

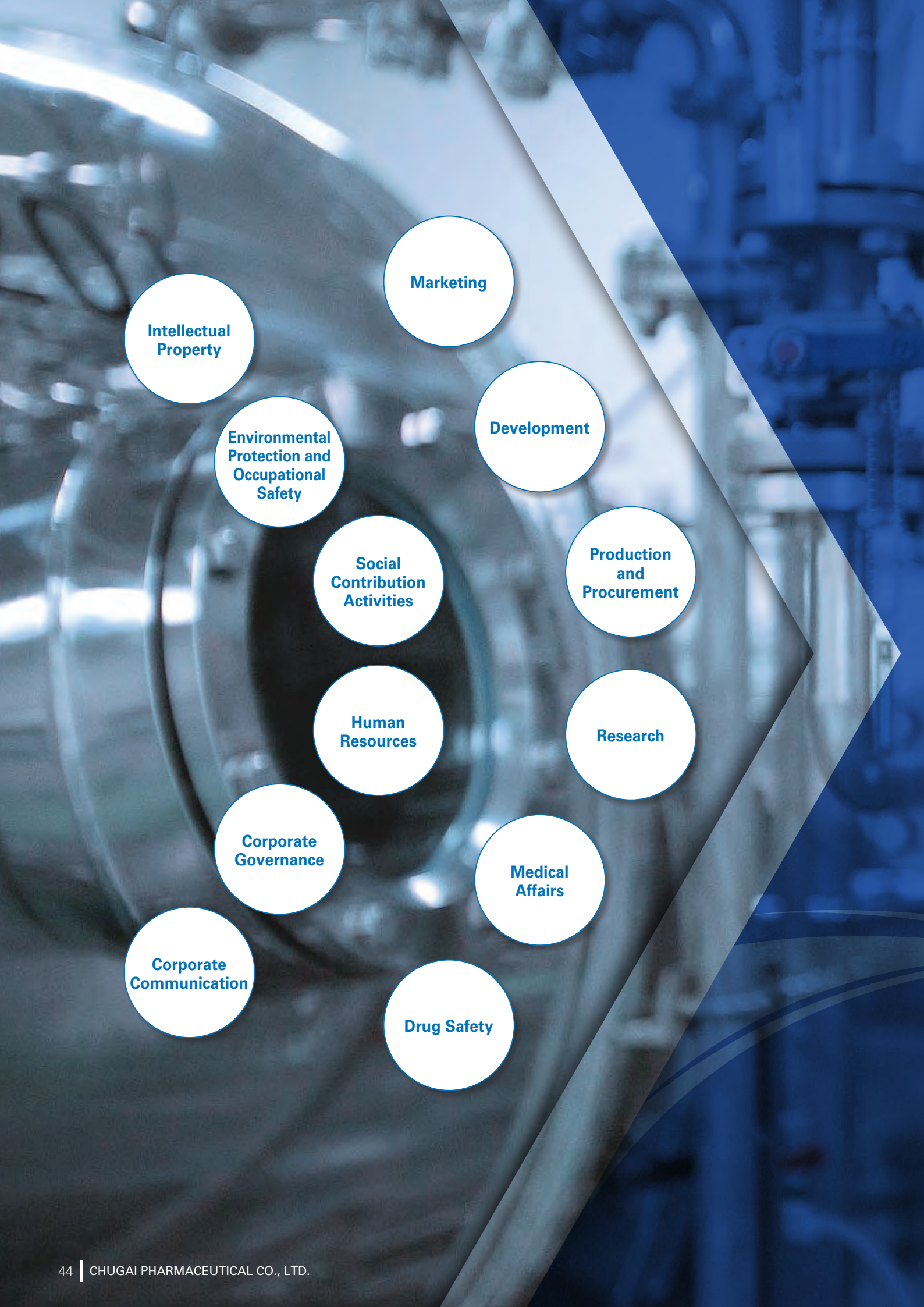
In our project to become a top pharmaceutical company, which started in 2009, we visualized the intangible strengths that Chugai has built, and shared 96 examples of those strengths within the Company.

Analysis of Value and Advantage

In a project to develop our public relations strategy, which started in 2013, we conducted internal and external interviews based on the 96 examples. We then evaluated those strengths from the standpoints of value to patients and competitive advantage, resulting in 25 categories.

Distillation Down to Seven Strengths

We organized these 25 categories through outside analysis and other means and distilled them down to seven strengths as a basic message to be used in communicating with stakeholders.


Marketing
Intellectual Property
Development
Environmental Protection and Occupational Safety
Social Contribution Activities
Production and Procurement
Human Resources
Research
Corporate Governance
Medical Affairs
Corporate Communication
Drug Safety

Performance Report and Future Initiatives

Under its business philosophy of "Innovation all for the patients," Chugai is innovating in all areas of its business operations with a focus on patient needs. In this section, we summarize our 2014 performance and action policies in each area, and describe Chugai's value creation initiatives.

Overview of Activities in 2014 46
Review of Operations 50
Marketing 52
Development 62
Production and Procurement 66
Research 68
Medical Affairs 72
Drug Safety 73
Intellectual Property 75
Environmental Protection and Occupational Safety 77
Social Contribution Activities 80
Human Resources 82
Corporate Governance 85
Corporate Communication 92
Board of Directors/Audit & Supervisory Board 94
Executive Officers 96

Overview of Activities in 2014

Items	Main initiatives	Main performance indicators in 2014
Marketing	• Promoting standards of care, regional healthcare and Personalized Healthcare (PHC)[1] • Contributing to advances in medicine as Japan's leading oncology drug and therapeutic antibody company • Offering patient-centered treatment proposals through consulting-based promotion • Conducting disease awareness and patient support activities in mainstay product areas	• Share of sales in the Japanese therapeutic antibody market: 35.4%[2] • Share of sales in the Japanese oncology market: 22.0%[2] • Education and internal certification program for MRs with a high level of expertise: 160 certified Top Oncology MRs, 110 Top Non-Oncology MRs who completed training courses and 30 certified Top Non-Oncology MRs (as of December 31, 2014)
Development	• Improving clinical development of drugs to address unmet medical need[3] • Increasing productivity and speed of global clinical development for early market launches • Conducting parallel development and regulatory filing of drug therapies and diagnostics that contribute to PHC • Strengthening lifecycle management to maximize product value	• Pipeline projects: 30 (as of January 28, 2015) • New products launched/new indications: 29 (2008-2014) • PHC-based development projects: 15 (as of January 28, 2015) • Projects in-licensed from Roche: 22 (2008-2014)
Production and procurement	• Providing a continuous stable supply of pharmaceuticals, raw materials and packaging materials • Strengthening global supply chain management • Continuously standardizing and optimizing purchasing processes to build fair, transparent relationships • Promoting purchasing that balances compliance, operational efficiency and cost reduction	• Invested in facilities to handle multiple antibody development projects simultaneously • Created and started operation of a world-class system for pharmaceutical quality management • Promoted fairness and transparency that includes cataloging of indirect materials in the electronic purchasing system
Research	• Continuously generating first-in-class[4] and best-in-class[5] drugs • Creating molecular targeted therapies[6] that contribute to PHC • Strengthening innovative proprietary research technologies and creating innovative antibodies • Providing support and education for researchers from Asia • Maintaining high animal welfare standards in accordance with international guidelines	• In-house products in pipeline research: 8 (as of January 28, 2015) • Expanded business at Singapore subsidiary Chugai Pharmabody Research Pte. Ltd. • Publications in academic papers and presentations at scientific conferences regarding Chugai's innovative proprietary technologies: 34 (2010-2014) • Published academic papers regarding Chugai's research findings: 122 (2010-2014) • R&D expenditures to revenues: 17.5%
Medical affairs	• Building a system for consistent management of medical affairs throughout Chugai • Strengthening systems for healthcare compliance[7] and governance of contract-based post-marketing studies • Promoting medical plans by area • Conducting contract-based post-marketing studies that conform to GCP and ethics guidelines	• Contract-based post-marketing studies: 15 (as of December 31, 2014) • Fields in which contract-based post-marketing studies are being conducted: 10 (as of December 31, 2014) • Staff with GCP Passport (JSCTR certification): 60 (as of January 31, 2015)
Drug safety	• Strengthening pharmacovigilance system to meet the world's strictest standards and most comprehensive global regulations • Continuously conducting post-marketing surveillance and disseminating timely information on appropriate use • Preparing and implementing risk management plans (RMPs)	• Cases for which safety information was collected from Japan and overseas according to global standards for clinical trials and post-marketing studies: About 170,000 adverse drug reaction reports (January-December 2014) • New RMPs prepared and carried out: 8 products (as of February 2015)

1. A treatment approach designed and implemented according to each patient's unique molecular and genetic profile
2. Copyright 2015 IMS Health Source: JPM 2014. Reprinted with permission. The scope of the market is defined by Chugai.
3. Medical need that is not adequately met due to a lack of effective treatments
4. An original drug that is highly novel and useful, and will significantly change the therapeutic system

Click on the white buttons to jump to the relevant pages on the Chugai website.

	Page reference	Items described in detail on website
• Participated at 26 locations nationwide in the 24-hour charity event Relay For Life • Customer inquiries answered by Chugai's Drug Information Center: 60,350 (includes telephone, e-mail and fax inquiries)	>52-61	Drug Information Center/Contributing to Patient-Centered Healthcare Initiatives for Patients and Consumers
• Projects co-developed with Roche Group: 27 (as of January 28, 2015) • Projects in response to development requests for unapproved drugs/indications: 12 (2011-2014)	>62-65	Development Pipeline/Co-Development and Joint Promotion with Roche/Conduct of Clinical Trials Reports & Downloads R&D Chugai's Approach to CSR
• Published research papers from the Pharmaceutical Technology Division: 64 (2010-2014) • Formulated procurement strategies for key materials and exchange of opinions with users • Issues of in-house newsletter *Purchasing News*: 6 • Internal e-learning held (for new employees and mid-career hires): 12 times	>66-67	A Global-Standard Regulatory Compliance and Quality Assurance System/Policy for Regulatory Compliance and Quality Assurance/Working with Business Partners Initiatives for Patients and Consumers Working with Business Partners
• Created new antibodies using Chugai's recycling antibody, sweeping antibody, bispecific antibody and other proprietary antibody technologies • In-house education and training for people who handle laboratory animals: 1 session attended by 540 people • In-house education for people who handle human-derived test materials: 1 session attended by 586 people	>68-71	Drug Discovery/R&D Infrastructure/R&D Structure/Chugai's View of Animal Welfare/Bioethics Initiatives in R&D/ Contributing to Patient-Centered Healthcare R&D Chugai's Approach to CSR Initiatives for Patients and Consumers
• Product Research Department: Published research papers: 110 (2010-2014) Academic conference awards: 9 (2010-2014)	>72	Future Post-Marketing Studies/Clinical Research Policy (Both information for healthcare providers in Japanese only)
• Papers and conference presentations on safety based on the results of post-marketing surveillance: 11 (2014)	>73-74	Post-Marketing All-Case Surveillance Initiatives for Patients and Consumers

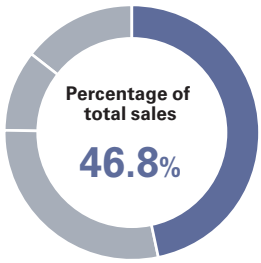
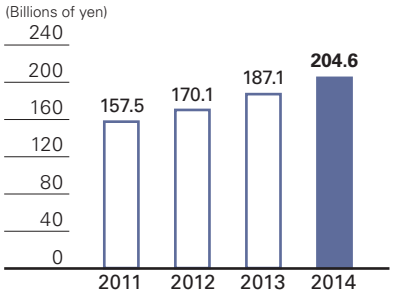
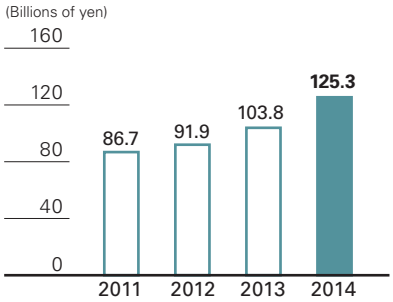
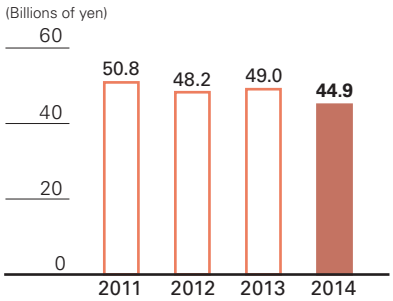
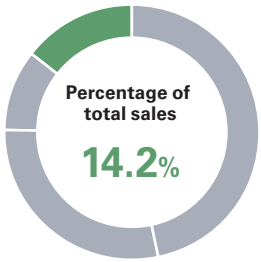
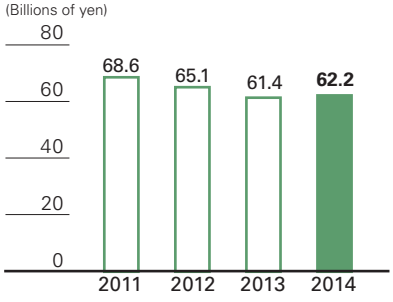
5. A drug that offers clear advantages over other existing drugs
6. A drug designed to specifically inhibit the action of a molecular target that is implicated in a disease process. Molecular targeted therapies play a central role in PHC, which uses advance testing for biomarkers.
7. Chugai defines healthcare compliance as compliance in general business operations related to conducting clinical testing, clinical research and non-clinical research, support operations, collecting medical information and providing drug information.

Items	Main initiatives	Main performance indicators in 2014
Intellectual property	• Protecting and effectively using rights for broadly applicable innovative technologies • Filing of high-quality patent applications and effectively allocating resources • Aggressive filing of patent applications outside Japan with a view to global co-development	• Patents held (including pending applications): 3,682 • New patents granted worldwide: 194 • Applications to register a patent term extension filed in Japan: 8 • Created a system for monitoring other companies' patents
Environmental protection and occupational safety	• Promoting global warming countermeasures, resource conservation and waste reduction • Thoroughly managing chemical substances • Disclosing environmental information • Enhancing environmental awareness and making environment-related contributions to local communities	• Energy consumption per employee compared with 2009: Down 10% (Chugai Group in Japan) • Amount of waste generated compared with 2013: Up 18% (Chugai Group in Japan) • Amount of landfill waste compared with 2013: Down 22% (Chugai Group in Japan) • Ratio of hybrid sales vehicles: 55.6%
Social contribution	• Conducting welfare initiatives for the elderly and people with disabilities • Nurturing the next generation of individuals who will carry science and technology forward • Supporting employee volunteer activities • Contributing to communities where Chugai Group facilities and sites are located	• Donation of welfare vehicles to provide transportation for home welfare services: Total of 203 vehicles over 30 years (total of five vehicles to five organizations in 2014) • Cumulative number of countries receiving free therapeutic drugs for treating lymphangiomas: 82 (program in its 24th year) • Video presentations given at Dr. Kitanomaru's Bio Pharmaceutical Laboratory exhibit: 38,208 (January - December 2014)
Human resources	• Fostering human resources who are competent in the global arena • Building work environments in which diverse people can succeed • Building sound labor-management relations • Creating safe, comfortable workplaces • Fostering high ethical standards through training on the BCG; making continuous efforts to build human rights awareness • Promoting compliance with the Pharmaceutical Affairs Law, fair competition codes, promotion codes, and other laws and regulations	• Implemented leader development program, all-employee program, division programs and Self-Innovation Program (SIP) • Employees posted through the Roche Human Resource Exchange Program: 113 (2004-2014) • Percentage of female managers[2]: 9.7% • Employees approved for telecommuting: 253 • New users of wiwiw (an online tool that supports employees who return to work after taking childcare leave): 48 • Employees taking childcare leave: 133 • Percentage of employees with disabilities: 2.06% • BCG and human rights training attendees: 13,516 (includes repeat attendees; Chugai Group in Japan)
Corporate governance	• Prompt decision-making, clarification of executive responsibilities and management transparency • Enhancing decision-making by introducing outside perspectives • Maintaining an internal control system	• Board of Directors meetings: 8 (average attendance rate of outside directors 89.5%) • Auditing system: 4 Audit & Supervisory Board Members (including 2 outside members)
Corporate communication	• Proactive disclosure of information to and promotion of IR activities for institutional investors, security analysts, individual investors and other stakeholders in Japan and overseas • Building good relationships with media outlets and disseminating information appropriately and in a timely manner (media relations) • Building and establishing the corporate brand	• Information events for the media and institutional investors: 18 • Security analysts and institutional investors in Japan with whom individual meetings/ conference calls were held: 400 • Briefings for individual investors and shareholders: 4 • Plant tours for shareholders or media: 2 • Attendees at General Meeting of Shareholders: 571 • Adopted new slogan and conducted activities to establish it (broadcast television commercials, placed newspaper advertisements and created brand website)

1. Source: Patent Result Co., Ltd.
2. Chugai Pharmaceutical Co., Ltd.

	Page reference	Items described in detail on website
• Improved efficiency by using electronic documents and visualizing workflows • Patent infringement lawsuits filed against generic drug companies: 1 • Industry ranking for scale of patented assets: 1st[1]	>75-76	
• Occupational incidence rate: 1.84 [(No. of occupational injuries and deaths/No. of hours actually worked) X 1,000,000] • Accidents accompanied by lost worktime: 4 (Chugai Group in Japan) • Lost workdays resulting from occupational accidents: 223 (Chugai Group in Japan)	>77-79	Chugai's Approach to CSR/Environmental and Safety Initiatives/Environmental Action Plans and Performance/ Occupational Safety and Health/Preventing Global Warming/Chemical Substance Management/Resource Conservation and Waste Management/Prevention of Air, Water and Soil Pollution/Education, Communication and Environmental Accounting Chugai's Approach to CSR | Environment and Safety
• Biology lab classes for children at the Japan Science Foundation's Science Museum: 113 participants in 6 labs • Endowed courses at Waseda University: Total of 15 lectures • Prepared an educational pamphlet on para-sports, and held an event for trying wheelchair basketball, a photograph exhibition and a talk show with para-athletes	>80-81	Chugai's Transparency Guidelines/Chugai's Social Contribution Activities/ Support for Para-Sports (Japanese only) Chugai's Transparency Guidelines | Initiatives for Society | Feature
• Conducted ethical and legal compliance survey within the Sales Division and Medical Affairs Division: 2,779 participants • Received the Minister's Prize for Excellence from the Ministry of Health, Labour and Welfare (MHLW) (Companies promoting gender equality) and the Tokyo Prefectural Labor Bureau Chief's Prize for Excellence (Family-friendly companies) at the Commendation of Companies Promoting Gender Equality and Work-Family Balance for 2014 • Selected as a "Nadeshiko Brand" in March 2015 by the Ministry of Economy, Trade and Industry and the Tokyo Stock Exchange	>82-84	Human Resource Strategy to Become a Top Japanese Pharmaceutical Company/Diversity Initiatives/Diversity Promotion System/Initiatives to Promote the Success of Diverse Employees/Facilitating Work-Life Balance/ Performance Data Related to Diversity/Our Commitment to Corporate Ethics/Creating Workplaces Free from Harassment Engagement with Employees | Diversity Initiatives | Chugai's Approach to CSR
• International Advisory Committee meetings: 1 • Established the Healthcare Compliance Committee	>85-91	Corporate Governance Report/The Resolutions concerning the Internal Control System by the Board of Directors/ Relationship with Roche Reports & Downloads | Management Policy
• Website ranked 1st in the pharmaceutical industry by Nikko Investor Relations Co., Ltd. • Won Second Prize in 17th Nikkei Annual Report Awards • Received Special Crossmedia Award at the 63rd Nikkei Advertising Awards • Won Prize for the Excellent Work at the 82nd Mainichi Advertisement Design Competition held by The Mainichi Newspapers Co., Ltd.	>92-93	Shareholder Information/Shareholder Meetings/ Shareholder Returns/Financial Results/Message to Individual Investors (Japanese only)/ Chugai Brand Story/ Videos (TV commercials) Shareholder Information | Financial Results | Chugai's Brand Website | Videos & Advertisements

Marketing

Therapeutic Fields	Sales	Major Products
Oncology	 	• Avastin (bevacizumab) • Herceptin (trastuzumab) • Rituxan (rituximab) • Tarceva (erlotinib) • Xeloda (capecitabine) • Neutrogin (lenograstim) • Perjeta (pertuzumab) • Kadcyla (trastuzumab emtansine) • Alecensa (alectinib)
Bone and Joint Diseases	 	• Actemra (tocilizumab) • Edirol (eldecalcitol) • Suvenyl (sodium hyaluronate) • Alfarol (alfacalcidol) • Bonviva (ibandronate sodium hydrate)
Renal Diseases	 	• Mircera (epoetin beta pegol) • Oxarol (maxacalcitol) • Epogin (epoetin beta)
Others	 	• Tamiflu (oseltamivir phosphate) • Sigmart (nicorandil) • CellCept (mycophenolate mofetil) • Pegasys (peginterferon alfa-2a) • Copegus (ribavirin)

(As of January 28, 2015)

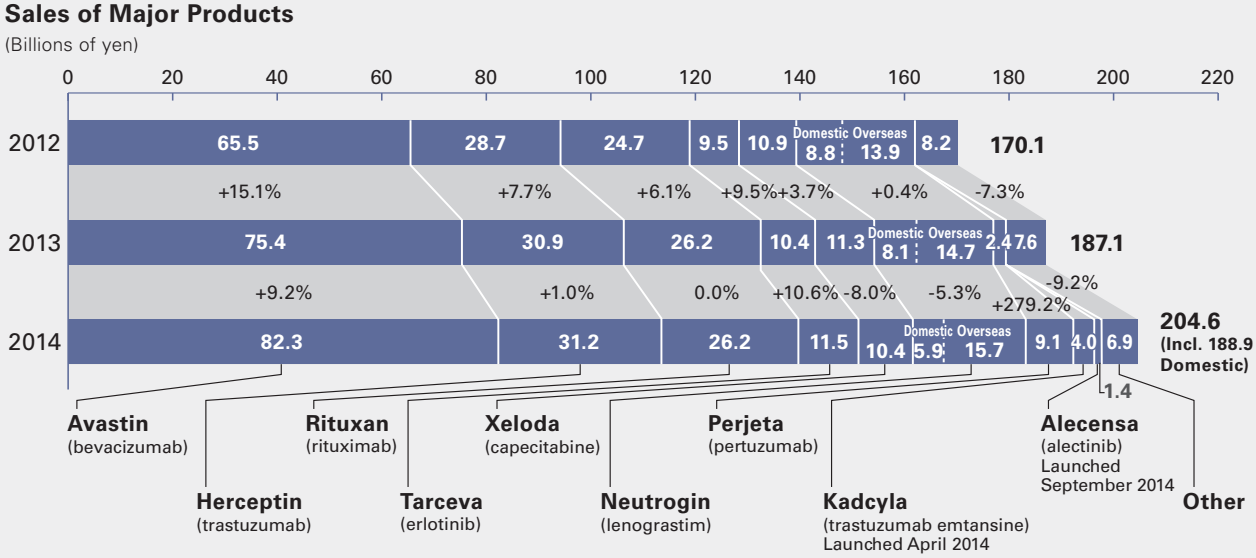
Research and Development

	Phase I	Phase II	Phase III	Filed
Oncology	**CKI27 (RG7304)** ◆ Solid tumors (Japan/overseas) **RG7321** Solid tumors **RG7596** Non-Hodgkin's lymphoma **RG7604** ◆ Solid tumors	**RG435 (Avastin)** Cervical cancer **GC33 (RG7686)** ◆ hepatocellular carcinoma	**AF802 (RG7853) (Alecensa)** ◆ Non-small cell lung cancer (overseas) **RG1273 (Perjeta)** ◆ Breast cancer (adjuvant) ◆ Gastric cancer **RG3502 (Kadcyla)** ◆ Breast cancer (adjuvant) ◆ Gastric cancer (II/III) **GA101 (RG7159)** Aggressive non-Hodgkin's lymphoma Indolent non-Hodgkin's lymphoma **RG7446** ◆ Non-small cell lung cancer ◆ Bladder cancer	**RG340 (Xeloda)** Gastric cancer (adjuvant)
Bone and Joint Diseases			**RG484 (Bonviva)** Osteoporosis (oral)	
Autoimmune Diseases		**MRA (RG1569) (Actemra)** Systemic sclerosis (overseas)	**MRA (RG1569) (Actemra)** Large-vessel vasculitis Giant cell arteritis (overseas) **SA237** Neuromyelitis optica	
Central Nervous System	**RG1577** ◆ Alzheimer's disease **RG1662** Improvement of intellectual ability in individuals with Down syndrome	**RG7090** Major depressive disorder	**RG1450** ◆ Alzheimer's disease	
Others		**RG3637** ◆ Idiopathic pulmonary fibrosis **CIM331** ◆ Atopic dermatitis **URC102** Gout (overseas) **ACE910 (RG6013)** Hemophilia A (I/II)	**RG3637** ◆ Asthma	

Originated in-house | Status changed in or after 2014. | ◆ PHC-based drug discovery

For details on diseases, products and development projects by therapeutic field, see "Development Pipeline" on pages 98-99 and "Basic Information" on pages 100-113.

Oncology



Avastin (bevacizumab)	Anti-vascular endothelial growth factor (VEGF) humanized monoclonal antibody Launch in Japan: June 2007
Herceptin (trastuzumab)	Anti-human epidermal growth factor receptor-2 (HER2) humanized monoclonal antibody Launch in Japan: June 2001
Rituxan (rituximab)	Anti-CD20 monoclonal antibody Launch in Japan: September 2001
Neutrogin (lenograstim)	Recombinant human granulocyte colony-stimulating factor (G-CSF) Launch in Japan: December 1991
Xeloda (capecitabine)	Fluoropyrimidine anti-tumor agent Launch in Japan: June 2003
Tarceva (erlotinib)	Epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor Launch in Japan: December 2007
Perjeta (pertuzumab)	HER2 dimerization inhibitory humanized monoclonal antibody Launch in Japan: September 2013
Kadcyla (trastuzumab emtansine)	Anti-HER2 antibody-tubulin polymerization inhibitor conjugate Launch in Japan: April 2014
Alecensa (alectinib)	ALK inhibitor Launch in Japan: September 2014

Overview

Cancer is the leading cause of death in Japan, with over 360,000 patients dying every year.[1] Chugai is the leading provider of anticancer agents in Japan, primarily for gastrointestinal, lung, breast and hematological cancer, and the products in our portfolio are standards of care around the world. We are committed to working for the benefit of patients by delivering cancer treatments that allow them to stand up against their disease with hope.

Our approximately 500 oncology medical representatives (MRs) continuously enhance their knowledge about diseases, standards of care and healthcare systems. Their expertise enables them to propose treatment options and side-effect management plans tailored to each patient, and to show the scientific basis behind those proposals to the various healthcare professionals involved, including doctors, pharmacists, nurses and pathologists. We call this approach "consulting-based promotion" to distinguish it from conventional promotion.

1. Source: Outline of Vital Statistics (2013) by Ministry of Health, Labour and Welfare

Review of 2014 Performance

General Overview

In 2014, sales in the oncology field in Japan increased ¥16.5 billion, or 9.6 percent, year on year to ¥188.9 billion. With patients awaiting innovative new treatments, Chugai followed the launch of Perjeta in 2013 with the launches of Kadcyla and Alecensa in April and September 2014, respectively, and promoted their appropriate use.

As a result, we increased our lead in the Japanese oncology market to a 22.0 percent[2] share, up 1.6 percentage points from 2013, maintaining our leading position in the field for the seventh consecutive year.

2. Copyright 2015 IMS Health Source: JPM 2014
Reprinted with permission.
The scope of the market is defined by Chugai.

Avastin
(bevacizumab)

Herceptin
(trastuzumab)

Tarceva
(erlotinib)

Perjeta
(pertuzumab)

Kadcyla
(trastuzumab emtansine)

Alecensa
(alectinib)

Performance by Product

Sales of Avastin, an anti-vascular endothelial growth factor (VEGF) humanized monoclonal antibody, increased ¥6.9 billion, or 9.2 percent, to ¥82.3 billion. Avastin is already an established standard of care for advanced or recurrent colorectal cancer at many medical facilities, and holds a solid position in the market. In lung cancer, an increasing number of doctors are making the decision to prescribe Avastin using image evaluation and other tools, and the accumulation of safety data is helping to broaden the range of patients who can receive treatment with this drug. In breast cancer, uptake of Avastin gained momentum, driven by findings that its use from the first-line setting in patients with inoperable or recurrent cancers reduces incidence of pain and other paraneoplastic syndromes. Use of Avastin also increased steadily for treatment of malignant glioma (a type of brain tumor) and ovarian cancer, two new indications added in 2013 for which innovative drugs had been long awaited.

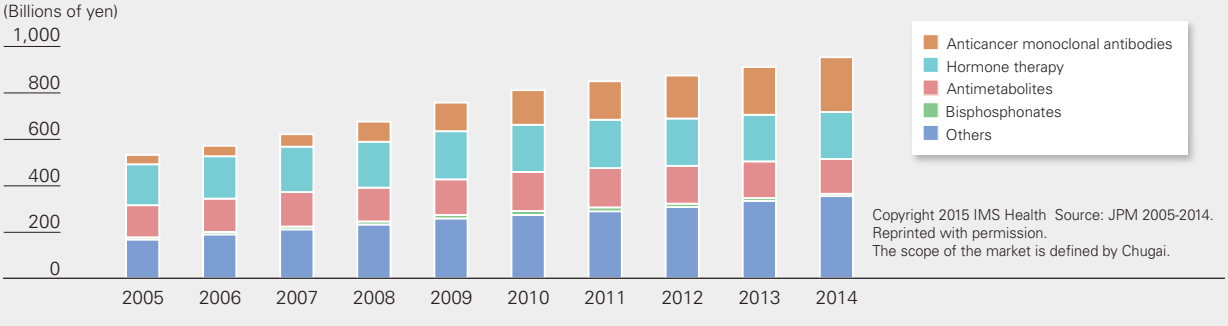
Herceptin, an anti-HER2 humanized monoclonal antibody; Perjeta, an HER2 dimerization inhibitory humanized monoclonal antibody; and Kadcyla, an anti-HER2 antibody-tubulin polymerization inhibitor conjugate, are all therapeutic antibodies that target HER2, a protein implicated in cancer cell growth. The availability of these agents has steadily advanced the therapeutic system for HER2-positive cancer and enabled Chugai to make a greater contribution to the life expectancy of patients.

Sales of Herceptin increased ¥0.3 billion, or 1.0 percent, to ¥31.2 billion. As a leading product in Personalized Healthcare, Herceptin has long been valued as a mainstay in the treatment of HER2-positive breast cancer. At the same time, information campaigns targeting healthcare providers have raised the rate of HER2 testing[3] for gastric cancer, further increasing the number of patients who can be treated with Herceptin.

Sales of Perjeta increased ¥6.7 billion, or 279.2 percent, to ¥9.1 billion, significantly exceeding our projections. Use of Perjeta increased particularly in first-line treatment backed by evidence that combination therapy with Herceptin improves overall survival (the length of time from diagnosis or start of treatment until death) in patients with HER2-positive inoperable or recurrent breast cancer.

Chugai launched Kadcyla in April 2014, after obtaining approval in September 2013. Kadcyla is an antibody-drug conjugate of a potent chemotherapeutic agent and trastuzumab (the active ingredient of Herceptin), which are joined with a stabilized linker. It provides the anti-tumor effect of trastuzumab while achieving greater efficacy and a better safety profile than standard combination chemotherapy. Sales in 2014

Anticancer Market in Japan



Copyright 2015 IMS Health Source: JPM 2005-2014.
Reprinted with permission.
The scope of the market is defined by Chugai.

were ¥4.0 billion, reflecting the positive assessment of the product's innovative mode of action from the time of its launch.

Alecensa, an ALK inhibitor developed from Chugai research, was launched in Japan in September 2014 for the treatment of *ALK* fusion gene-positive unresectable, recurrent/advanced non-small cell lung cancer. This drug demonstrates an anti-tumor effect by selectively inhibiting the activity of ALK, a receptor tyrosine kinase. A clinical trial in Japan indicated a high level of efficacy, which led to high expectations for the product even before its launch. Sales in 2014 totaled ¥1.4 billion. Since this drug obtained approval in a relatively short time, we are conducting all-case registration surveillance, taking steps to ensure appropriate use and collecting safety data.

Sales of Xeloda, a fluoropyrimidine anti-tumor agent, decreased ¥0.9 billion, or 8.0 percent, to ¥10.4 billion due to contraction of the 5-fluorouracil market and intensified competition. In addition to promoting combination therapy with oral Xeloda and oxaliplatin (a regimen called XELOX), a worldwide standard of care, we continued to focus on providing guidance for side effect management. As a result, evaluation of this product improved further. Xeloda has also established a leading position in postoperative adjuvant chemotherapy to prevent the recurrence of colon cancer after surgery. In addition, uptake of Xeloda for advanced or recurrent gastric cancer has increased steadily as a result of our efforts to highlight its efficacy, particularly in combination with Herceptin.

Sales of Tarceva, an epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor, increased ¥1.1 billion, or 10.6 percent, to ¥11.5 billion. In non-small cell lung cancer, the use of Tarceva in the first-line setting has accelerated after it obtained approval for first-line treatment in patients with *EGFR* mutations in 2013.

Sales of Rituxan, an anti-CD20 monoclonal antibody, were stable at ¥26.2 billion. This medicine holds a well-established position as a standard therapy for non-Hodgkin's lymphoma, and is showing solid sales growth.

Sales in Japan of Neutrogin (overseas name: Granocyte), a recombinant human granulocyte colony-stimulating factor (G-CSF), decreased ¥2.2 billion, or 27.2 percent, to ¥5.9 billion. The decrease in sales reflected market contraction due to expansion of outpatient chemotherapy that has reduced the frequency of neutropenia and the impact from competing products including biosimilars.[4] On the other hand, due to the impact of the depreciation of the yen, overseas sales increased ¥1.0 billion, or 6.8 percent, to ¥15.7 billion.

3. A diagnostic test can determine if a patient's breast or gastric cancer cells have overexpression of a protein called HER2. Herceptin and Perjeta target HER2 and are administered only to patients whose tumors are identified as HER2-positive.
4. Follow-on versions, produced by other manufacturers, of biopharmaceutical products; also called follow-on biologics. Unlike generic versions of synthetic agents, biosimilars are not completely identical to the original drugs.

2015 Strategy and Outlook

In 2015, Chugai will continue to provide evidence-based information and propose treatment options tailored to patients based on our large portfolio of products that can benefit patients with various cancer types, pathologies and lines of therapy.

We will work to further expand the use of Avastin in the treatment of lung cancer and breast cancer. For lung cancer, we will focus on making Avastin a treatment option for a broader range of patients and proposing maintenance therapy so that their treatment can be continued longer. Moreover, we will respond precisely to research on combination therapy with EGFR tyrosine kinase inhibitors such as Tarceva, which has shown promise in terms of efficacy. For breast cancer, we will continue to highlight the quality of life improvements made possible by starting patients on Avastin in early lines of therapy.

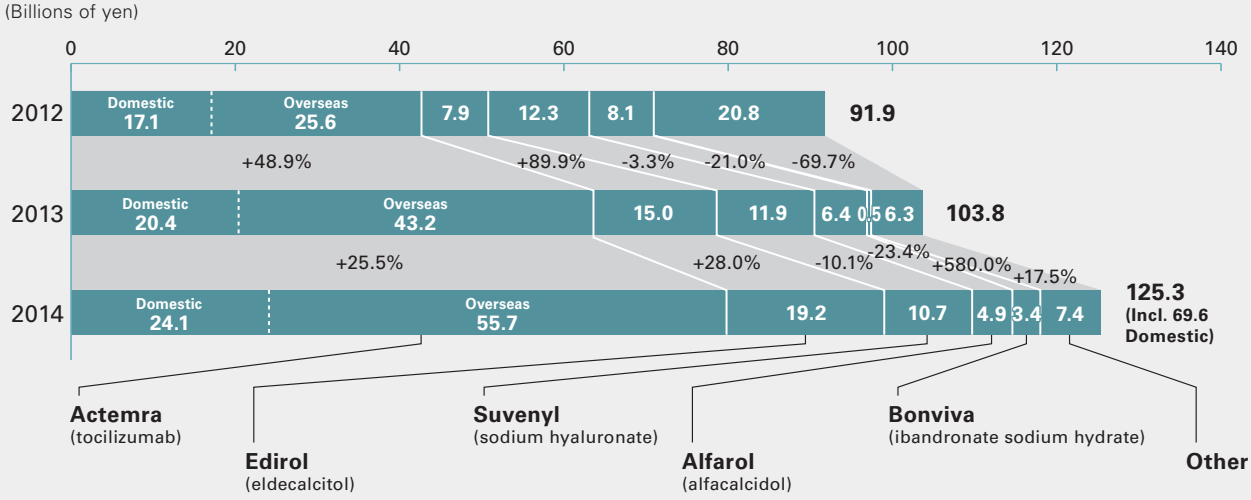
We will work to foster understanding of the characteristics and position of Herceptin, Perjeta and Kadcyla as we prepare to expand the indications of Perjeta and Kadcyla to include breast cancer (adjuvant chemotherapy) and gastric cancer. In addition, we will promote the steady uptake of Perjeta in first-line treatment of metastatic breast cancer and Kadcyla in second-line treatment of metastatic breast cancer.

Sales of Alecensa are expected to grow strongly in 2015, as awareness of ALK inhibitors is already established among healthcare professionals. Chugai will highlight this product's high response rate and potential for improving quality of life while continuing efforts to ensure appropriate use and provide accurate safety information from all-case registration surveillance.

With Xeloda, we will accelerate uptake by highlighting the convenience and safety of the XELOX regimen in colorectal cancer and by promoting the use of combination therapy with Herceptin in gastric cancer based on clinical evidence.

For Tarceva, we will work to further expand first-line use by taking advantage of Chugai's strength in making comprehensive treatment proposals for lung cancer.

Bone and Joint Diseases



Actemra (tocilizumab)	Humanized anti-human IL-6 receptor monoclonal antibody Launch in Japan: June 2005 (Castleman's disease) April 2008 (rheumatoid arthritis) May 2013 (new formulation: subcutaneous injection)
Suvenyl (sodium hyaluronate)	Agent for joint function improvement Launch in Japan: August 2000
Edirol (eldecalcitol)	Active vitamin D_3 derivative Launch in Japan: April 2011
Alfarol (alfacalcidol)	Active vitamin D_3 derivative (1α(OH) D_3) for improving bone metabolism Launch in Japan: January 1981
Bonviva (ibandronate sodium hydrate)	Bisphosphonate Launch in Japan: August 2013

Overview

Chugai has been active for more than three decades in the field of bone and joint diseases. Our role in this field expanded further in 2005 with the launch of Actemra, the first therapeutic antibody created in Japan. Actemra is the only approved drug in the world that targets interleukin-6 (IL-6), a protein that causes inflammation. Now, nine years after its launch, it is sold in more than 90 countries. With worldwide Roche Group sales reaching 1 billion Swiss francs, Actemra has become a global medicine. For rheumatoid arthritis (RA), the primary indication of Actemra, the advent of biologics has shifted the therapeutic goal from alleviation of pain and other symptoms to early and sustained remission (decrease in or disappearance of symptoms) and prevention of bone and joint destruction. To contribute further to the treatment of RA, we are making efforts at a global level to expand treatment options, including the launch of a subcutaneous formulation in 2013. In addition to RA, Actemra is approved for rare diseases with limited treatment methods, including Castleman's disease, systemic juvenile idiopathic arthritis (sJIA) and polyarticular juvenile idiopathic arthritis (pJIA).

In the osteoporosis segment, "locomotive syndrome," which refers to the loss of mobility of the legs and back due to advanced age or lifestyle factors, has received growing attention in Japan due to its impact on quality of life. This has boosted awareness of the importance of treatment. In 2011, we launched Edirol, a next-generation active vitamin D_3 derivative that improves on Alfarol, and in 2013, we launched Bonviva, a bisphosphonate agent. These additions to our product lineup reflect our commitment to meeting the therapeutic needs of osteoporosis patients.

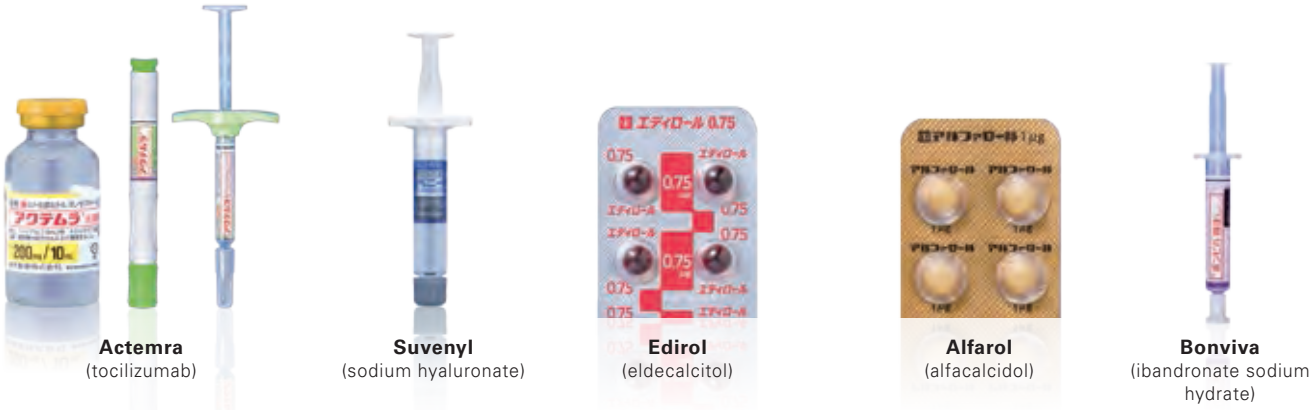
Review of 2014 Performance

General Overview

In 2014, sales in the bone and joint diseases field in Japan increased ¥9.0 billion, or 14.9 percent, year on year to ¥69.6 billion. Sales growth was driven largely by further acceleration in the uptake of Actemra, our core product in this field in Japan and overseas. In the osteoporosis segment, use of Edirol and Bonviva IV Injection also grew steadily.

Rheumatoid Arthritis (Japan)

Sales of Actemra in Japan increased ¥3.7 billion, or 18.1 percent, to ¥24.1 billion in 2014. The domestic market for biologics is expanding, driven by successive



Actemra
(tocilizumab)

Suvenyl
(sodium hyaluronate)

Edirol
(eldecalcitol)

Alfarol
(alfacalcidol)

Bonviva
(ibandronate sodium hydrate)

launches of new drugs and a growing patient population. Patients and their healthcare providers can now choose from a wider array of treatments to fit treatment objectives and patient lifestyles. In this changing market landscape, Actemra was increasingly chosen as the first-line biologic treatment, and posted strong growth.

Behind the growth in use of Actemra is the increasing recognition of its efficacy. Clinical trials have shown that Actemra maintains high remission rates over a sustained period while preventing joint destruction. Recent research also indicates that using Actemra first when administering biologics is highly effective. The benefit of blocking IL-6 in RA treatment has been reported at numerous scientific conferences in Japan and around the world, and the benefit of treatment focused on IL-6 is now widely recognized. Another strength of Actemra is the follow-up all-case registration surveillance of approximately 5,500 cases that was conducted to accumulate data on the product's long-term safety profile in Japanese patients.

In addition, we expanded the value of the product in terms of flexibility and convenience during treatment with two types of subcutaneous formulation launched in 2013: a pre-filled syringe and an auto-injector. Use of these formulations has grown rapidly. Another major factor driving growth was the lifting of the two-week limit on prescriptions in June 2014, allowing Actemra to be prescribed for one month or longer. Compared to the intravenous formulation, the subcutaneous formulations significantly shorten the administration time and reduce the frequency of hospital visits because patients can self-inject. These formulations also eliminate the need for hospital beds and other infrastructure necessary for a drip infusion, and reduce demands on medical staff. The result has been an increase in the number of facilities, primarily clinics, for patients who prefer to be administered Actemra by a doctor. The auto-injector is the first such device for RA treatment in Japan enabling users to inject with the push of a button. Its design allows even patients with impaired finger dexterity resulting from the symptoms of RA to safely and easily administer the medicine without fear of needles.

In 2014, we expanded the inner diameter of the injection needle, reducing administration time from 20 seconds to 15 seconds to further enhance convenience for patients.

Rheumatoid Arthritis (Overseas)

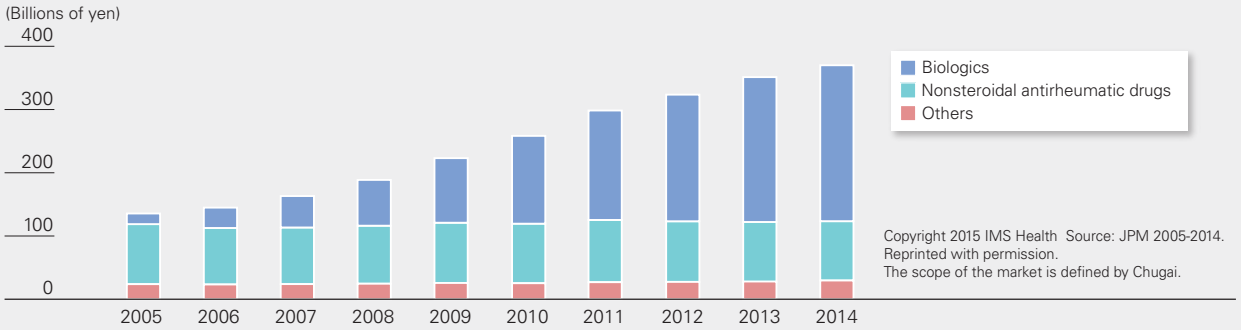
Sales of Actemra outside Japan (exports to Roche for sale in regions other than Japan, South Korea and Taiwan) increased ¥12.5 billion, or 28.9 percent, to ¥55.7 billion. Actemra IV formulation obtained regulatory approval in the European Union, where it is known as RoACTEMRA, in 2009, and in the United States in 2010. In the market for biologics in Europe and the United States, where subcutaneous formulations are used more than in Japan because of geographic and other factors, the pre-filled syringe formulation obtained approval in the United States in 2013 and in the European Union in April 2014, which contributed to faster growth than in Japan. RoACTEMRA was also approved for early RA in the European Union in September 2014.

In the U.S. and European markets, the efficacy and safety of Actemra/RoACTEMRA as the only IL-6 inhibitor is widely recognized. The European League Against Rheumatism (EULAR) issued new treatment recommendations in 2013 giving Actemra/RoACTEMRA the same grade of recommendation as earlier biologics. In 2014, a proposed update of clinical practice guidelines was announced by the American College of Rheumatology, with biologics including Actemra added as first-line treatments along with anti-TNF agents.

Osteoporosis and Osteoarthritis

Sales of Edirol, an active vitamin D_3 derivative from Chugai research, increased ¥4.2 billion, or 28.0 percent, to ¥19.2 billion. Due to its superior effectiveness in increasing bone mass and preventing bone fractures, Edirol is used more than any other vitamin D_3 derivative. Edirol is the first vitamin D_3 derivative to receive a Grade A recommendation in the osteoporosis prevention and treatment guidelines,

Rheumatoid Arthritis Market in Japan



which has helped to broaden recognition and understanding of the product as a base treatment. As a result, use of Edirol by medical institutions increased in 2014 and prescriptions expanded, primarily for new patients. In addition to prevention of fractures, recent research has focused on Edirol's other potential benefits such as prevention of falls, further raising regard for the product. We will continue to study the potential for active vitamin D_3 derivatives in helping improve patients' quality of life.

Uptake of Bonviva IV Injection, a bisphosphonate agent, has increased rapidly since its launch in Japan in August 2013. Sales increased ¥2.9 billion, or 580.0 percent, year on year to ¥3.4 billion. This product has demonstrated effectiveness with a once-monthly intravenous injection, and is especially convenient for patients who have difficulty taking oral formulations. It is therefore expected to improve adherence to treatment. Our efforts to disseminate information to healthcare providers have resulted in very high recognition of the usefulness of Bonviva IV Injection.

In the osteoarthritis segment, sales of Suvenyl decreased ¥1.2 billion, or 10.1 percent, to ¥10.7 billion due to competition from rival products and generics. Suvenyl contributes to treatment as the straight-chain hyaluronate preparation with the highest molecular weight. It is recognized not only for its viscoelasticity but also for its superior effects such as anti-inflammatory and analgesic action. We will work to promote understanding of these features and educate people about the importance of early treatment.

2015 Strategy and Outlook

In the RA segment, we anticipate further significant growth for Actemra in 2015, and will continue to contribute to the treatment of RA around the world.

In Japan, we will focus our efforts on establishing Actemra as a first-line therapy by spreading awareness of the product's high and sustained remission rate and highlighting the benefit of blocking IL-6 in RA treatment based on evidence accumulated in basic and clinical research. At the same time, we will broaden recognition of Actemra's high cost-effectiveness and conduct a study to evaluate the economic benefit of treatment with Actemra to Japanese patient lifestyle. In addition, we will enhance our efforts to provide information to medical institutions about the subcutaneous injections so that patients can safely and reliably self-inject this product at home.

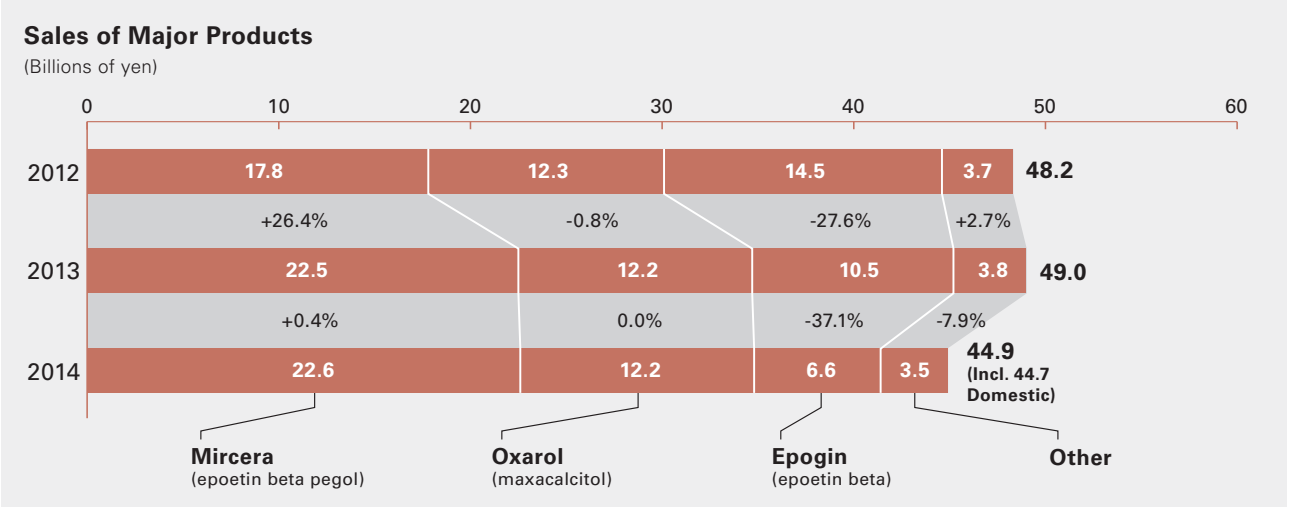
Outside Japan, we will accelerate the spread of understanding regarding the significance of blocking IL-6. We will strengthen cooperation with the Roche Group as we continue to foster recognition of Actemra's characteristics, particularly its high efficacy as a biologic monotherapy, to expand its use in first-line treatment.

In the osteoporosis segment, we will make treatment proposals that distinguish between the use of Edirol and Bonviva, which have different characteristics, and generate evidence on combined use of these two products. As a leader in the field of osteoporosis, we will educate people about the importance of measuring bone density to promote early detection and treatment so that more patients will seek timely treatment.

In the osteoarthritis segment, we will promote further understanding of the straight-chain high-molecular-weight sodium hyaluronate preparation Suvenyl, and build awareness about cartilage protection and early treatment.

Chugai has a large portfolio of products for the treatment of rheumatoid arthritis, osteoporosis and osteoarthritis – the primary underlying diseases that cause locomotive syndrome – as well as other products that can benefit elderly patients. Therefore, we will also focus on making comprehensive treatment proposals for the elderly.

Renal Diseases



Mircera (epoetin beta pegol)	Continuous erythropoietin receptor activator Launch in Japan: July 2011
Oxarol (maxacalcitol)	Agent for secondary hyperparathyroidism Launch in Japan: September 2000
Epogin (epoetin beta)	Recombinant human erythropoietin Launch in Japan: April 1990

Overview

Since the 1990 launch of Epogin, a renal anemia treatment, Chugai has led the industry in building awareness of the importance of early treatment of renal anemia. Our ongoing contributions to the treatment of renal disease in Japan include the 2011 launch of Mircera, an innovative long-acting erythropoietin-stimulating agent (ESA) with a significantly lower dosing frequency than existing medicines.

Around 90 percent of patients beginning dialysis require treatment for anemia, and improvement of anemia is essential for maintaining their quality of life. Studies suggesting that early treatment of anemia in patients with pre-dialysis renal failure* may slow disease progression have also increased awareness of the importance of treating anemia. Chugai not only provides agents for renal anemia, but also secondary hyperparathyroidism and hyperphosphatemia treatments, which are necessary in dialysis therapy. We also provide related information to help dialysis facilities as part of our comprehensive support.

* Patients who have reduced renal function, but do not yet require dialysis

Mircera
(epoetin beta pegol)

Oxarol
(maxacalcitol)

Epogin
(epoetin beta)

Review of 2014 Performance

In 2014, sales in the renal diseases field in Japan decreased ¥4.2 billion, or 8.6 percent, to ¥44.7 billion, reflecting the impact of competing products in the market.

In treatments for renal anemia associated with chronic kidney disease (CKD), in the pre-dialysis segment attention is focused on public awareness campaigns to promote early diagnosis and treatment of renal anemia. In the dialysis segment, however, the size of the market is contracting due to downward pressure on medical costs and the aging of patients. At the same time, the number of approved medicines has increased.

In this market environment, sales of Mircera increased ¥0.1 billion, or 0.4 percent, to ¥22.6 billion. Mircera can maintain stable hemoglobin levels with a dosing frequency of just once every two or four weeks. In addition, its serum half-life is the same after both intravenous and subcutaneous administration, allowing consistent treatment from pre-dialysis to dialysis. As a result, use of Mircera in treatment of pre-dialysis patients continued to grow in 2014. The product is

recognized for benefits such as better convenience for patients and longer duration of action. Awareness of the benefits of Mircera is spreading and its use is accelerating, particularly in new patients. Meanwhile, in treatment of dialysis patients, Mircera has built solid support among healthcare professionals who have seen its advantages firsthand. A growing number of treatment facilities are achieving better control of hemoglobin levels by administering a dose every two weeks. Nevertheless, market uptake has been slower than planned, in part because the revisions to the National Health Insurance drug reimbursement price have lowered the prices of rival products.

Sales of Epogin decreased ¥3.9 billion, or 37.1 percent, to ¥6.6 billion, reflecting the switch to Mircera and impact from competing products, including biosimilars.

Sales of Oxarol, an agent for secondary hyperparathyroidism, were stable at ¥12.2 billion. Oxarol maintained its leading market position, backed by substantial clinical data showing that treatment with an active vitamin D derivative can extend survival.

2015 Strategy and Outlook

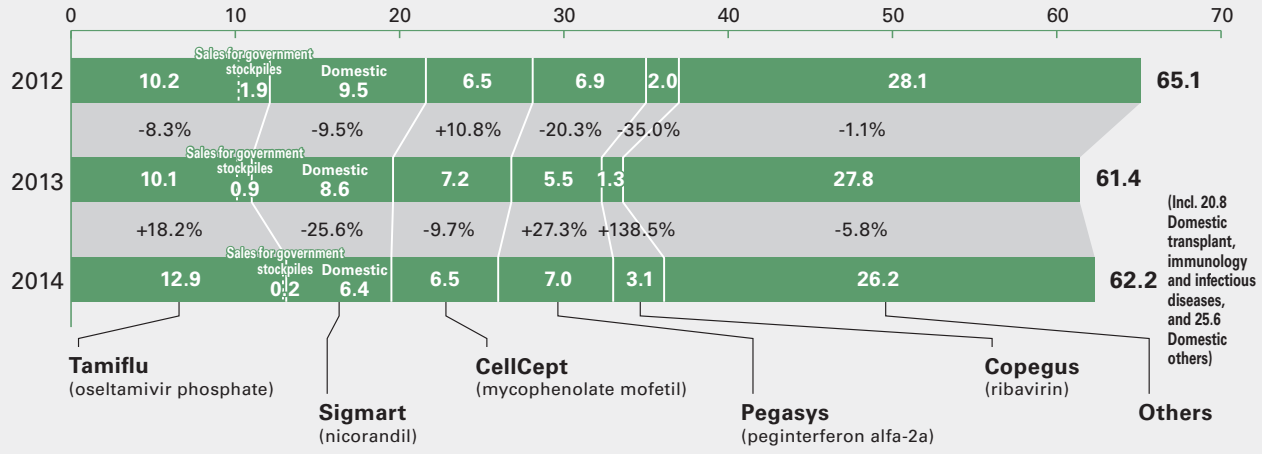
In 2015 in the renal diseases field we will continue to accelerate the uptake of Mircera. We will establish Mircera as a drug that can help to improve patients' prognosis and quality of life through its use from the pre-dialysis to dialysis stage, because it helps to keep hemoglobin above a certain level during the critical period just before and after the start of dialysis. Especially in the expanding pre-dialysis segment, we will accelerate penetration by leveraging its usefulness. We will also contribute to treatment of renal diseases in this segment by proactively providing information about Rituxan, which obtained approval in August 2014 for the additional indication of refractory nephrotic syndrome.

For Oxarol, we will promote renewed recognition of the product profile by disseminating information to firmly establish its position in the market ahead of the emergence of competing products. We will also promote awareness about the benefits of early treatment of secondary hyperparathyroidism, which is emphasized in treatment guidelines.

Transplant, Immunology and Infectious Diseases, and Others

Sales of Major Products

(Billions of yen)



Overview

At Chugai, we are also active in the transplant, immunology and infectious diseases field, which includes influenza and chronic hepatitis, as well as other fields. In the influenza area, Chugai plays an important role as a provider of the anti-influenza agent Tamiflu. We contribute to influenza treatment by disseminating information on the appropriate use of Tamiflu as well as on its safety and effectiveness, including for prevention of the disease, based on extensive clinical data accumulated over 13 years.

Tamiflu (oseltamivir phosphate)	Anti-influenza agent Launch in Japan: February 2001
Sigmart (nicorandil)	Anti-anginal agent Launch in Japan: April 1984
CellCept (mycophenolate mofetil)	Immunosuppressant Launch in Japan: November 1999
Pegasys (peginterferon alfa-2a)	Peginterferon alfa-2a agent Launch in Japan: December 2003
Copegus (ribavirin)	Anti-viral agent Launch in Japan: March 2007

In chronic hepatitis, we help raise awareness of the importance of early detection and treatment for chronic hepatitis C. The peginterferon alfa-2a agent Pegasys was approved for the treatment of compensated liver cirrhosis caused by hepatitis C, and of chronic hepatitis B, ahead of competing products, as a result of our efforts to make this product available to a broader range of patients. We are also developing products in other areas of significant unmet medical need including severe asthma and central nervous system diseases.

Review of 2014 Performance

In 2014, sales in the transplant, immunology and infectious diseases field in Japan increased ¥2.0 billion, or 10.6 percent, year on year to ¥20.8 billion. Sales in the Others field in Japan decreased ¥3.0 billion, or 10.5 percent, to ¥25.6 billion.

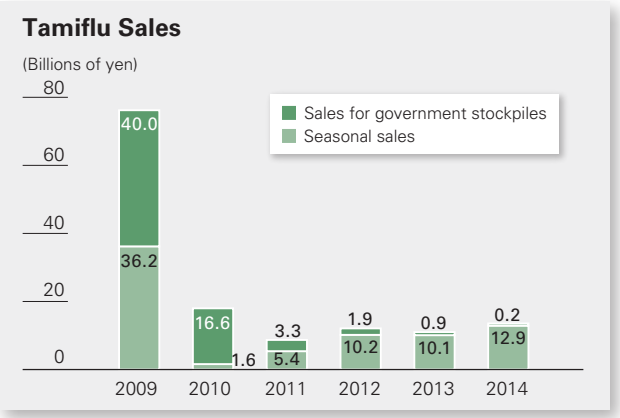
Tamiflu sales increased ¥2.0 billion, or 18.2 percent, to ¥13.0 billion, with seasonal sales of ¥12.9 billion, or ¥2.8 billion (27.7 percent) higher than in the previous year, and sales for government stockpiles of ¥0.2 billion, or ¥0.7 billion (77.8 percent) lower. We highlighted the drug's efficacy and the benefits of its unique dry syrup formulation.

Sales of CellCept, an immunosuppressant, decreased ¥0.7 billion, or 9.7 percent, to ¥6.5 billion. CellCept is used to treat refractory rejection after kidney transplants and to help prevent rejection after kidney, heart, liver, lung and pancreas transplants. The need for transplantation medicines has been rising in Japan, driven by advances in transplantation therapy.

Tamiflu
(oseltamivir phosphate)

Pegasys
(peginterferon-α-2a)

Copegus
(ribavirin)



Sales of Pegasys increased ¥1.5 billion, or 27.3 percent, to ¥7.0 billion, and sales of Copegus increased ¥1.8 billion, or 138.5 percent, to ¥3.1 billion. The number of patients with chronic hepatitis C is decreasing in Japan, reflecting advances in drug therapy. However, the use of triple combination therapy (peginterferon plus ribavirin and a protease inhibitor) expanded rapidly for patients with a specific virus type (genotype 1), and the use of Pegasys and Copegus likewise increased. Pegasys has been positively appraised in combination therapy with Copegus for compensated liver cirrhosis caused by hepatitis C, and also contributes to the treatment of hepatitis as the only peginterferon indicated for chronic hepatitis B.

2015 Strategy and Outlook

In the area of anti-influenza agents, we expect sustained competitive pressure in 2015, but will continue to promote proper understanding of Tamiflu-resistant viruses. In addition, by proactively providing information earlier, we will work to build solid awareness of the extensive safety and efficacy data on Tamiflu.

In the area of chronic hepatitis C, the move toward interferon-free treatment is expected to continue due to the launch of medicines that do not have to be administered in combination with interferon. However, there is no evidence that interferon-free therapy will produce the same degree of tumor suppression as interferon. Therefore, we will continue to focus on contributing to treatment particularly for patients with high risk factors for cancer.

To prepare for the launches of products for severe asthma and central nervous system diseases, which are expected later this decade, we will take steps such as training MRs and establishing the necessary marketing organization.

Patient Support and Disease Awareness Activities

Disease Awareness Activities

Chugai participates in and co-sponsors a variety of activities to support cancer patients and their families.

One such activity is the Relay For Life, an awareness support campaign that forges ties in the fight against cancer. This event, a 24-hour walk-a-thon in which cancer patients, their families and supporters compete as relay teams, was held in 43 locations throughout Japan in 2014. Chugai employees have participated as volunteers in the Relay For Life since 2007. A total of 474 employees took part as "Team Chugai" at 26 locations in 2014. As in 2013, Chugai used iPads to offer an educational quiz on lung cancer, which 1,463 people took at 17 locations. As participants answered questions on the iPad, Team Chugai members provided explanations to deepen their understanding of lung cancer.

Chugai employees participate as volunteers in the Relay For Life.

Measures to Support Healthcare

Based on its business philosophy of "Innovation all for the patients," Chugai contributes to improving the level of healthcare with support that goes beyond simply providing pharmaceuticals.

As treatments become more diverse and sophisticated, multidisciplinary team care has become an increasingly important approach. Chugai has been at the forefront of planning and holding workshops and other events that provide an opportunity for interdisciplinary communication. Many healthcare providers have found these workshops useful.

At the same time, because the aging society and declining birthrate substantially alter the structure of Japanese society, Chugai uses webinars on medical administration, committees to discuss local activity and other methods to disseminate the latest information on models for future medical service systems. Consequently, Chugai has a strong reputation among medical administrators.

To raise the efficiency of healthcare, Chugai proactively conducts e-promotion linked to various media. For example, in response to the diversifying channels and devices healthcare providers use to obtain information, we began providing information accessible by tablet computers and smartphones. We also improved the accessibility of product information such as package inserts and product news releases. Moreover, we have worked to enhance information for patients, primarily on safety.

Fundraising Activities

Chugai conducts fundraising activities to assist children in need around the world and patients suffering from rare intractable diseases.

Chugai collected donations for and participated in the global charity event Roche Children's Walk 2014. Approximately 2,900 Chugai employees helped raise funds, which were matched by the Company. Half of the funds were donated to Exchange Salon Hikari, which is operated by the nonprofit organization Fuyodo 2100 to provide support for disabled children and their families who are evacuees from the Great East Japan Earthquake. The other half was donated through Roche to assist orphaned children in Malawi.

For over 20 years Chugai has worked with the nonprofit organization Shuhei Ogita Fund (http://www.fund-ogita.org/) to provide OK-432, an anticancer agent and agent for treating lymphangiomas,* free of charge to children worldwide suffering from incurable lymphatic malformations. This fund helps to make the treatment available to children around the world who suffer from this disease, regardless of their local medical situation or financial difficulties.

* A rare disease in which lymphatic fluid abnormally pools in the lymphatic vessels to form cysts in parts of the body. In many cases, it is found at birth. Unlike cancer, lymphatic malformations are benign, but can retard children's development, and occasionally the cysts compress the respiratory tract and become life-threatening.

Development

Chugai's Development System

Guided by its business philosophy, "Innovation all for the patients," Chugai has established a lifecycle management system that coordinates multiple operations to bring innovative pharmaceuticals to patients as quickly as possible. Our clinical development function, for example, draws up clinical development plans based on the latest scientific findings and invites medical institutions to conduct clinical trials. Our manufacturing function examines commercial production to turn candidate compounds into pharmaceutical products and manufactures investigational drugs for clinical trials. Our drug safety function ensures a high level of safety in clinical trials by understanding and beginning assessments of each drug's safety profile from the early stages of clinical trials. Dealing with regulatory authorities, including filing applications for manufacturing and marketing approval, is handled mainly by our regulatory affairs function. Leaders from each function are assigned to development projects, and lifecycle leaders, who have been given authority over certain personnel matters, provide strong leadership for cross-divisional lifecycle teams to expedite the progress of each project and filing of applications for regulatory approval.

Acceleration of Global Development

We are making various changes aimed at speeding up global development to maximize the value of our in-house products.

For example, in developing Alecensa (development code: AF802), which was launched in September 2014, we followed a development model with a higher probability of success. As a result, we were able to shorten development to a mere seven years (For details, see the following "Oncology" section). In addition, to expedite the start of phase III multinational studies, we are including patients with the target disease in phase I clinical trials, which are normally conducted on healthy adult subjects, to determine the efficacy of a drug at an earlier stage. This is called early proof-of-concept (PoC),[1] and allows us to design global development plans and negotiate with partners earlier to facilitate a smooth transition to phase III multinational studies. Using this approach, we were able to out-license ACE910 to Roche less than two years after the start of clinical development. In August 2014, we amended the business agreement with Roche regarding out-licensing to expedite the development process for products from Chugai research and to use our resources more efficiently. Among the changes, we will offer Roche first refusal rights for overseas development of all products upon achievement of early PoC.

For SA237 and CIM331, Chugai has taken a new approach by managing multinational studies. We are working to strengthen our clinical science functions and raise our competitiveness in clinical trial design. As part of the ongoing reform of our development system, a chief medical officer (CMO) was appointed from outside the Chugai Group in March 2014, and in April 2015 we established the Translational Clinical Research Division.

1. Proof-of-concept (PoC) is a demonstration 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.

Oncology

Overview

In 2014, Chugai launched two new products and obtained approval for one project in the oncology field. Three development projects for compounds from Chugai research are currently under way, and we are also developing 13 compounds in-licensed from Roche, with one already filed for regulatory approval. Of the projects in our pipeline, 10 are based on Personalized Healthcare (PHC).

Products from Chugai Research

Alecensa (generic name: alectinib), an anaplastic lymphoma kinase (ALK) inhibitor, was launched in Japan in September 2014 following approval in July 2014 for

New Chief Medical Officer (CMO)

In managing multinational clinical studies, Chugai must not only understand the needs of patients and healthcare professionals throughout the world, but also be able to effectively engage with regulators and global partners. With this in mind, Chugai Pharma USA, LLC, a wholly owned subsidiary of Chugai, appointed Athos Gianella-Borradori, M.D. as its chief medical officer (CMO). The CMO is responsible for overseeing all clinical development activities in the United States and representing Chugai in communications with U.S. regulatory authorities and clinical trial investigators. Dr. Gianella-Borradori, a hematologist-oncologist, has held senior positions in research and development at several global pharmaceutical companies, and will use his expertise to increase awareness of Chugai's achievements to facilitate expansion of its clinical development activities in the United States.

the treatment of *ALK* fusion gene-positive unresectable, recurrent/advanced non-small cell lung cancer. After the product was designated as an orphan drug by the Ministry of Health, Labour and Welfare, we filed for approval based on the results of a phase I/II clinical trial in Japan, and it received priority review. As a result, the launch of Alecensa was exceptionally fast.

Overseas, a phase III multinational study of Alecensa was started by Roche in August 2014. It is the first drug from Chugai research to receive Breakthrough Therapy designation from the U.S. Food and Drug Administration (FDA), and is expected to contribute significantly to the treatment of patients around the world.

The PI3K class I inhibitor PA799 and the MEK inhibitor CIF were removed from the pipeline in 2014 after a reconsideration of priorities.

Products In-Licensed from Roche

We are conducting two projects to develop Perjeta (development code: RG1273), a HER2 dimerization inhibitory humanized monoclonal antibody launched in September 2013, for the additional indications of HER2-positive breast cancer (adjuvant) and gastric cancer. Each of these projects is moving steadily through phase III multinational studies. Kadcyla (development code: RG3502), an anti-HER2 antibody-tubulin polymerization inhibitor conjugate, obtained approval in September 2013 and was launched in April 2014 for HER2-positive inoperable or recurrent breast cancer. Kadcyla is currently being evaluated in a phase III multinational study as a potential treatment for HER2-positive breast cancer (adjuvant) and a phase II/III multinational study for gastric cancer. By expanding the indications of these drugs that target HER2, we expect them to play a significant role in the treatment of HER2-positive cancer, along with our existing core product Herceptin (generic name: trastuzumab).

For MPDL3280A, an engineered anti-PDL1 monoclonal antibody, phase III multinational studies for the potential treatment of non-small cell lung cancer and bladder cancer started in February 2014 and January 2015, respectively. A protein called programmed death-ligand 1 (PD-L1) expressed on the surface of tumor cells results in T cell tolerance induced via the PD-1/PD-L1 pathway, allowing the tumor to evade attack by T cells. MPDL3280A binds to PD-L1 and blocks the PD-1/PD-L1 pathway to restore T cell immune activity, and has gained attention as a new type of anticancer agent.

We filed for approval of Zelboraf (development code: RG7204), a BRAF inhibitor, for the treatment of melanoma in April 2014, obtained approval in December 2014 and launched it in February 2015. Roche Diagnostics K.K. filed for approval of a companion diagnostic to detect mutations of the *BRAF* gene, which was also granted in December 2014. In January 2015, administration of anti-VEGF humanized monoclonal antibody Avastin (development code: RG435) began in a phase II clinical trial in Japan for the potential treatment of cervical cancer.

In December 2014, we filed for approval of Xeloda (development code: RG340), a fluoropyrimidine anti-tumor agent, for the additional indication of gastric cancer (adjuvant).

We have discontinued development of the humanized anti-MET monoclonal antibody RG3638 for non-small cell lung cancer in accordance with the recommendation by an independent data monitoring committee to stop a phase III multinational study (the METLung study).

We also discontinued development of Avastin for

Oncology Development Pipeline (As of January 28, 2015)

Development Code	Expected Indication	Status	Generic Name	Dosage Form	Origin (Collaborator)
AF802 (RG7853)	◆ Non-small cell lung cancer	Approved: July 2014	alectinib	Oral	In-house (Roche)
		Phase III: (Overseas)			
RG7204	◆ Melanoma	Approved: Dec. 2014	vemurafenib	Oral	Roche
RG340	Gastric cancer (adjuvant)	Filed	capecitabine	Oral	Roche (Yakult Honsha)
RG1273	◆ Breast cancer (adjuvant)	Phase III: (Multinational study)	pertuzumab	Injection	Roche
	◆ Gastric cancer	Phase III: (Multinational study)			
RG3502	◆ Breast cancer (adjuvant)	Phase III: (Multinational study)	trastuzumab emtansine	Injection	Roche
	◆ Gastric cancer	Phase II/III: (Multinational study)			
GA101 (RG7159)	Aggressive non-Hodgkin's lymphoma	Phase III: (Multinational study)	obinutuzumab	Injection	Roche (Nippon Shinyaku)
	Indolent non-Hodgkin's lymphoma	Phase III: (Multinational study)			
MPDL3280A (RG7446)	◆ Non-small cell lung cancer	Phase III: (Multinational study)	—	Injection	Roche
	◆ Bladder cancer	Phase III: (Multinational study)			
RG435	Cervical cancer	Phase II	bevacizumab	Injection	Roche
GC33 (RG7686)	◆ Hepatocellular carcinoma	Phase II: (Multinational study)	—	Injection	In-house (Roche)
CKI27 (RG7304)	◆ Solid tumors	Phase I	—	Oral	In-house (Roche)
		Phase I: (Overseas)			
RG7321	Solid tumors	Phase I	pictilisib	Oral	Roche
RG7596	Non-Hodgkin's lymphoma	Phase I	polatuzumab vedotin	Injection	Roche
RG7604	◆ Solid tumors	Phase I	taselisib	Oral	Roche

● Designates change in status in 2014 and thereafter ◆ PHC-based drug discovery

the additional indication of breast cancer (adjuvant) and RG7414, an anti-EGFL7 humanized monoclonal antibody, because the predetermined efficacy criteria were not satisfied in clinical trials.

New Development Projects

Among projects that moved into the clinical phase of development in 2014, a phase I clinical trial for RG7596 as a potential treatment for non-Hodgkin's lymphoma started in Japan in July. RG7596 is an antibody-drug conjugate composed of the microtubule inhibitor MMAE linked to an anti-CD79b monoclonal antibody. It is designed for direct delivery of MMAE into target cells via CD79b, which is expressed on malignant B-cell lymphocytes. It is thus expected to inhibit tumor cell growth while limiting effects on normal cells.

A phase I clinical trial for RG7604 as a potential treatment of solid tumors started in Japan in September 2014. RG7604 is a small-molecule anticancer agent that selectively inhibits PI3K. Compared with RG7321, which is also in phase I, it has been shown to exhibit stronger inhibitory activity against PI3Kα mutations.

Bone and Joint Disease/ Autoimmune Diseases

We are working to maximize the value of Actemra (development code: MRA), a product of Chugai research, in Japan and around the world. A new subcutaneous formulation obtained approval in Japan and the United States in 2013, and in the European Union in April 2014. The product also obtained approval in the European Union under the name RoACTEMRA in September 2014 for use in patients with early rheumatoid arthritis. In Japan, a phase III clinical study for Actemra as a potential treatment of Takayasu's arteritis (a type of large-vessel vasculitis) started in October 2014 following its designation as an orphan drug for this indication in June 2014. Takayasu's arteritis and giant cell arteritis, which is currently the target of a phase III clinical study by Roche overseas, are both types of large-vessel vasculitis, and are pathologically similar. However, clinical differential diagnosis is required because there are differences in the age of onset and affected sites.

SA237 is an IL-6 inhibitor that Chugai is developing to follow Actemra. A Chugai-managed phase III multinational study for the potential treatment of neuromyelitis optica (NMO) started in February 2014. Specifically, two studies are under way: one for monotherapy (U.S. and Canada) and another for combination therapy with existing treatments (Japan, Europe and Taiwan). SA237 is a next-generation therapeutic antibody that was developed by applying recycling antibody technology, one of Chugai's proprietary innovative antibody engineering technologies. Recycling antibodies are engineered to reduce antibody clearance and enable a single molecule to bind to a target antigen repeatedly. Using this technology, SA237 exhibited plasma persistence four times that of Actemra in nonclinical trials. The results of repeated administration in a phase I clinical trial confirmed the concept of extending serum half-life. This drug is expected to improve convenience for patients in terms of dosage amount and frequency. In June 2014, SA237 was designated as an orphan drug by the U.S. FDA.

A project to add the indication of enthesopathy for Suvenyl failed to meet the primary endpoint in 2013, and after considering the future direction of the project, Chugai discontinued development in 2014. We also discontinued development of RG7415, an anti-interferon alpha humanized monoclonal antibody, in view of the progress of development at Roche.

Central Nervous System/ Other Diseases

Central Nervous System

In the central nervous system field, Chugai is developing four compounds in-licensed from Roche.

Bone and Joint Diseases/Autoimmune Diseases Development Pipeline (As of January 28, 2015)

Development Code	Expected Indication	Status: Phase I	Phase II	Phase III	Filed	Approved		Generic Name	Dosage Form	Origin (Collaborator)
Bone and Joint Diseases										
RG484	Osteoporosis							ibandronic acid	Oral	Roche (Taisho Pharmaceutical)
Autoimmune Diseases										
MRA (RG1569)	Rheumatoid arthritis (new formulation: subcutaneous injection)						(Overseas: E.U.) April 2014	tocilizumab	Injection	In-house (Roche)
	Large-vessel vasculitis									
	Giant cell arteritis				(Overseas)					
	Systemic sclerosis			(Overseas)						
SA237	Neuromyelitis optica				(Multinational study)*			—	Injection	In-house

Designates change in status in 2014 and thereafter

* Multinational study managed by Chugai

In May 2014, we started a phase III multinational study for RG1450, an anti-amyloid-beta human monoclonal antibody. RG1450 is intended for use before the onset of symptoms and in the early stages of Alzheimer's disease, and expectations are rising for this drug in early intervention. The study targets patients most likely to respond to treatment based on levels of amyloid deposition, as the compound is also seen as a possible disease-modifying drug (a drug that acts to inhibit recurrence and slow progression of the disease).

A new project in our pipeline is RG1662, a $GABA_A\alpha5$ receptor antagonist with the expected indication of improvement of intellectual ability in individuals with Down syndrome. A phase I clinical trial on healthy adults started in Japan in May 2014. RG1662 is expected to increase cognitive and memory ability in individuals with Down syndrome by inhibiting excessive activity of GABA, the dominant inhibitory neurotransmitter. The clinical study is assessing the compound's effect on both cognitive function and adaptive behavior.[2]

We discontinued development of RG1678, glycine reuptake inhibitor, in view of the progress of development at Roche.

2. Adaptive skills needed in everyday living – for example, reading, writing, language, personal relationship building, and dressing skills

Other Diseases

ACE910 is an anti-factor IXa/X bispecific antibody that employs Chugai's proprietary antibody engineering technologies. A phase I clinical trial of ACE910 as a potential treatment for hemophilia A started in August 2012, and Chugai signed an out-licensing agreement with Roche in July 2014. Replacement therapy to supplement blood coagulation factor VIII (FVIII) is the established standard of care for hemophilia A, and in recent years routine supplementation has been increasingly used to prevent bleeding. However, intravenous injections three times a week are required in standard replacement therapy protocols, and difficulty in venous access is a problem for infants in particular. Moreover, autoantibodies (inhibitors) against FVIII develop in some patients who receive FVIII formulations, making it difficult to stop bleeding. ACE910 shows promise as an antibody that can prevent bleeding with once-weekly or less frequent subcutaneous administration, regardless of the presence of inhibitors. Phase I clinical trial data presented in December 2014 showed that once-weekly subcutaneous administration of this drug reduces bleeding frequency in patients with or without inhibitors. It therefore has the potential to change the existing therapy for hemophilia A. Another key feature of ACE910 is that it applies Chugai's proprietary ART-Ig technology for commercial production of bispecific antibodies.

CIM331 is an anti-IL-31 receptor humanized monoclonal antibody that originated from Chugai research. A Chugai-managed phase II multinational study of this drug as a potential treatment for atopic dermatitis started in December 2013 in Japan, the United States and Europe, and is proceeding smoothly. CIM331 works by blocking the binding of IL-31, which is related to the itchiness of atopic dermatitis, to its receptors, and thus has the potential to prevent itching and improve dermatitis by cutting off the itch-scratch cycle.

A phase II clinical trial started in July 2014 to investigate the URAT1 inhibitor URC102 as a potential treatment for gout. URC102 is a small-molecule compound originating from one of our satellite labs, C&C Research Laboratories in South Korea, and is being co-developed with JW Pharmaceutical Corporation of South Korea. The compound is expected to reduce the level of serum uric acid by promoting its excretion through inhibition of URAT1.

Chugai started a phase II multinational study of RG3637, an anti-IL-13 humanized monoclonal antibody, for the potential indication of idiopathic pulmonary fibrosis in October 2014.

Chugai has stopped development of RG7652, an anti-PCSK9 human monoclonal antibody, following Roche's discontinuation of development.

Central Nervous System/Other Diseases Development Pipeline (As of January 28, 2015)

Development Code	Expected Indication	Status: Phase I	Phase II	Phase III	Filed	Approved	Generic Name	Dosage Form	Origin (Collaborator)
Central Nervous System									
RG1450	◆ Alzheimer's disease			(Multinational study)			gantenerumab	Injection	Roche/MorphoSys
RG7090	Major depressive disorder			(Multinational study)			basimglurant	Oral	Roche
RG1577	◆ Alzheimer's disease						—	Oral	Roche
RG1662	Improvement of intellectual ability in individuals with Down syndrome						—	Oral	Roche
Other Diseases									
RG3637	◆ Asthma			(Multinational study)			lebrikizumab	Injection	Roche
	◆ Idiopathic pulmonary fibrosis			(Multinational study)					
CIM331	◆ Atopic dermatitis			(Multinational study)*			—	Injection	In-house
URC102	Gout			(Overseas)			—	Oral	In-house/ JW Pharmaceutical
ACE910 (RG6013)	Hemophilia A			(I/II)			—	Injection	In-house (Roche)

Designates change in status in 2014 and thereafter ◆ PHC-based drug discovery

* Multinational study managed by Chugai

Production and Procurement

Features of Chugai's Production Functions

Chugai is enhancing its production technologies and working toward a more robust production system based on the belief that its production functions create value through stable supply to patients and healthcare providers and product creation that allows the Company to deliver innovative pharmaceuticals to patients as soon as possible.

Chugai has been accumulating new knowledge and experience backed by continuous innovation, particularly in the manufacture of therapeutic antibodies, where our technologies are at Japan's top level. Our production of biopharmaceuticals began more than 30 years ago. With Actemra, we became the first in Japan to manufacture a therapeutic antibody and subsequently have achieved commercial-scale production of a series of pharmaceuticals developed using new antibody technologies. In addition, our on-site improvements have reduced work that must be re-done, enabling us to manufacture investigational new drugs in a short time.

Our production bases are spread around the globe, with three domestic plants in Utsunomiya, Ukima and Fujieda. We have also created a rigorous quality control system in line with global standards, including compliance with GMP.*

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

Antibody production cell culture: Cells are transplanted in a 10,000-liter bioreactor for cultivation.

Cell separation: Cells are eliminated from the culture medium.

Measures to Enhance Production Functions

Chugai focuses on enhancing its production functions for accelerated market launches and simultaneous development based on continuous generation of development projects that are more innovative.

One measure is the establishment of a seamless integrated production system. Formerly, investigational new drug production and post-marketing production each had their own exclusive facilities and staff. However, raising the level of GMP and sharing technologies for flexible use of both lines immediately reduced the time required for development while accommodating a staged increase in scale from clinical development to post-marketing production. The extremely rapid acquisition of regulatory approval for Alecensa and other products exemplifies the success of this measure. To expedite multiple development projects, we employ cell-culture tanks with single-use disposable bioreactors at the Ukima plant. This makes washing and inspection after cultivation unnecessary, allowing cultivation of the next batch without interruption and thus dramatically raising capacity utilization (currently two such 2,000-liter units are in operation, with two additional 2,000-liter units to be installed in 2015).

Overview of Production Bases

Plant	Features	Products Manufactured
Utsunomiya plant (Tochigi Prefecture)	One of Japan's largest facilities for cultivating biological active pharmaceutical ingredients (APIs) and a state-of-the-art production line for injectable formulations	Biological APIs: Actemra APIs Injectable formulations: Actemra, Avastin, Epogin and others
Ukima plant (Tokyo)	Manufactures and packages solid and injectable formulations and biological APIs. Started manufacturing investigational new drugs in 2013.	Biological APIs: Epogin APIs and others Injectable formulations: Oxarol and others Solid formulations: Alecensa and others
Fujieda plant (Shizuoka Prefecture)	Integrated production line from API synthesis to formulation and packaging. Also supplies its APIs overseas.	API synthesis: Edirol and others Solid formulations: Edirol, Tarceva, Xeloda and others

Future development of drugs using recycling antibody, sweeping antibody and other technologies is expected to entail production of diverse small-dose pharmaceuticals. For this purpose, we are working to set up a production system for small volumes of multiple products, including installation of tray fillers to handle various types of syringes on the same production line during the formulation process.

Reliable Distribution of Pharmaceuticals

To ensure a stable and continuous supply of safe, high-quality pharmaceuticals, Chugai is strengthening its supply chain management to optimize each step from raw material procurement to production and distribution. As part of that effort, we established a global supply chain to reliably meet demand in countries around the world. We share global demand information and collaborate with Roche to leverage our experience as the supplier of Japan's first original therapeutic antibody to overseas markets.

Also, with the globalization of our suppliers of raw materials and intermediates and our production bases for finished products, we are ensuring shipping quality between bases and developing risk countermeasures, such as increasing the locations that produce essential products, based on our experience from the Great East Japan Earthquake. In ways such as these, we are working to maintain and improve the reliability of distribution in Japan and overseas by strengthening our measures for supply chain management as it becomes increasingly complex and global.

Chugai Distribution Co., Ltd. handles distribution of pharmaceuticals in Japan. For stable and safe distribution, the company uses a computer system for inventory management and inspection, and the staff employs original methods for the careful packaging of products to enable easy sorting and prevent damage when recipients open the cartons.

Measures for Stable Procurement

Raw material procurement is a key business activity in providing a stable and continuous supply of high-quality pharmaceuticals to healthcare providers and patients. However, the stable procurement of raw materials is constantly exposed to risks such as discontinued production due to the merger or closing of suppliers, spikes in prices or problems with availability due to fluctuations in the balance of raw material supply and demand, or delays in delivery caused by accidents at suppliers. Chugai takes a number of measures to avoid these risks and maintain a stable supply of raw materials. For each raw material, we monitor market trends and the financial condition of suppliers; conduct quality assessments, price analysis and delivery management; and analyze risks at production facilities, such as natural disasters. In this way, we ensure a stable supply of pharmaceuticals.

Quality Assurance

Placing top priority on patients, Chugai seeks to provide high-quality products and services that offer outstanding efficacy and safety. From this perspective, Chugai's Quality Assurance Department is working closely with each manufacturing site to improve product quality.

Quality assurance functions have diversified in recent years as the product supply process has become more complex and the scope of cooperation between our quality assurance and development operations has broadened for smoother product development. Quality requirements are becoming increasingly stringent with Japan's accession to the Pharmaceutical Inspection Convention and the Pharmaceutical Inspection Co-operation Scheme (PIC/S) in July 2014 and the start of implementation of the international Pharmaceutical Quality System guideline.

In view of these trends, Chugai conducts consistent GMP throughout the product lifecycle from development to manufacturing, and is strengthening oversight of GMP management to promote more rigorous and high-level quality assurance. As part of its efforts to strengthen oversight, Chugai has created a world-class system for pharmaceutical quality management that began operation in April 2014.

Chugai's products are provided to patients worldwide, and we have affiliated manufacturing sites around the world, including Roche's production facilities. We carry out GMP consistently from the development stage to ensure that we continue to deliver high-quality medicines to patients everywhere.

Building Fair, Transparent Relationships with Business Partners

Chugai emphasizes cooperation with its business partners and works on a daily basis to promote various initiatives to ensure fair and transparent relationships with them as equals.

We have been standardizing and optimizing our process for purchasing indirect materials, such as office supplies, to ensure healthy competition. In 2011, we restructured our electronic purchasing system, which was introduced in 2005 as an optimal mechanism for building fair and transparent business relationships.

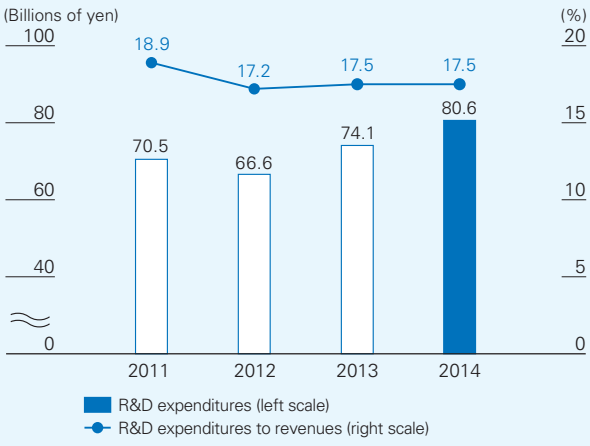
Research

Basic Policy and Allocation of Resources

Chugai's raison d'etre is to generate a steady stream of innovative products to address unmet medical need and benefit the medical community and human health around the world. Based on this principle, our key priority is to create new drugs with first-in-class or best-in-class potential. We are also a major player in Personalized Healthcare (PHC), where treatment is fitted to individual patients based on molecular and genetic profiles of their cells. Accordingly, we are focusing on the creation of molecular targeted therapies that are suitable for PHC and we are also partnering with the Roche Group's Diagnostics Division for simultaneous development of companion diagnostics.

In allocating research resources, we prioritize projects based on criteria such as a compound's potential for development as a novel medicine that can be clearly differentiated; whether it has a scientific basis for addressing unmet medical need; and whether it is a project that will enable PHC. At various decision points during research, we focus first and foremost on patient needs, reflecting our belief that creating medicines that patients and healthcare providers truly need, will lead to Chugai's medium-to-long-term growth.

R&D Expenditures (Core Basis)



Strengths of Chugai's Research Organization

Chugai has three core strengths in its research operations.

The first is our years of accumulated knowledge and the benefits of the merger with Nippon Roche. Before the merger, Chugai had been engaged in research and development of biopharmaceuticals for more than 30 years and had a top-class research platform in Japan for biopharmaceuticals and therapeutic antibodies. Nippon Roche, meanwhile, had discovered Xeloda, the global standard of care for cancer, and established a world-class technology platform for the discovery of synthetic agents. The merger of these two companies in 2002 created an industry-leading technology platform excelling in both biopharmaceuticals and small molecule drugs.

The second strength is access to Roche's global research infrastructure. The ability to share Roche's research resources and infrastructure, which include a rich compound library for use in high throughput screening[1] and a database of information on compounds, represents a significant advantage for Chugai in terms of cost and efficiency, and has dramatically increased our research productivity. While we enjoy the benefits of these assets of the Roche Group, independence of research and development activity has been ensured.

The third strength is our research system's environment of open innovation [2] Chugai cooperates and collaborates with cutting-edge research institutions, and has steadily engaged in joint research, while contributing its own technology and know-how. Combined with recognition of our proprietary technologies, this has helped us to build strong external networks. Chugai also conducts research at satellite labs (research subsidiaries).

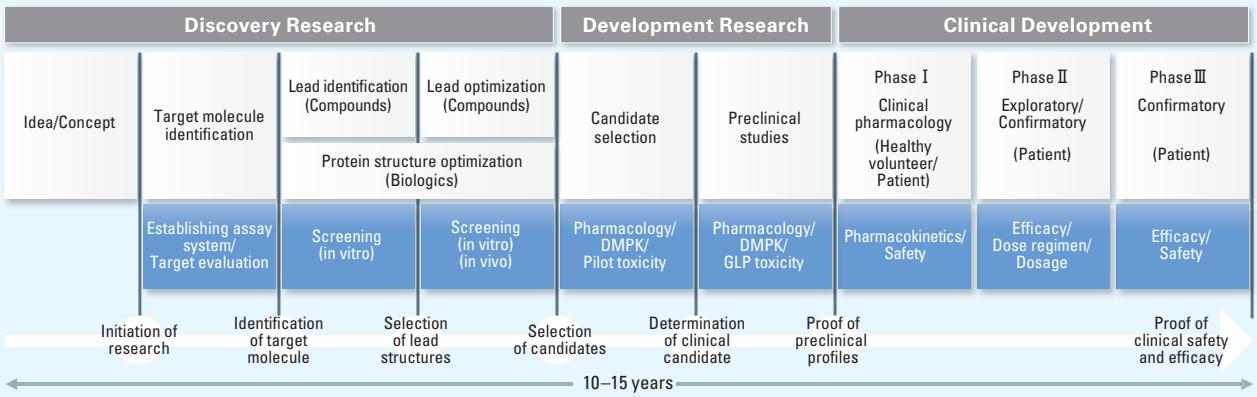
1. A technology that conducts evaluations at a high speed with automated robots or other means to select chemical compounds having activities for drug creation targets from a library consisting of a vast number of compound types with various structures
2. Generating innovative, new value by utilizing the technologies and development capabilities of external research networks in addition to in-house capabilities.

Recent Outcomes of Research Activities and Continuous Creation of Innovative Products

There are still many patients with diseases for which no sufficiently effective treatment is established. These areas of unmet medical need remain because they cannot be addressed with conventional technologies. Chugai's research has been developing new technologies to address these areas of unmet medical need. The development of bispecific antibody technology, which is used in ACE910, is a representative example. Moreover, to maximize the value of our proprietary technologies, we further refine and apply them to other target molecules. By repeating this cycle of developing original technologies to address unmet medical need, then developing innovative therapies and conducting drug discovery that applies these technologies, we can continuously generate new first-in-class and best-in-class drugs.

Chugai granted licenses to Roche in May 2014 for its proprietary innovative antibody engineering

Process and Milestones of Drug Development



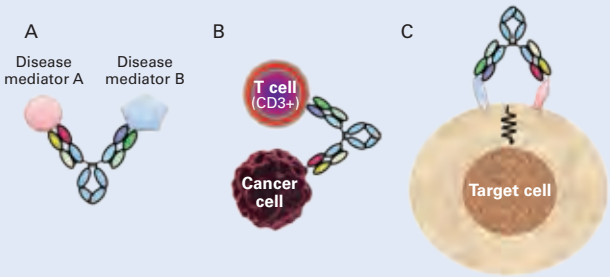
technologies that were developed in this way, including recycling ant body, which extends a therapeutic antibody's duration of efficacy, sweeping antibody, which eliminates disease-causing antigens from plasma, and bispecific antibody. Moreover, we have expanded drug discovery research by operating satellite labs as part of our open innovation initiatives. This led to the successful establishment of stable cell lines of colon cancer stem cells in October 2012, which we published in an academic paper. In addition, URC102, a small-molecule compound discovered at C&C Research Laboratories in South Korea, a joint venture between Chugai and JW Pharmaceutical Corporation of South Korea, has already entered clinical development. New drug targets have also been identified at the University of Tokyo Research Center for Advanced Science and Technology and Forerunner Pharma Research Co., Ltd., a multidisciplinary research institution adjacent to the RIKEN Yokohama Institute. We will effectively incorporate these findings into drug discovery research to further enhance our development pipeline. Moreover, we established Chugai Pharmabody Research Pte. Ltd. (CPR) in Singapore in 2012 to accelerate antibody creation.

In recent years, many projects from Chugai's research have entered clinical development. Of the 20 new compounds in our development pipeline in 2014, 35 percent were developed in-house. PHC-related projects represented 50 percent of our total pipeline (including projects in-licensed from Roche).

Note: For details on Chugai's innovative proprietary antibody technologies, see our website (http://www.chugai-pharm.co.jp/english/profile/rd/index.html).

Drug Discovery Using Bispecific Antibodies

Antibodies normally bind with only one type of target molecule, but a bispecific antibody can bind simultaneously to two different disease mediators (Figure A), and is therefore expected to enhance drug efficacy. Bispecific antibodies are attracting attention because they not only display the effects of two drugs in a single drug, but also are expected to display new functions unachievable by conventional antibodies. These include bridging tumor cells and immune cells (Figure B) to enhance antitumor effect, inducing intercellular signals by bridging different sites on the same cell (Figure C) or facilitating access between two different molecules (for example, an enzyme and a substrate) to trigger the drug's action, as with ACE910. By developing proprietary technologies to address unmet medical need, such as ART-Ig technology for effective large-scale production of bispecific antibodies, and maximizing their value by applying them to various target molecules, Chugai will continuously create first-in-class and best-in-class drugs.



Progress of Development Projects

January 1, 2014 – January 28, 2015

	Number of Projects	Breakdown		
		New Molecular Entities	Additional Indications	Additional Dosage and Administration/ Formulations
Approved	4	2	1*	1
Filed	2	1	1	—
Started phase III	7	5	2	—
Started phase II	3	2	1	—
Started phase I	3	3	—	—
Development suspended	8	—	—	—

* Includes approval of Actemra for early RA in the European Union

Bioethics in R&D

To ensure that research using human-derived test material is carried out appropriately, Chugai has established Ethical Guidelines for Research That Uses Human-Derived Test Material and a Research Ethics Committee. More than half of the members of this committee are from outside the Company to conduct fair evaluations from a pluralistic frame of reference. Moreover, we strive to ensure that research is conducted with respect for human rights by offering guidance to our researchers on the necessary ethical knowledge and standards required when conducting research on human-derived test material, including the Declaration of Helsinki and protection of personal information.

Chugai's View of Animal Welfare

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 act so as to minimize their pain, keeping in mind the scientific conditions.

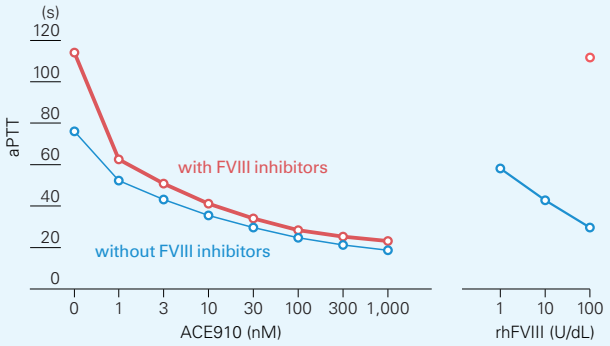
The Institutional Animal Care and Use Committee has added an examiner from outside the Company to assess the validity of research using laboratory animals from a more objective viewpoint and make appropriate improvements to reflect changes in the social environment and scientific progress. At the same time, an institutional qualification program was adopted for researchers and animal handlers to cultivate concern for animal welfare through education and training. These measures were positively evaluated by AAALAC International,[3] a global independent evaluation organization, and Chugai has maintained full accreditation since 2007.

Research Technology Reflected in ACE910

Hemophilia A and Issues with Conventional Treatments

Hemophilia A is a bleeding disorder caused by a congenital deficiency or abnormal function of blood coagulation factor VIII. Overall, there are approximately 40,000 registered patients in Japan, the United States and Europe and approximately 140,000 worldwide, but the total number of people with hemophilia A, including those who are undiagnosed, is estimated to be more than 300,000. Current treatment of hemophilia A, which centers on administration of factor VIII, consists of on-demand therapy for administration in bleeding episodes and regular replacement therapy to prevent bleeding (prophylaxis). In recent years, regular replacement therapy has spread as an effective method of preventing the onset and progress of joint disease due to repeated bleeding in the joints. However, the necessity of frequent (three times a week) intravenous administration in children, whose narrow blood vessels are difficult to see, and the loss of therapeutic effect due to the appearance of neutralizing antibodies called inhibitors during factor VIII therapy are major issues. Under these circumstances, Chugai explored approaches for resolving these issues with a mission to address the high unmet medical need for hemophilia A therapies. Our efforts were underpinned by our many years of experience and knowledge in the area of blood from the research, development and sale of erythropoietin and recombinant human granulocyte colony-stimulating factor (G-CSF) and cultivation of the antibody technologies developed in the process of creating Actemra. This led to the idea of a bispecific antibody (ACE910: phase I/II clinical trial under way in Japan) that mimics the function of factor VIII by simultaneously binding to activated factor IX and factor X.

Plasma Coagulation Accelerating Action of ACE910



Source: Chugai data

3. Association for Assessment and Accreditation of Laboratory Animal Care International, a private nonprofit organization that promotes the humane treatment of animals in scientific research through voluntary inspection and accreditation programs. More than 900 facilities in 37 countries have been accredited.

Academic Support Activities

Chugai actively promotes exchanges with researchers and healthcare providers around the world and particularly the fostering of young researchers in Asia.

The Chugai Academy for Advanced Oncology (CHAAO)[4] held its largest event, the International Academy for Advanced Oncology (IAAO) 2014, over two days in Tokyo in August 2014. The main topic of this fifth annual forum was "Convergence for Breakthroughs in Oncology Therapy." Thirteen influential oncologists working at the forefront of their field gave lectures on cutting-edge cancer therapy. In addition to scientific presentations, the event included a lecture on the recently trending topic of conflict of interest, with a presentation of measures in Japan, the United States and Europe. There was also a panel discussion on the need for cooperation and the proper relationship between academia and pharmaceutical companies in drug creation. Moreover, a lecture on cancer immunotherapy, which has drawn considerable attention in recent years, generated especially lively discussion with presentations of three topics covering basic to clinical research that provided a hint of the breakthroughs to come in this new area of oncology.

Chugai conducts an international joint research fellowship program through the Tokyo Biochemical Research Foundation (TBRF). Each year, the foundation invites young postdoctoral researchers from Asia to conduct joint research at universities and scientific research institutions in Japan for one to two years. Since its launch in 1995, the program has supported 77 researchers from 15 Asian countries and regions. At a meeting in March 2014, nine researchers from India, Indonesia, South Korea, Thailand, China, Nepal and Bangladesh presented their findings. For details on the program, see the TBRF website (http://www.tokyobrf.or.jp/english/).

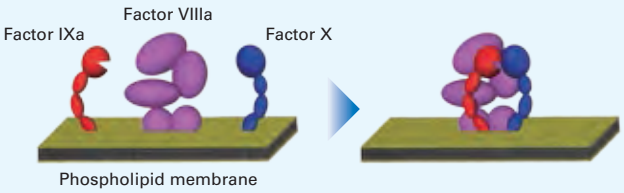
4. Founded in October 2009 to contribute to the establishment and advancement of infrastructure for cancer treatment in Japan. To bring cancer treatment in Japan to a world-class level, CHAAO promotes deeper academic exchange between the world's top specialists in oncology and healthcare professionals who play a leading role in cutting-edge research and treatment of cancer in Japan.

Drug Creation Using Bispecific Antibody Technology

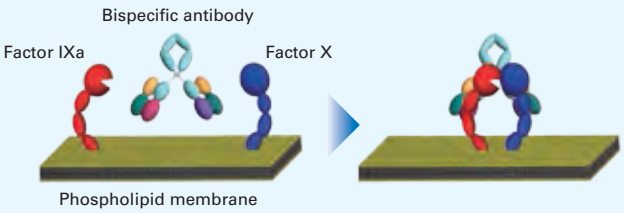
Bispecific antibodies, which bind to two different types of antigen, have a more complex structure than conventional antibodies, making high-efficiency output and purity for large-scale production extremely difficult. Chugai overcame these challenges by establishing ART-Ig, a proprietary technological platform for creating bispecific antibodies. As a result, we have achieved a production volume and purity equivalent to conventional therapeutic antibodies with a manufacturing process on a 2,500-liter scale.

Non-clinical studies for ACE910 created this way have shown that it simultaneously binds to factor IX and factor X, activating factor X by activated factor IX and promoting the blood coagulation that occurs as a result. It also demonstrated its efficacy in the presence of factor VIII inhibitors. In the results of a phase I study in Japan announced at the American Society of Hematology Annual Meeting in December 2014, once-weekly subcutaneous administration demonstrated a prophylactic efficacy profile irrespective of the presence of inhibitors.

Mode of action of current treatment



Mode of action of ACE910



Medical Affairs

Medical Affairs System

In addition to creating a steady flow of innovative drugs, Chugai recognizes the importance of ensuring that the value of its products is delivered appropriately to patients, which will lead to better treatment. Promoting safe and appropriate use of new products, verifying the efficacy of products in clinical practice and validating medical data with transparent post-marketing clinical studies play a key role in that effort.

At the same time, healthcare compliance requirements for pharmaceutical companies are being tightened worldwide. In Japan, separation of marketing and medical affairs[1] and enhancement of transparency and fairness in post-marketing clinical studies have become pressing issues.

Chugai has been working to further promote healthcare compliance and strengthen its medical affairs functions, which serve as a bridge between healthcare and pharmaceutical industries. We have also made several organizational changes. In 2012, we shifted all functions related to medical science by establishing the independent Medical Affairs Division and unified medical plan[2] and post-marketing development functions. In 2013, we launched a system for consistent management of medical plans throughout the Company with the establishment of a Medical Coordination Section in each branch nationwide. In 2014, we reorganized the Medical Affairs Division to strengthen organizational governance and compliance in these unified activities.

1. Activities to generate data useful for patient treatment based on knowledge gained in clinical studies.
2. Comprehensive medical policies planned by pharmaceutical companies for each drug

Initiatives to Strengthen Medical Affairs Functions

Chugai's Medical Affairs Division draws up medical plans from a scientific standpoint and carries out various related activities to address unmet medical need and provide useful solutions to patients.

Based on the relevant medical plan, we perform non-clinical studies (basic research for post-marketing development) and clinical studies (contract-based post-marketing studies) and focus on validating and providing useful data as a science-based solution. In the last several years, many innovative products have been launched, and the Company has established its own medical affairs system and implemented post-marketing clinical studies with the same level of rigor as clinical trials for new drug development. As a result, we now have a research structure that conforms to the GCP[3] guidelines of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).

At the same time, we are strengthening promotion of medical affairs and enhancing communication activities at our branches to accurately disseminate information solutions to healthcare providers in each area. We are also focusing on development and education of medical staff. We have established training programs for acquisition of clinical research associate certification (the GCP Passport of the Japan Society of Clinical Trials and Research) and scientific training for medical representatives (MRs), and we are working to improve learning tools and e-learning programs.

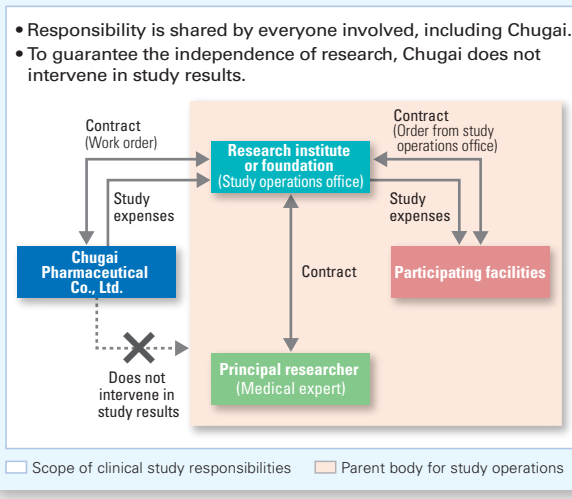
3. Good Clinical Practice, a set of standards for conducting pharmaceutical clinical trials

Contract-Based Post-Marketing Studies

Raising transparency and addressing conflicts of interest in post-marketing clinical studies have become key issues, reflecting society's growing interest in drug development after launch and scandals at pharmaceutical companies since 2013.

Since 2012, Chugai has developed its own post-marketing clinical study scheme under the name "contract-based post-marketing studies" to guarantee the independence and transparency of research. We conduct post-marketing studies with thorough efforts such as clear disclosure of research-related payments, relationships and conflicts of interest. We will continue working to validate new clinical data and disseminate more appropriate information solutions to healthcare providers as we contribute to raising the level of clinical studies in Japan.

Chugai's Contract-Based Post-Marketing Study Framework



Drug Safety

Drug Safety Approach and System

In Japan and overseas, Chugai handles numerous biopharmaceuticals, molecular targeted therapies and other pharmaceuticals with innovative modes of action. Expert safety evaluation is essential for promoting the appropriate use of these pharmaceuticals around the world and gaining acceptance from patients and healthcare providers, while speedy decision-making is crucial for timely collection and provision of safety information and ensuring safety. Consequently, Chugai has established the Drug Safety Division and built a safety system directly linked to management. Based on this system, Chugai works with Roche to enhance its world-class operations. By carefully evaluating and disclosing the risk-benefit balance to patients and healthcare providers, Chugai increases its credibility.

Measures to Enhance Drug Safety

Promoting Safety Evaluation and Appropriate Use

The Drug Safety Division is at the core of measures to collect and evaluate information on the safety and efficacy of drugs after their market launch. One such measure, post-marketing surveillance, is conducted on new drugs under actual treatment conditions, mainly to collect safety information that is unobtainable in a clinical trial. At Chugai, the Drug Safety Division is responsible for planning post-marketing surveillance, managing its progress and analyzing the results in coordination with product lifecycle teams and the Marketing & Sales Division. Medical representatives (MRs) handle tasks such as requests to medical institutions, data collection and follow-up. Post-marketing surveillance is conducted according to fixed protocols. The data forms are collected from medical institutions through electronic systems, and the accumulated data are analyzed as quickly as possible. This evaluated safety information is shared with medical institutions and officially announced inside and outside the Company via scientific conferences, papers and other means.

The numerous innovative new drugs such as anticancer drugs or biopharmaceuticals require wider-ranging and more rigorous management, such as thorough management of distribution, including wholesalers and dispensing pharmacies, and confirmation of conditions of use, in addition to surveillance in which all patients to whom a product is being administered are registered (all-case registration surveillance). Ahead of other companies, Chugai conducted large-scale all-case registration surveillance, particularly for Avastin, Tarceva and Actemra. With the launches of Kadcyla in April 2014 and Alecensa in September 2014, we began post-marketing surveillance (all-case registration surveillance for Alecensa) together with rigorous safety measures. We plan to conduct the same safety measures for Zelboraf, which obtained approval in December 2014. With this extensive experience, we lead the industry in drug safety evaluation and safety measures. Now, even when we launch drugs that do not have all-case registration surveillance as a condition of approval, our MRs first explain the drug information, after which we check the facilities and organizational requirements of medical institutions to ensure that physicians are obtaining adequate information on the relevant drug. In this way, we have implemented a rigorous process for ensuring the appropriate use of our pharmaceuticals.

Safety Analysis and Adverse Drug Reaction Reports

Chugai is committed to highly transparent, speedy and timely reporting and release of drug safety information. In 2014, we collected safety information on 170,000 cases and evaluated it from a medical standpoint. We have established a system for recording evaluations in a global database and conducting signal detection of adverse drug reactions. With this system, we promptly disclose information on phenomena that may have a causal relationship, and on frequent or serious reactions, to regulatory authorities in Japan, the United States, Europe and Asia. Aside from our large volume of safety information, our Drug Safety Division is staffed with medical doctors with abundant clinical experience. As full-time division employees, they conduct safety evaluations with a high level of expertise.

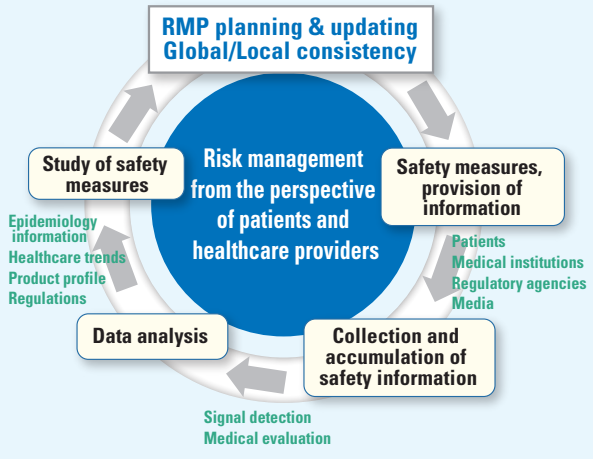
Moreover, we compile information on and typical examples of potential risk factors for the inherent adverse drug reactions of each product. We distribute patient information leaflets on adverse drug reactions to medical institutions and academic societies, in addition to posting information on the Company website, while MRs respond to inquiries from medical institutions individually. In addition, we have established a group that specializes in safety communications to provide accurate information in a timely manner and proactively conduct activities for more robust communication with customers. These activities help to reduce the incidence and aggravation of adverse drug reactions by creating an environment for treatment that takes high-risk patients into consideration.

Introduction of the Risk Management Plan (RMP)

A sweeping revision of pharmaceutical jurisprudence in Europe has energized pharmacovigilance activities and discussions worldwide in recent years. Demands include an expanded scope of safety information collection, globally standardized safety management systems, and an increase in transparency by ensuring the quality of information from collection to provision and promoting direct communication with medical institutions, patients and other parties. There is a growing consensus that companies should collect and analyze information consistently from the preclinical and clinical stages and should conduct evaluations that consider the balance between benefit and risk, rather than taking the conventional approach of focusing mainly on post-marketing studies. The European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA) are also placing greater emphasis on pharmacovigilance in the drug approval process. Under these conditions, Chugai has set up a world-class safety management system that can accommodate the pharmaceutical jurisprudence and review procedures of regulatory agencies in Japan, the United States and Europe. In addition, to establish a plan – do – check cycle in our pharmacovigilance activities, we have drawn up and applied RMP measures to eight of our products since 2012, ahead of our competitors (as of February 2015). RMP became mandatory in Japan in April 2013, but we implemented it early because we consider RMP to be part of Chugai's commitment to patients and medical institutions, not just a legal obligation. Consequently, we have also come to view it as an opportunity to enhance our pharmacovigilance system and align it with global standards. Our efforts to date have included establishing a signal detection system, conducting evaluations with a high level of expertise, and making speedy decisions on measures to ensure safety.

In applying RMP, we were particularly aware of the need to strengthen our ability to analyze safety information data from an epidemiological standpoint. As a result, we are working to improve the precision of analysis through a specialized internal group in charge of epidemiology functions and proactively cooperating with specialist companies and others to help upgrade Japan's epidemiological database. We are also conducting new measures such as establishing signal detection and assessment tools for adverse events to assess potential risks and conduct more precise safety evaluations. In addition, based on the strong track record we have compiled ahead of our competitors, we are driving the industry in ways such as proactively working to formulate industry-wide RMP-related suggestions and guidance.

Organization Oriented to Risk Management



Globalization of Safety Information

To standardize safety information worldwide and conform to global safety standards, Chugai is establishing specific pharmacovigilance-related interactive communication protocols with Roche and other partner companies, and making arrangements for their smooth operation. In addition to standardizing safety evaluations for each product and sharing information on adverse drug reactions, we have already established a worldwide framework for speedy decision-making on safety measures and methods of response in coordination with Roche. By enhancing cooperative measures in these ways, Chugai aims to provide patients and medical institutions with truly valuable safety data and contribute to healthcare worldwide.

Intellectual Property

Basic Approach

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. Under our basic policy, which emphasizes high-quality patent applications and effective allocation of resources, we have established a strong framework for cooperation within the Company. Our aim is to maximize the value of our products and technologies with IP rights and utilize them as a source of earnings through patent out-licensing.

How Our IP Strategy Creates Value

The Intellectual Property Department and the Research Division cooperate closely from the early stages of research and development to move R&D projects forward and secure a competitive advantage by conducting multifaceted analyses from an IP standpoint. In line with our basic policy, 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 our inventions related to formulation, production method, diagnostic method and Personalized Healthcare in addition to those for the substance and use. For significant drug discovery technologies such as innovative antibody technologies, we take advantage of accelerated examination programs and the Patent Prosecution Highway* to quickly establish rights globally. By viewing these product and technology patents in a matrix, we can strategically deploy them to optimize product protection and secure a technological advantage over our competitors. In addition, we are actively engaged in open innovation, and aggressively file patent applications for the research findings that emerge from our research networks with universities and research institutions.

Investigating and analyzing the patents of other companies is also an important component of our IP strategy. We are therefore enhancing our patent search and analysis functions and promoting the use of patent information. In particular, the rights in antibody engineering technology are becoming more complex every year, so we are building our own related patent database and using it to plan IP strategies, including monitoring trends at other companies.

* Under the Patent Prosecution Highway, applicants whose patent applications are determined to satisfy the conditions for patentability in the country where the application was first filed (for example, Japan) can request an accelerated examination of the corresponding application filed in a second country (for example, the United States).

Features of Chugai's IP Strategy

One feature of our IP strategy is that we take full advantage of our benefits as a member of the Roche Group. Naturally, for our own inventions we file patent applications and promote the acquisition of rights and their use based on our own initiative and judgment. Accordingly, Chugai takes responsibility for matters in Japan and overseas such as formulating application strategies for individual products, selecting countries where applications will be filed, and strategies for acquisition of rights. On the other hand, because the Roche Group including Genentech has abundant know-how and experience regarding patent applications, rights acquisition and use in the United States and Europe, we endeavor to choose our best options while coordinating closely within the Group at all times. We also provide full support for patent applications, rights acquisition and use in Japan by Roche and Genentech to maximize the value of their IP.

Another feature is our high proportion of antibody-related technology patent applications compared with the competition. We consider antibody engineering technologies to be important for our R&D strategy, and actively conduct research and development both to cultivate our basic technologies and to apply them to product development. Accordingly, in our IP strategy, we also focus on proactively applying for patents for antibody-related technologies and promoting rights acquisition and use. In fact, antibody engineering technologies have accounted for about 30 percent of our patent applications over the past three years as we work to secure rights for these proprietary technologies with broadly applicable patents. Because these patent applications ensure not only a technological advantage over our competitors, but also competitive advantages for our products, we consider them to be extremely important IP assets.

While properly asserting Chugai's legitimate rights, we aim to strategically use IP to contribute to our business activities with a balance of competition and cooperation.

IP Strategy Project

Reforming our system for utilizing IP is one of the strategies of ACCEL 15, Chugai's mid-term business plan. The aim of this strategic theme is to radically enhance the strategy and system for IP, both offensively and defensively, to accelerate the creation and expansion of new value globally based on Chugai IP.

The creation of innovative new drugs is the foundation of Chugai's business model, which is distinguished by its high-level capabilities for the requisite drug creation technologies. Consequently, the two main points of our IP strategy are using

product-related patents to maximize the length of time our product rights are protected and using technology-related patents to secure competitive advantages.

The IP strategy project clearly states these strategic objectives in a "top down" fashion. In addition, specific measures to achieve these objectives are conducted from the "bottom up" with the establishment of internal working teams made up of a large number of employees. Specific measures are as follows.

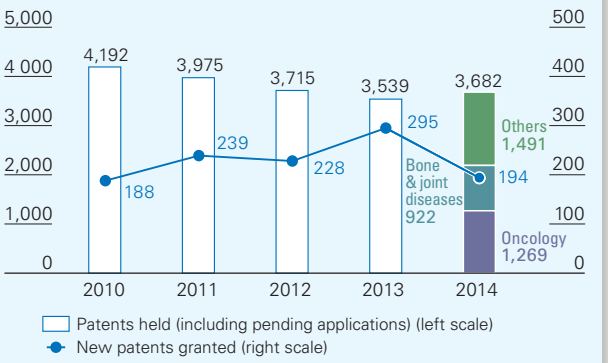
- Studying successful examples of product lifecycle extension through patents and establishing an application strategy
- Strengthening the system for monitoring other companies' patents and promoting the use of patent information
- Planning a strategy for innovative drug discovery technology-related patent applications, acquisition of rights and use
- Strengthening the network of external experts and planning effective utilization measures
- Taking measures to foster cost-consciousness and improve productivity

Moreover, human resources are essential for carrying out these strategies. To create a global patent strategy, we are strengthening internal employee training by offering overseas opportunities for patent work experience while securing capable external human resources to promote diversity and incorporate new knowledge and experience.

Current Patent Portfolio

Chugai currently holds 3,682 patents worldwide, including patents pending. By therapeutic area, oncology accounts for the largest share of patents with approximately 35 percent of the total, a proportion that reflects Chugai's product portfolio. In 2014, Chugai acquired 194 patents worldwide, primarily in its main markets of Japan, the United States and the European Union. These include patents protecting GC33 and SA237, which were developed from Chugai research, and SMART-Ig, our innovative antibody technology. On the other hand, we abandon patent applications that are no longer needed or transfer them to others in order to reduce costs. In 2014, we abandoned or transferred a total of 268 applications. With this approach, we are seeking to increase the overall value of our patent portfolio not only by securing high-value patents but also by conducting periodic reviews to determine whether or not patents should be maintained. In addition, we promote the efficient use of IP information by centralizing it in a patent management system so that it can be shared Company-wide.

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



AIPPI World Intellectual Property Congress

The World Intellectual Property Congress, the annual meeting of the International Association for the Protection of Intellectual Property (Association Internationale pour la Protection de la Propriété Intellectuelle; AIPPI) was held in Toronto, Canada in September 2014. A representative from Chugai participated as a speaker in a workshop on biosimilars, providing an overview of the current conditions and issues for biosimilars to a group of IP specialists from pharmaceutical companies and patent law firms from around the world. The discussion was lively, with introductions of the current status of biosimilar screening for marketing authorization in Canada by an examiner from the regulatory organization Health Canada and recent biosimilar patent litigation in Europe by a lawyer from the United Kingdom.

Masahisa Yamaguchi, Department Manager of the Intellectual Property Department, speaks at AIPPI.

Environmental Protection and Occupational Safety

Framework for Promoting Environmental Protection Activities and Occupational Safety

Environmental Protection Activities

Basic Approach

At Chugai, measures to minimize our impact on the environment are rooted in one of our core values – "We care about the global environment" – and based on environmental laws and regulations, with the aim of contributing to the protection of the global environment as set forth in the Chugai Business Conduct Guidelines.

Chugai Environmental Policy

We believe the supreme value to the future of "one and only Earth" and, therefore, we continue our efforts to reconcile our business activity with nature and the environment.

Regulatory Compliance
Chugai complies with all legislation and regulations, internal regulations and self-imposed standards relating to environmental protection.

System to Facilitate Action
Each year Chugai sets an environmental action plan and goals, and is continuously working to protect the environment.

Environmental Protection Activities
To minimize its impact on the environment, Chugai works to prevent global warming, conserve resources, reduce waste and prevent environmental pollution at every stage of the product lifecycle, from research and development to manufacturing, transportation, marketing and disposal.

Education and Training
Chugai provides regular education and training to its employees to deepen their knowledge and appreciation of environmental protection.

Information Disclosure
Chugai actively discloses information about its environmental protection activities both internally and externally and works to improve communication with communities.

Medium-to-Long-Term Targets

In its mid-term environmental plan for 2014, Chugai set a target of reducing energy consumption per employee by 10 percent from the 2009 level. In 2014, we reduced energy consumption per employee by 10 percent compared with 2009, achieving the target.

In 2014, we set the following four medium-to-long-term targets for 2020.

- Reduce energy consumption per employee (gigajoules) by 20 percent compared with 2010.
- Discontinue the use of specified chlorofluorocarbons (CFCs).
- Achieve zero emissions of waste (a waste recycling ratio of 99 percent or more) at our three sites.
- Achieve fuel efficiency above the average of 16 km/l for our MR fleet.

Measures to Prevent Global Warming

Progress toward 2014 short-term targets was as follows.

- CO_2 emissions decreased 2 percent, or 2.4 tons from 2013.
- The total amount of CFCs and hydrochlorofluorocarbons (HCFCs) used was 4,726 kg, a decrease of 73 kg from 2013.
- The ratio of fuel-efficient vehicles was 55.6 percent, maintaining a level higher than the 2012 target of 50 percent. Fuel consumption was 14.3 km/l for gasoline-powered vehicles and 17.6 km/l for diesel-powered vehicles.

Waste and Recycling

Industrial Waste

In 2014, the amount of industrial waste generated was 2,616 tons (an increase of 410 tons compared with 2013), the amount of landfill waste was 39 tons (a decrease of 11 tons), and the recycling ratio was 74 percent (an increase of 1 percentage point). The amount of landfill waste (2014 target: 50 tons or less) was substantially better than the target, but the amount of industrial waste generated (2014 target: 2,000 tons or less) and the recycling ratio (2014 target: 75 percent or higher) did not reach their targets due to an increase in production and other factors.

In 2015, Chugai aims to further reduce the amount of landfill waste by working to recycle waste that is not currently recyclable in order to raise the recycling ratio and reduce the final disposal ratio toward its medium-to-long-term target of achieving zero emissions of waste at its three plants by 2020. In addition, recognizing our responsibility for disposed waste, we will enhance our on-site inspections of waste contractors to ensure proper waste management.

Water Resources

Water is an important raw material for pharmaceutical manufacturing, and is currently valued as a crucial global resource. Chugai has been building awareness of the effective use of water by monitoring the volume consumed and discharged each year. In 2013, we conducted a whole effluent toxicity (WET) test on wastewater discharged from our sites into rivers to ascertain its ecological impact, and confirmed that there were no problems.

In 2015, Chugai plans to test wastewater from all its plants and research laboratories.

Environmental Accounting

Environmental accounting data compiled in 2014 are shown below. Investments in 2014 totaled ¥832 million, while costs were ¥1,439 million. Major investments included refrigeration-related equipment and expenditures for heat source conversion. The economic benefit was ¥51 million.

2014 Investments and Costs for Environmental Protection

(Millions of yen)

Breakdown of costs	Investments	Costs
(1) Business area costs	810	1,167
(2) Upstream and downstream costs	—	36
(3) Administration costs	21	228
(4) R&D costs	—	2
(5) Social activity costs	2	7
(6) Environmental remediation costs	—	—
Total	832	1,439

Establishing a Training System for ISO14001 Internal Auditors

The Chugai Group has established an in-house system to train internal auditors with world-class auditing skills for ISO14001, a set of international standards for environmental management systems. The objective in establishing the training system is to become a top pharmaceutical company in the environmental area by being involved in high-level environmental activities through high-quality internal audits.

The program, which is supported by the International Register of Certificated Auditors (IRCA) in the U.K., was created as a unique three-day training course that includes on-site experience. As the result of an assessment by IRCA, the program is the first and currently the only course in Japan to be certified as an ISO14001 internal auditor training course.

Moreover, Chugai has entered into a contract with IRCA for its Organisations Employing Auditors (OEA) scheme for priority receipt of specialized audit information, technical support and other services. We are the first pharmaceutical manufacturer in Japan to join the scheme, and the first in the world to do so at the internal auditor level.

In 2014, nine new internal auditors received IRCA certification under this system.

Occupational Safety and Health

Occupational Safety and Health System

In December 2011, Chugai established its Guidelines for Health and Safety as the basis for health and safety management in the Chugai Group. We are improving and implementing safety and health management systems throughout the Company under our policy of placing priority on ensuring employee safety in all business operations. Safety management, health management, mental health programs and other activities are carried out uniformly at all sites.

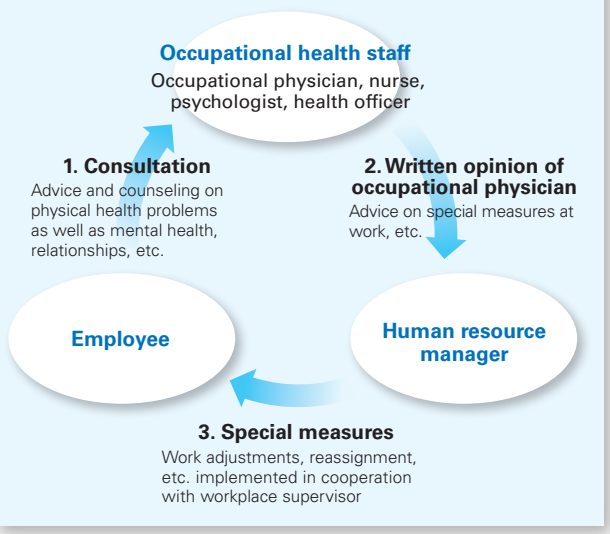
Safety and Health Risk Assessment

Safety and health risk assessment consists of activities for advance discovery of unidentified risk factors to reduce unforeseen workplace accidents. In 2014, the Chugai Group introduced a workplace safety and health patrol to eliminate known risk factors in tandem with a target of minimizing workplace accidents. We are conducting efficient and effective improvements by evaluating risks in each workplace using common standards to determine priority risks to be addressed.

Health Management

Chugai has occupational physicians, nurses, psychologists, health officers and other occupational health staff to provide necessary support not only for employees who are unwell or on leave due to illness or injury, but for all employees who need consideration for their health conditions at work, including those with abnormalities found in health checkups, those who work long hours, pregnant women, and employees with disabilities. Health staff, human resource managers and workplace supervisors cooperate as shown in the chart below left.

Basic Health Management Structure



Support for Return to Work after Mental Health Leave

Support for employees returning to work after mental health leave is conducted within a framework similar to that for health management. Due to a program that provides individualized support for returning to work, the number of employees with problems that recur within a year of their return has fallen substantially. In addition, Chugai also conducts ongoing awareness activities including training for managers on promoting understanding of mental health problems and dealing with them appropriately.

Coordination among Internal Help Lines

The managers in charge of the internal help lines for health, career, harassment and compliance meet regularly to coordinate support for problem-solving. In addition, Chugai coordinates areas such as employee training and information provision.

Creating Healthy, Energetic Workplaces

To prevent problems such as poor mental health or harassment, Chugai conducts measures to vitalize workplaces and improve the working climate to create highly productive environments where employees can work energetically. Since 2013, our health management and human capital development organizations have collaboratively conducted team coaching training at a total of 20 workplaces, and post-training surveys have shown improvement in work engagement, workplace identification and other items.

Team coaching training

Social Contribution Activities

Welfare Vehicle Donation Program

Chugai's program to donate specially equipped welfare vehicles began in 1985 as part of activities to commemorate the Company's sixtieth anniversary. Five vehicles were donated in 2014, bringing the cumulative total over the 30 years of the program to 203.

In Japan's super-aging society, the number of senior citizens and disabled people requiring nursing care has been increasing. The welfare vehicles donated by Chugai are used to transport elderly and disabled people who receive nursing care at home.

The vehicles donated by Chugai are wagon-type vans with a capacity of two (including the driver) in the front, and space to accommodate up to four wheelchair passengers in the rear or a gurney and two wheelchairs. A lift facilitates loading and unloading.

This 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.

Donation ceremony in Okegawa City, Saitama Prefecture

Donated vehicle

Biology Lab Classes to Show Children the Fun of Science

As part of its social contribution activities, Chugai hosts various lab classes to show children that science can be fun. In 2014, elementary school students observed cells and extracted DNA, and junior high school students learned about the lumination mechanisms of organisms. In addition, Chugai and Roche Diagnostics K.K. presented a class for high school students on using real-time PCR[1] to verify beef, pork and poultry contained in foods.

1. A method that uses real-time measurement of a polymerase chain reaction (PCR), which amplifies a specified DNA fragment, to quantitatively analyze DNA based on the resulting amplification curve.

Endowed Courses on Medical Treatment

As a way of contributing to society, Chugai has established endowed courses at universities to raise interest in health and medical treatment among the next generation. One such course at Waseda University was held for the fourth year from October 2014 to January 2015.

Support for Para-Sports

Chugai co-sponsors the Japanese Para-Sports Association as an official partner to support top athletes competing around the world. To help realize the para-sports philosophy of "creating a vital and inclusive society," Chugai actively provides assistance to para-sports through promotional and awareness-raising activities including preparation and distribution of an educational pamphlet on para-sports and

Transparency Guidelines

In addition to complying with Japan's Pharmaceutical Affairs Law and other laws and ordinances, Chugai works to increase its transparency and reliability by observing the industry's self-imposed norms based on the high ethical standards set by the Japan Pharmaceutical Manufacturers Association. As a further measure, we have formulated two original sets of guidelines for transparency.

We have established "Transparency Guidelines for Chugai Activities Involving Medical Institutions, etc." for information on funding (including goods) provided to Japanese medical institutions, healthcare professionals and other parties, and "Guidelines for Cooperation between Chugai and Patient Groups" for information on funding and other compensation (including labor and other services) provided to patient groups in Japan. In accordance with the guidelines, both sets of information are disclosed on Chugai's website (http://www.chugai-pharm.co.jp/english/csr/transparency/guideline_01.html) after the settlement of accounts for each fiscal year.

Chugai aims to maintain the trust of society by conducting corporate activities based on transparency and high ethical and moral standards.

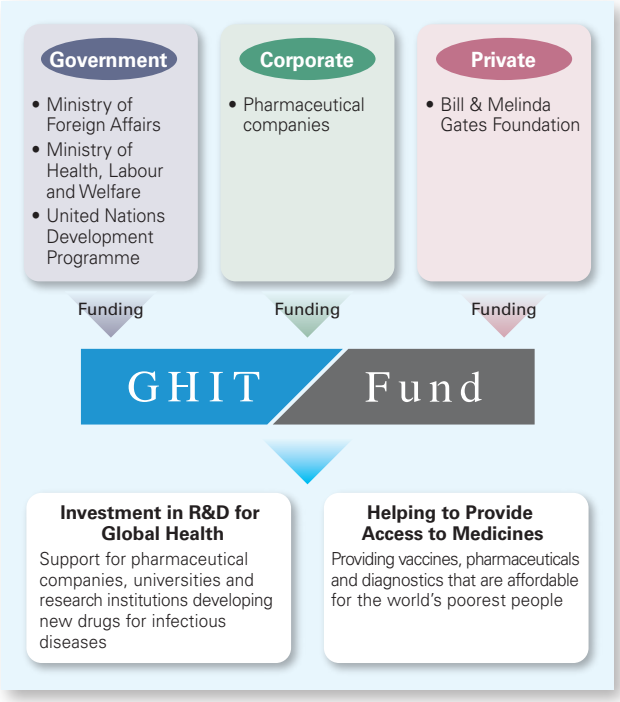
holding an event that provides an opportunity to try wheelchair basketball.

Participation in a Public-Private Partnership for Global Health

In December 2014, Chugai joined the Global Health Innovative Technology Fund (GHIT Fund) to promote Japan's international contributions in the area of global health.

Overview of the GHIT Fund

The GHIT Fund is a public-private partnership initiated in Japan to support new drug development that makes more direct use of the country's medical technologies, scientific innovations and knowledge to rectify the disparity in health between industrialized and developing countries. It was jointly established in April 2013 with funding of approximately ¥10 billion from five Japanese pharmaceutical companies, the Japanese government (the Ministry of Foreign Affairs and the Ministry of Health, Labour and Welfare), the Bill & Melinda Gates Foundation[2] and the United Nations Development Programme. The fund's vision is one in which the crushing burden of infectious disease no longer prevents billions of people in the developing world from seeking the level of prosperity and longevity now common in the industrialized world. The main feature of the fund is the participation of and funding from a consortium of pharmaceutical companies and the Japanese government to promote new drug development for global health.



Initiatives of the GHIT Fund

The GHIT Fund conducts activities to provide support for pharmaceutical companies, universities and research institutions that are working to develop new vaccines, pharmaceuticals, diagnostics and other medicines for infectious diseases; to promote collaboration in global pharmaceutical research and development; and to increase access to medicines in developing countries.

Infectious diseases such as HIV/AIDS, malaria, tuberculosis and neglected tropical diseases (NTDs)[3] are one of the most serious areas of unmet medical need worldwide, affecting nearly 40 percent of the world's population. Controlling these diseases in developing countries will require highly effective, low-cost therapies, vaccines and diagnostics. By promoting global cooperation with research and development organizations inside and outside Japan, the GHIT Fund contributes to the development of new drugs for people in developing countries suffering from infectious diseases, as well as for the improvement of global health.

Significance of Chugai's Participation

Chugai's mission is "to dedicate itself to adding exceptional value through the creation of innovative medical products and services for the benefit of the medical community and human health around the world." Toward that end, we have been working to contribute to global health as a member of the Roche Group, and participation in the GHIT Fund is part of these efforts. Moreover, we believe that exploring possible applications for our innovative drug discovery technologies for infectious and other diseases will contribute to global healthcare.

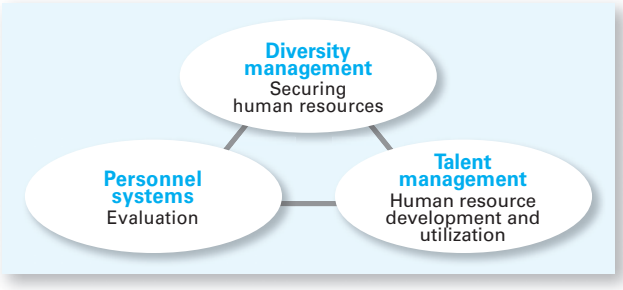
As a partner in the GHIT Fund, we expect promoting the development of new medical technologies will go beyond basic social responsibility, leading to the promotion of health and sound economic growth in developing countries. In addition, we are participating in this public-private partnership in the belief that it is a necessary long-term investment in Japan's future growth.

2. The world's largest charitable foundation, established in 2000 by former Chairman of Microsoft Corp. Bill Gates and his wife Melinda. Guided by the belief that every life has equal value, the foundation works to help all people lead healthy, productive lives.
3. Neglected tropical diseases (NTDs) are parasitic, bacterial and viral infections spread mainly in tropical areas. It has been reported that approximately one billion individuals are infected with NTDs and half a million people die each year worldwide. Because NTDs are quite rare in industrialized countries, they have not attracted widespread attention.

Human Resources

Human Resource Strategy to Become a Top Pharmaceutical Company

People are an invaluable asset in generating a company's growth and development. Based on that fundamental principle, Chugai is building its human resource management on the three pillars of diversity management, talent management and personnel systems. The number of women active as managers and leaders is increasing, and the proportion of women among next-generation leaders and middle management is rising. The number of women who work while raising children has also risen, and role models for women have diversified. Non-Japanese employees and mid-career hires have increased as well, and their diverse values are vitalizing the organization. We are fostering an organizational culture of respect for diverse values, not only in attitudes but also through further measures in areas such as systems, mechanisms and working styles to make diversity in human resources a value of our organization. In this way, we will generate innovation and become a top pharmaceutical company.



Diversity Management

Chugai has placed priority on diversity management to enable a rich variety of employees to work enthusiastically and create new value. To begin addressing this issue, we launched a management working team in 2010 to deal with gender issues and established the Diversity Office in 2012 to promote measures for different nationalities, senior employees and women. We have conducted e-learning and distributed educational guidebooks to all employees, and in 2014 held training for all managers on management of increasingly diverse departments and teams. We have been promoting the active participation of women by working to raise awareness about careers through methods such as forums in every division and meetings where participants can exchange opinions with a female company director. In 2014, we also introduced training to nurture female leaders. The

A View of Diversity from the Clinical Development Division's BEYOND Project

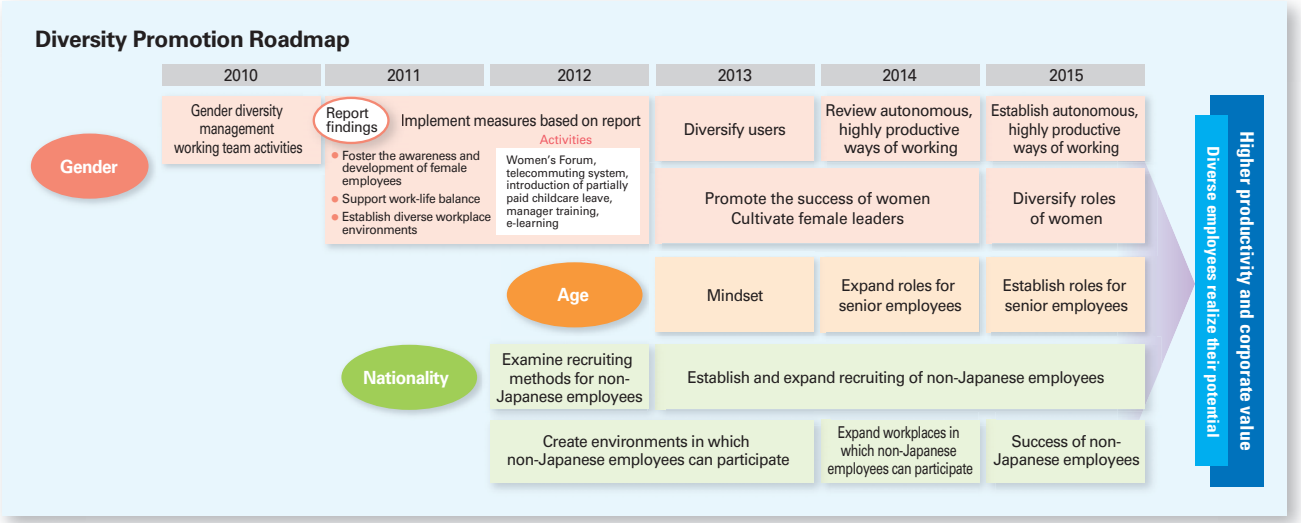
BEYOND (Best Yield of Next Development) is a productivity improvement project that began in earnest in January 2013. The project works cross-divisionally, conducting various reforms that are best from an overall perspective for further raising the productivity of clinical development and promoting visualization of work.

Most of the approximately 15 members have other concurrent duties, fitting in their project member duties as appropriate. Membership is diverse, not just in terms of position and department, but also including employees who have recently returned from childcare leave and mid-career hires with wide-ranging experience. In our many discussions from the perspective of the common good, we place importance on diverse viewpoints and values, and as a result, this project has created an environment in which these diverse opinions can easily be expressed.

Reform leader Yumiko Uematsu (center) and project members

Diversity is indispensable to generating innovation with a sense of speed. I believe diversity is becoming rooted in employee attitudes and Chugai's corporate culture. Moreover, reform leaders cannot rely only on their own expertise, but must manage in a way that helps employees to display their abilities to the utmost. I hope our activities help to accelerate diversity and generate innovation with a sense of speed.

Yumiko Uematsu
Manager
Clinical Development Process Innovation and Improvement Initiative Office
Clinical Development Division



percentage of female managers has increased to 9.7 percent, and we will continue our efforts to expand the number of female next-generation leaders.

As our workforce becomes more diverse, we have expanded our working systems and provide information through forums such as lunchtime gatherings and the Company intranet to help employees balance work and life events such as childcare or nursing care. Initiatives in 2014 included offering online video support for post-childcare-leave career development for employees and their managers, providing career development training for 50-year-old employees on the assumption that they will continue working to the age of 65, and expanding our portal site for nursing care based on feedback from a nursing care seminar held in 2013. With more employees providing childcare or nursing care and growing opportunities to work with people overseas, the ratio of employees using our telecommuting system has also risen. In addition, we have established a website that provides information and support for non-Japanese employees to create a better environment for working together with other employees. In recognition of the Diversity Office's efforts to encourage women to demonstrate their full potential at work and to support a balance between work and childcare and nursing care, Chugai received the Minister's Prize for Excellence (Companies promoting gender equality) (shown here) from the Ministry of Health, Labour and Welfare (MHLW) and the Tokyo Prefectural Labor Bureau Chief's Prize for Excellence (Family-friendly companies) at the Commendation of Companies Promoting Gender Equality and Work-Family Balance for 2014 hosted by the MHLW. In addition, in March 2015 the Ministry of Economy, Trade and Industry and the Tokyo Stock Exchange selected Chugai as a "Nadeshiko Brand" because of the Company's exceptional efforts in promoting the success of women.

NADESHIKO BRAND 2015

Awards ceremony of the Commendation of Companies Promoting Gender Equality and Work-Life Balance for 2014

Facilitating Work-Life Balance

Based on the desire to retain employees and support family life, Chugai has developed a full range of programs, including childcare leave and a part-time working system for childcare, that allow employees to continue working, for example, during child-rearing years. In 2008 and 2011, Japan's Ministry of Health, Labour and Welfare certified Chugai under the Act on Advancement of Measures to Support Raising Next-Generation Children, and the Company is currently conducting its Phase 3 Action Plan.

Moreover, beginning from 2007, labor and management have been promoting the reduction of excessive working hours. Since summarizing their approach to work-life balance as "the pursuit of work-life synergy" in 2013, they have been working to make the concept understood and adopted by employees. Under this concept, when individuals and workplaces come up with original ways to work and live, and pursue synergy between the two, it helps to expand the potential of individuals and raise the productivity of the organization, thus becoming a win-win relationship for the Company and each employee.

Talent Management System

Chugai conducts talent management to secure and nurture the leaders and core human resources who will carry out its management strategies to become a top

pharmaceutical company. Specifically, in April 2014 each organization continued its efforts from the previous year by holding discussions on medium-to-long-term human resource development policy, drafting a human resource development plan and creating a talent pool.[1] Based on the development plans, the organizations carried out strategic employee placement and training designed to strengthen leadership from a Company-wide perspective.

In addition, we clarified our succession plan by selecting successor candidates for a total of 87 general managers and department managers in Japan. We are currently implementing development plans for these candidates to help them hone a variety of skills and cultivate a wide-ranging perspective to ensure that they can display leadership on a global level.

This talent management system will enable Chugai to systematically and continuously develop and turn out the next generation of leaders and core employees while strengthening human resources and boosting motivation throughout the Company.

1. A group of candidates for the next generation of leaders

Three Goals of the Talent Management System

Goal 1	**Formulate and implement human resource development plans** according to the capabilities and aptitude of individual employees
Goal 2	**Build and manage a talent pool** from which to select successor candidates
Goal 3	**Formulate and implement a succession plan** to serve as a framework for evaluation, selection, development and assignment

Equal Opportunity and Fairness in Recruiting

Based on its equal opportunity policy, Chugai treats and compensates its employees equally regardless of gender, age, nationality or disability. In accordance with this policy, we actively seek to hire disabled people in addition to hiring new university graduates, mid-career professionals and non-Japanese. As of December 31, 2014, the ratio of employees with disabilities in the Company was 2.06 percent.

Moreover, we maintain fair and impartial hiring practices by using a diverse team of interviewers to evaluate candidates' abilities, skills and experience.

Career Development Framework

Having already revised its personnel system and introduced diversity management and a talent management system, Chugai revamped its career development framework in 2012 and has been working to firmly establish it.

Our career policy is to "Support employee autonomy and mutual growth by placing importance on providing employees with opportunities to realize and nurture their own value." With the career declaration system as the basic cycle, we focus on workplace dialogue and management centering on the awareness of the employee concerned and the support and advice of his or her superior to facilitate self-directed career development. We also supplement the basic cycle with various measures to promote further autonomy and mutual growth.

Maintaining the Work Environment

In December 2011, Chugai established basic rules on occupational safety and health. Based on our policy of placing priority on ensuring employee safety in all operations, we are taking proactive measures to upgrade our safety and health system, ensure safety, prevent occupational injuries, promote health maintenance and create comfortable work environments. In creating a framework to give individualized attention to each employee's issues, we have set up physical and mental health counseling services in which specialists including occupational health physicians, nurses and psychologists cooperate with human resource managers and workplace supervisors. Employees at all facilities can freely access these services.

BCG and Human Rights Training

Chugai conducts annual training for all employees. In the first half of the year, the content focuses on corporate ethics, and in the second, on respect for human rights.

The theme for the first half of 2014 was "The fair and transparent business activities we aim for." This training reviewed global anti-bribery regulations and changes in the operating environment such as measures to secure transparency in the healthcare industry and considered the importance of dealing with these issues while conducting fair business activities.

The two themes in the second half were "Strengthening promotion of compliance" and "The individual's right to work: Social minorities." The first theme shared the significance of and targets for strengthening promotion of compliance, an area where the entire Company made efforts in 2014, and confirmed the importance of individual awareness and action. The second used interviews with social minorities – schizophrenics and LGBT[2] and HIV-positive people – to consider their thoughts on working and what they can contribute. Employees learned that fostering an organizational culture of respect for diverse values entails creating workplaces that enable diverse members to display their individual capabilities while working together as an organization, which in turn is reflected in the results of the organization.

2. An acronym for the lesbian, gay, bisexual and transgender sexual minority

Corporate Governance

Management Decision-Making, Execution and Oversight of Business Operations

To expedite business operations and clarify executive responsibilities, Chugai has adopted an executive officer system to keep decision-making on management issues of primary importance separate from business execution. The Board of Directors is in charge of the former, while executive officers are entrusted by the board with the authority to conduct the latter. The Executive Committee makes decisions concerning business execution. In execution of business, since March 2012 the chief executive officer (CEO) has ultimate responsibility for decisions on Companywide management strategies and other important matters, and the chief operating officer (COO) is responsible for decisions on business execution.

Board of Directors

The Board of Directors makes decisions on management issues of primary importance and receives quarterly reports on the state of business execution as well as reports on key decisions made by the Executive Committee. It is also responsible for oversight of the execution of business operations. The board consists of five directors from Chugai and five outside directors, totaling ten directors. Two of the outside directors are from the Roche Group.

In 2014, the Board of Directors convened eight times.

Executive Committee

The Executive Committee makes important executive decisions. It consists of key executive officers, including the CEO and COO, and the full-time Audit & Supervisory Board Members.

In addition, the IR Committee, Risk Management Committee, Corporate Social Responsibility Committee and Healthcare Compliance Committee have been established under the Executive Committee.

Chugai's Management Following the Strategic Alliance and the Current Effectiveness of Corporate Governance

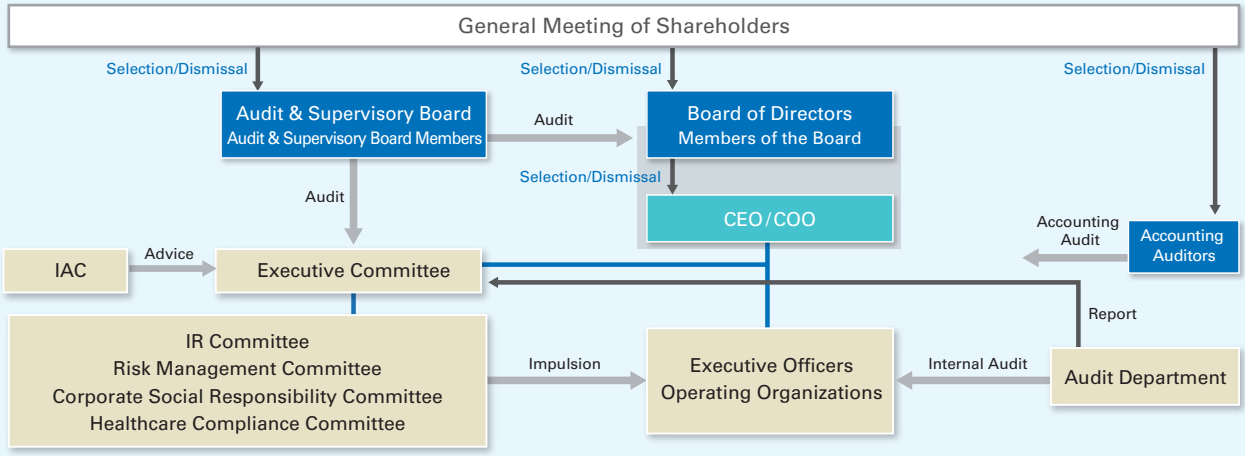
Franz Bernhard Humer
Outside Director
Chairman, Diageo plc
Former Chairman of the Board of Directors of ROCHE HOLDING LTD

I was the Chairman of the Board of Directors and CEO of ROCHE HOLDING LTD when Roche and Chugai integrated their management in 2002 by entering into a strategic alliance. We rated Chugai positively as an alliance partner not only for the strengths of its R&D and marketing operations, but also in terms of its management and corporate governance capabilities. We considered Chugai an excellent company, particularly for its prompt decision-making based on its executive officer system and its productivity improvement initiatives.

Since then, I have served as an outside director of Chugai from 2002 through 2007 and again in 2013 and 2014. I am pleased that over this period Chugai's corporate governance has continued to evolve. In addition to appointing outside directors, the Company has incorporated external perspectives by operating the International Advisory Council (IAC) to gain a broad range of opinions from specialists in various fields inside and outside of Japan as well as by focusing on increasing management transparency. Lively exchange of opinions among the Board of Directors, which is responsible for key decision-making and oversight of business execution, has made the meetings extremely effective for appropriate decision-making. The creation of Chugai's international research network is just one example of the successes engendered by this system.

I expect Chugai to further enhance its corporate governance to expedite global management and accelerate various business operations.

Chugai's Corporate Governance System



Introduction of Outside Perspectives

To reflect diverse stakeholder viewpoints in business decisions, Chugai has taken measures to obtain outside perspectives, such as nominating outside directors and establishing a council made up of domestic and overseas specialists.

International Advisory Council (IAC)

Chugai has established the International Advisory Council (IAC) composed of industry leaders and other professionals from around the world. The IAC works to enhance decision-making by providing valuable advice on how to deal with changes in the global business environment and appropriate business conduct.

Outside Directors

Chugai has appointed outside directors to reflect the views of a broader range of stakeholders in management decision-making.

Outside directors point out issues and give advice concerning Chugai's management at their discretion. Those from Roche do so from a global perspective while the others do so from their abundant experience and knowledge as corporate executives, physicians or university professors.

The rate of attendance by outside directors at the eight board meetings in 2014 was 89.5 percent on average, the highest being 100 percent and the lowest 33.3 percent.

Members of the IAC

IAC Chairman

- **Henry L. Nordhoff (U.S.)**
  Former Chairman of the Board, Gen-Probe, Inc.

IAC Advisors

- **Virginia Bottomley (U.K.)**
  Former Health Secretary
- **William M. Burns (U.K.)**
  Former Chief Executive Officer of the Pharmaceuticals Division, F. Hoffman-La Roche Ltd
- **Andrew von Eschenbach (U.S.)**
  Former Commissioner of the Food and Drug Administration
- **Victor Halberstadt (Netherlands)**
  Professor, Leiden University
- **Andre Hoffmann (Switzerland)**
  Vice Chairman, ROCHE HOLDING LTD
- **Dr. Franz B. Humer (Switzerland)**
  Chairman, Diageo plc
  Former Chairman, ROCHE HOLDING LTD
- **Robert A. Ingram (U.S.)**
  Former Vice Chairman of Pharmaceuticals, GlaxoSmithKline plc
- **Arnold J. Levine (U.S.)**
  Professor at the Institute for Advanced Study, Princeton University
  Discoverer of the p53 cancer suppressor protein
- **Abraham D. Sofaer (U.S.)**
  George P. Shultz Distinguished Scholar and Senior Fellow at the Hoover Institution, Stanford University
  Former legal advisor to the U.S. Department of State
- **Sonosuke Kadonaga (Japan)**
  President, Intrinsics

Reasons for Election of Outside Directors

Name	Outside Position	Reason for Election
Yasuo Ikeda	Vice-Chairman of the Board of Directors, Musashi Academy of the Nezu Foundation, University Professor of Waseda University, Professor Emeritus of Keio University	Recommended or appointed based on the Company's judgment that he will provide appropriate advice and monitoring with respect to the Company's management and business by leveraging his abundant experience and knowledge as a doctor and university professor and can properly execute the duties of an outside director. Designated as an independent director based on the regulations of Tokyo Stock Exchange, Inc., to which notification has been submitted.
Masayuki Oku	Chairman of the Board, Sumitomo Mitsui Financial Group, Inc., Outside Director, Kao Corporation, Outside Director, Komatsu Ltd., Outside Director, Panasonic Corporation, Outside Audit & Supervisory Board Member, Nankai Electric Railway Co., Ltd.	Recommended or appointed as the Company expects that he will provide advice and monitoring by leveraging his abundant experience and knowledge of corporate management and other fields. Designated as an independent director based on the regulations of Tokyo Stock Exchange, Inc., to which notification has been submitted.
Franz B. Humer	Chairman, Diageo plc Former Chairman, ROCHE HOLDING LTD	Recommended or appointed based on the Company's judgment that he can provide appropriate advice and monitoring with respect to the Company's management and business based on his abundant experience and knowledge as a manager of global pharmaceutical companies and can properly execute the duties of an outside director.
Daniel O'Day	Chief Operating Officer of Roche Pharmaceuticals Division, Member of the Roche Corporate Executive Committee and Member of the Genentech Board of Directors	Managerial member of the Roche Group, to which the Company belongs. Recommended or appointed based on the Company's judgment that he can provide appropriate advice and monitoring with respect to the Company's management and business from a global perspective and can properly execute the duties of an outside director.
Sophie Kornowski-Bonnet	Head of Roche Partnering, Member of the Enlarged Roche Corporate Executive Committee	Managerial member of the Roche Group, to which the Company belongs. Recommended or appointed based on the Company's judgment that she can provide appropriate advice and monitoring with respect to the Company's management and business from a global perspective and can properly execute the duties of an outside director.

Auditing System

Audits by Audit & Supervisory Board Members

Chugai has an Audit & Supervisory Board, and audits of management decision-making and business execution are conducted independently from business operations by four Audit & Supervisory Board Members, including two outside members.

Audit & Supervisory Board Members express their opinions in real time from the standpoint of appropriate corporate governance in a variety of occasions including meetings of the Board of Directors, the Executive Committee (full-time Audit & Supervisory Board Members only) and the Audit & Supervisory Board.

Internal Audits

The Audit Department, with a staff that includes certified internal auditors and certified fraud examiners, conducts audits of the status of the Chugai Group's business execution from various standpoints, such as the effectiveness, efficiency and compliance of business activities, including those of subsidiaries in Japan and overseas, reports and makes recommendations to the Executive Committee; and reports to the Audit & Supervisory Board.

In addition, the Audit Department conducts internal control assessments based on the Financial Instruments and Exchange Act, J-SOX, and other criteria to help maintain sound operations. Chugai also dispatches its auditing staff as Audit & Supervisory Board Members at subsidiaries in Japan.

Accounting Auditors

KPMG AZSA LLC handles accounting audits and internal control audits.

Cooperative Auditing

Audit & Supervisory Board Members, the Audit Department and the accounting auditors cooperate closely by regularly exchanging information to improve the effectiveness of their respective audits. Audit & Supervisory Board Members and the accounting auditors confirm each other's audit plans and hold regular meetings to exchange opinions on matters including the results of quarterly audit reports. In addition, they work to strengthen governance at Group companies by coordinating with Audit & Supervisory Board Members at subsidiaries in Japan on quarterly reports, fiscal year-end reports and other matters. The Office of Audit & Supervisory Board Members ensures the independence and enhances the auditing functions of Audit & Supervisory Board Members.

Officer Remuneration

Chugai's fundamental policy for remuneration of directors and Audit & Supervisory Board Members is to facilitate maximization of the Chugai Group's corporate value. Remuneration levels and the remuneration system are designed to link compensation of officers with the Company's performance and promote shared values with shareholders.

Remuneration of directors consists of three components: fixed regular compensation, bonuses paid according to performance, and stock options granted as a long-term incentive. These components are paid by resolution of the Board of Directors based on the Company's criteria within the limits on remuneration approved by the general meeting of shareholders. The Remuneration Committee, mainly composed of outside directors and people with experience as outside directors, sets policies and details concerning remuneration of directors with specific titles to ensure the objectivity and transparency of the remuneration-setting process.

Remuneration of outside directors and Audit & Supervisory Board Members (including outside members), which consists solely of fixed regular compensation, is paid by resolution of the Board of Directors for outside directors and through consultation with the Audit & Supervisory Board for Audit & Supervisory Board Members. The amounts are set within the limits approved by the general meeting of shareholders.

A resolution was passed in the 98th annual general meeting of shareholders held in March 2009 to abolish the retirement benefits system for directors. A resolution was passed in the 95th annual general meeting of shareholders held in March 2006 to abolish the retirement benefits system for outside directors and Audit & Supervisory Board Members (including outside members).

Amount of Remuneration Paid to Directors and Audit & Supervisory Board Members

	Total Remuneration, etc. (Millions of yen)	Total Remuneration, etc. by Type (Millions of yen)				Number of Eligible Officers
		Regular Compensation	Bonuses	Common Stock Options	Stock Options as Stock based Compensation	
Directors (excluding outside directors)	745	304	220	104	117	6
Outside Directors	45	45	—	—	—	4
Total	790	569		104	117	10
Audit & Supervisory Board Members (excluding outside members)	63	63	—	—	—	2
Audit & Supervisory Board Members (outside members)	22	22	—	—	—	2
Total	85	85		—	—	4

1. Amounts are rounded to the nearest million yen.
2. The table above includes two directors who resigned during 2014.
3. The amount of remuneration (regular compensation and bonuses) paid to all directors is no more than ¥750 million per year as per the resolution passed in the 96th Annual General Meeting of Shareholders held in March 2007.
   Apart from this, the maximum amounts of compensation paid to directors in the form of stock acquisition rights allocated as stock options are ¥125 million per year for common stock options and ¥150 million per year for stock options as stock-based compensation as per the resolution passed in the 98th Annual General Meeting of Shareholders held in March 2009.
4. The amount of remuneration for all Audit & Supervisory Board Members was no more than ¥100 million per year as per the resolution passed in the 95th Annual General Meeting of Shareholders held in March 2006.
5. The amount of bonuses shown in the table above is the amount of the provision of reserve for bonuses to directors during 2014.
6. The amounts of common stock options and stock options as stock-based compensation and the number of eligible officers shown in the table above are the amounts that were posted as expenses for 2014 and the number of officers in 2014, respectively.
7. In addition to the total remuneration, etc. shown in the table above, the following amounts were paid as retirement benefits corresponding to the period from the time each officer assumed office to the abolishment of the retirement benefits system for directors and Audit & Supervisory Board Members.
   One retired director: ¥54 million
   One retired outside director: ¥1 million

   A resolution was passed in the 98th Annual General Meeting of Shareholders held in March 2009, to abolish the retirement benefits system for directors with executive power, and to pay retirement benefits corresponding to the residual term up to the abolishment of the system to each concerned director remaining in office after the closing of the 98th Annual General Meeting of Shareholders, at the respective time of their retirement.
   Also, a resolution was passed in the 95th Annual General Meeting of Shareholders held in March 2006 to abolish the retirement benefits system for directors and Audit & Supervisory Board Members with no executive power, and to pay retirement benefits corresponding to the residual term up to the abolishment of the system to each concerned director and Audit & Supervisory Board Member remaining in office after the closing of the 95th Annual General Meeting of Shareholders, at the respective time of their retirement.
8. In 2014, the amount of remuneration received by two outside directors, namely Franz Bernhard Humer and Daniel O'Day, as officers from the parent company of the Company or subsidiaries of the said parent company totaled ¥1,832 million (converted into yen at the average exchange rate in 2014).
9. In addition to the bonuses in 2014 shown in the table above, and apart from the ¥185 million in provision of reserve for bonuses to directors presented in the Business Report for 2013, ¥34 million has been paid to five directors as bonuses for 2013.

Amount of Remuneration Paid to Each Representative Director

	Total Consolidated Remuneration, etc. by Type (Millions of yen)				Total Consolidated Remuneration (Millions of yen)
	Regular Compensation	Bonuses	Common Stock Options	Stock Options as Stock-Based Compensation	
Osamu Nagayama (Representative Director)	125	148	45	58	376
Motoo Ueno (Representative Director)	55	24	17	18	114
Tatsuro Kosaka (Representative Director)	55	30	17	21	122

1. Amounts are rounded to the nearest million yen.
2. Total amount of remuneration paid to each representative director is presented.
3. Other than the representative directors in the table above, no director or Audit & Supervisory Board Member received total remuneration of more than ¥100 million.

Relationship with Roche

Roche, the parent company of Chugai, owns 59.9 percent of Chugai's outstanding shares based on the strategic alliance agreement between the two companies. Roche and Chugai have agreed to cooperate in maintaining the listing of Chugai's common stock on the First Section of the Tokyo Stock Exchange.*

The aim of this alliance is to establish a new business model that differs from conventional corporate acquisitions and joint ventures. Although ROCHE HOLDING LTD includes Chugai in its consolidated accounts, Chugai functions as an independent listed company and makes all of its own management decisions based on the principle of self-governance. Chugai believes that autonomy and diversity are key to generating innovation, that maintaining its independent management brings diversity to the Roche Group, and that the pharmaceuticals it creates as a result contribute to all stakeholders, including patients and minority shareholders. In its business dealings with the Roche Group, Chugai conducts all transactions fairly using third-party prices to protect the interests of minority shareholders. Two of Chugai's ten directors are from the Roche Group. However, they do not comprise a majority of the Board of Directors, and thus Chugai considers its management independence to be secure.

Chugai will continue to manage its business with autonomy and independence as a publicly listed company.

* The Tokyo Stock Exchange requires delisting if the ratio of tradable shares to listed shares is less than 5 percent.

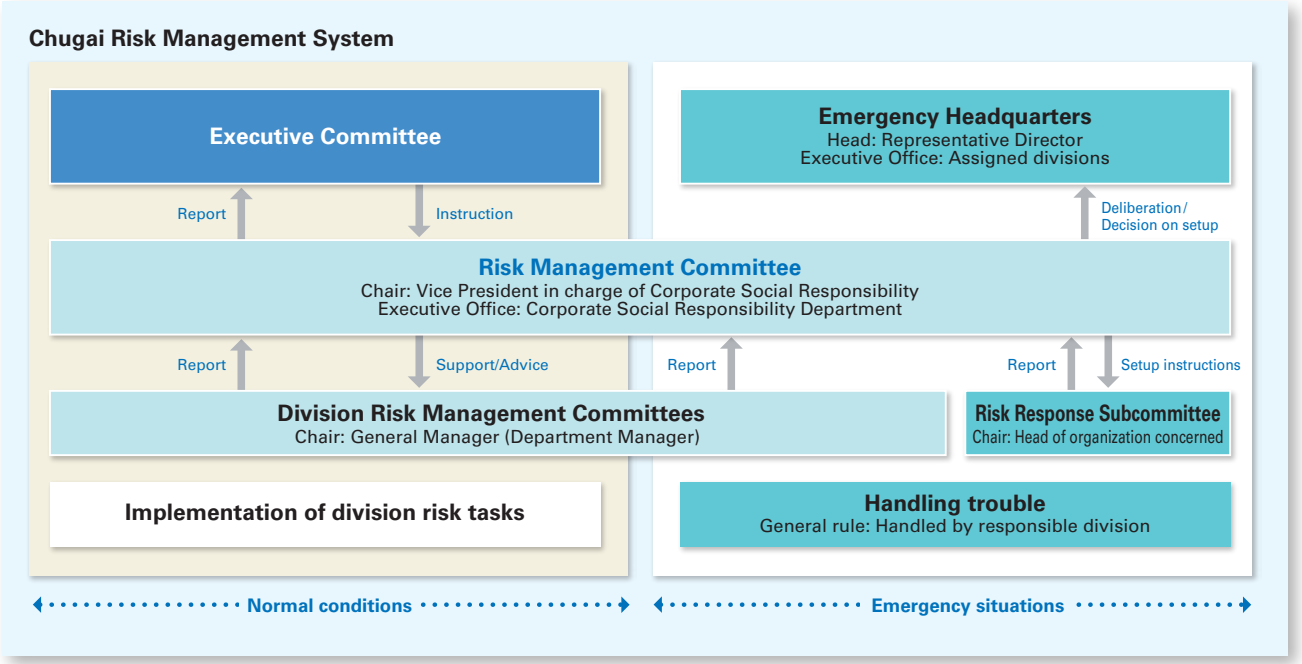
Restrictions on Roche's Shareholding

Period	Maximum Shareholding Percentage
Oct. 1, 2002 – Sept. 30, 2007	50.1%
Oct. 1, 2007 – Sept. 30, 2012	59.9%
Oct. 1, 2012 and thereafter	Cooperate in maintaining Chugai's listing

Maintenance and Management of Internal Controls

In maintaining its internal control system, Chugai established the Chugai Business Conduct Guidelines (Chugai BCG) as standards for management decision-making and employee behavior. The Corporate Social Responsibility Committee created under the Executive Committee, together with the Corporate Social Responsibility Department, ensure that the guidelines are implemented throughout the Company.

In addition, Chugai has prepared for the system of internal controls over financial reporting under the Financial Instruments and Exchange Act. We have formulated a basic policy for the establishment, management and assessment of internal controls over financial reporting, formulated a system of controls that ensures reliable financial reporting and implemented control design effectiveness assessments. We select business processes to be assessed based on the results of the assessments of Company-wide internal controls and evaluate the design and operation of internal controls after identifying and analyzing financial reporting risks.



Risk Management

Chugai has established Risk Management Regulations to prevent risks that could affect the Company's business activities, as well as to ensure prompt and appropriate handling of problems that arise. We have also established a Risk Management Committee under the Executive Committee, and Division Risk Management Committees. The Risk Management Committee identifies Company-wide risks that may significantly affect management and submits a progress report to the Executive Committee concerning preventive measures for such risks. Division Risk Management Committees summarize and create risk maps of all the risks facing their divisions, make proactive efforts to prevent such risks, and submit reports on the progress of those efforts to the Risk Management Committee. (For details of business risks, see pages 126-127.)

Compliance

Rooted in its belief that corporate ethics take priority over profit, Chugai places paramount importance on respect for life, and strives for fair and transparent corporate activities based on high ethical standards, along with sincere scientific initiatives.

As well as strictly complying with laws and regulations such as the Law for Ensuring the Quality, Efficacy and Safety of Drugs and Medical Devices and the voluntary Code of Practice for the industry established by the Japan Pharmaceutical Manufacturers Association (JPMA), Chugai proactively takes part in the activities of the Fair Trade Council of the Ethical Pharmaceutical Drugs Marketing Industry, the JPMA Code Committee and other organizations. In addition, by establishing its own guidelines, Chugai works to ensure a high level of ethics, morality and transparency in its various business activities including collaboration with medical institutions and other parties and cooperation with patient groups. To further promote compliance in healthcare, Chugai has also established internal organizations such as the Healthcare Compliance Committee and the Medical Affairs Division to promote internal consistency.

Chugai has put in place Compliance Regulations for its compliance system. These regulations are promoted by the Corporate Social Responsibility Committee and the Corporate Social Responsibility Department. In light of increasing societal demands for greater compliance in the pharmaceutical industry, in 2014 we strengthened compliance measures Company-wide. In addition to working to enhance compliance education in each of our training programs, we conducted compliance risk management measures in each organizational unit. Moreover, every six months the Corporate Social Responsibility Department conducted monitoring surveys regarding compliance status. Surveys were conducted internally, as well as for subsidiaries in Japan and overseas affiliated companies, and results were reported to the Corporate Social Responsibility Committee. Each organization works to ensure thorough legal compliance in the workplace through BCG promotion managers and assistants and holds corporate ethics courses twice a year, among other programs.

The BCG Hotline and the internal and external Harassment Hotlines have been established to receive employee inquiries and reports concerning compliance with laws, Company rules and the Chugai BCG.

Disclosure Policy

Chugai conducts interactive corporate communication activities to deepen mutual understanding and build relationships of trust with its stakeholders, such as patients, healthcare providers, shareholders, investors and employees. In order to achieve these objectives, Chugai ensures that information related to its business activities is made available in a transparent, fair and consistent manner to all stakeholders.

Chugai's policy for disclosing information to shareholders and investors is to make timely, appropriate and fair disclosure of information in accordance with the Financial Instruments and Exchange Act and relevant rules of the stock exchange on which Chugai's shares are listed in order to receive fair valuation in capital markets. In addition, measures to allow easy access to disclosed information have been established to ensure transparency.

Chugai has established an IR Committee composed of the CFO and general managers of the Corporate Communications Department, the Corporate Planning Department, the Finance & Accounting Department, the Corporate Social Responsibility Department and the General Affairs Department as a corporate management committee. The IR Committee holds regular meetings and is responsible for the establishment, revision and internal dissemination of the information disclosure policy, and for the management and promotion of information collection, disclosure and other related activities.

Top management, including the Chairman and key executive officers, has primary accountability for disclosure. In addition, the Corporate Communications Department takes the lead in coordinating with relevant departments to disclose information promptly.

Note: For further details on policies for disclosure to shareholders and investors, securities analysts and other capital market participants, please refer to Chugai's website (http://www.chugai-pharm.co.jp/english/ir/policy/disclosure.html).

External Recognition

Selection as Stock for Socially Responsible Investment Indices

In 2014, Chugai was selected for the first time as a component of the Dow Jones Sustainability Asia Pacific Index. The index, which covers companies in Japan, Asia and Oceania, is one of the Dow Jones Sustainability Indices (DJSI), which is one of the world's premier indices for socially responsible investment (SRI). Jointly complied by S&P Dow Jones Indices LLC of the United States and RobecoSAM AG of Switzerland, DJSI determines its component stocks each year based on an assessment in terms of economic, environmental and social sustainability. Out of 600 major companies in the region that applied for inclusion in 2014, the top 148 were selected, including 65 Japanese companies.

Chugai has also been selected for inclusion continuously since 2003 in another global SRI index, the FTSE4Good Index Series. This series is maintained by the FTSE Group in the U.K., which offers a variety of stock and other investment indices. It tracks the stocks of about 2,000 listed companies in 25 countries worldwide and selects candidates that meet international criteria related to the environment and society. As of December 31, 2014, 782 companies were listed, of which Chugai was one of 176 Japanese companies.

Chugai has been selected as a component of these global SRI indices in recognition of its proactive initiatives from the standpoint of corporate sustainability in areas including the environment, society and governance. Chugai will continue to fulfill its social responsibility as a healthcare company.

MEMBER OF
Dow Jones Sustainability Indices
In Collaboration with RobecoSAM

FTSE4Good

Corporate Communication

Communication with Society

Chugai emphasizes communication with stakeholders to increase its corporate value. As such, we are working to enhance communication not only with our shareholders and investors, but with the general public.

Since 2013, we have been conducting a project to develop our public relations strategy with the aim of establishing our corporate brand. By sharing Chugai's unique strengths with our stakeholders outside the Company, we aim to gain their recognition and understanding. Chugai's strengths have been identified and shared inside the Company as part of our project to become a top pharmaceutical company, which started in 2009. Using these strengths as a basis, through interviews inside and outside the Company, outside evaluations and analysis and other measures, we established Chugai's seven unique strengths. (For details on the seven strengths, see "Chugai's Seven Unique Strengths" on page 43.)

In December 2014, we adopted a new slogan, "INNOVATION BEYOND IMAGINATION." The slogan conveys the commitment of the Company and the strong desire of its employees to make Chugai a top pharmaceutical company that continuously creates not only the products anxiously awaited by people around the world but also unprecedented medicines that exceed all expectations. We have updated our corporate advertising with new slogans, and plan to build a corporate image of continuously creating what has never existed before, using the theme of art and architecture created based on unique concepts.

Strandbeest, a work by Dutch kinetic artist Theo Jansen, walks using the power of the wind. In Chugai's advertisements, it depicts the new world engendered by unprecedented creation. These advertisements won the Prize for the Excellent Work at the 82nd Mainichi Advertisement Design Competition held by The Mainichi Newspapers Co., Ltd. and sponsored by the Ministry of Economy, Trade and Industry.

Nikkei Shimbun, national morning edition, December 24, 2013

"Chugai's Activity Fields: New Medicine, New Me" in the *Nikkei Shimbun* electronic edition (appeared from December 24, 2013 to June 30, 2014)

Chugai's advertisements in the print and electronic editions of the *Nikkei Shimbun* newspaper received a Special Crossmedia Award at the 63rd Nikkei Advertising Awards for pioneering new potential and raising the value of newspaper advertising.

External Recognition

Chugai Receives the Second Prize for the Second Consecutive Year at the 17th Nikkei Annual Report Awards

The annual report was highly evaluated for two reasons. First, it explained the Company's management policies and business operations with Chugai's business philosophy "Innovation all for the patients" at its core. Second, the report used specific examples of Chugai's seven strengths identified through interviews inside and outside the Company, outside evaluations and other measures, as well as a special feature to show how we will use these strengths to create corporate value.

Media Relations Initiatives

Chugai conducts media relations activities on a daily basis to proactively disseminate information through methods including press releases, assistance with information gathering, various types of presentations, observation tours and informal discussions with management. Recognizing the important role played by the media in conveying corporate information to all its stakeholders, Chugai works to build and maintain good relationships with media outlets while disclosing information appropriately and in a timely manner.

Communication with Shareholders and Investors

General Meeting of Shareholders

Unlike many Japanese companies, which have fiscal years ending in March, Chugai's fiscal year ends in December. As a result, we are able to avoid holding our general meeting of shareholders on the same day as other companies. Convocation notices for the general meeting of shareholders are normally sent out more than four weeks prior to the meeting date.

The 104th annual general meeting of shareholders was held on March 26, 2015. After the presentation of the business report through narration and materials, shareholders deliberated on agenda items concerning appropriation of retained earnings and election of directors and Audit & Supervisory Board Members. All agenda items were approved and passed by a majority.

IR Activities

Coinciding with financial results announcements, Chugai holds information meetings and conference calls for investors, analysts and the media. These meetings provide opportunities to explain the state of the Company's business directly to shareholders and investors. In August 2014, we held an information meeting for Alecensa, an anticancer agent that obtained approval in July, to explain its usefulness in Personalized Healthcare and our safety measures. In addition, the President held discussions with institutional investors and securities analysts over three days during August and September. This was our first initiative to deepen mutual understanding by providing an opportunity for direct discussion between the President and market participants in small groups. We will continue to expand these face-to-face investor relations activities featuring senior management to properly convey Chugai's corporate value to the market. In December, we held an information meeting on research and development to give an overview of and progress report on projects that are the focus of attention (products in our HER2 franchise, anti PD-L1 antibody RG7446 and ACE910).

Director, Executive Vice President & CFO Yoshio Itaya was selected as both the sell-side (securities companies) and buy-side (institutional investors) "All-Japan Executive Team Best CFO" in the healthcare and pharmaceuticals sector.* This was his second consecutive year of selection by the sell side in recognition of his stance of increasing convenience for and enhancing communication with shareholders, investors and analysts in Japan and overseas.

* Initiated by Institutional Investors LLC in 2013, this competition ranks candidates based on a survey of securities analysts and institutional investors around the world, including Japan.

In May 2014, we conducted a factory tour for individual shareholders, a new initiative started in 2013 to increase shareholder communication. The tour of the Utsunomiya plant, where our flagship product Actemra is produced, gave shareholders a first-hand view of the manufacturing process for the biopharmaceuticals that are one of Chugai's strengths.

Senior management also holds overseas roadshows and in 2014 visited institutional investors in Europe, the United States and Asia. Moreover, in addition to participating in domestic and overseas conferences hosted by securities companies, Chugai is enhancing its outreach to individual investors by holding information meetings for them at branches of securities companies throughout Japan.

In addition, Chugai has integrated reporting to communicate its corporate value, which includes both financial and non-financial aspects. Since *Annual Report 2012*, we have integrated the traditional annual report with the corporate social responsibility (CSR) report.

The Chugai website is another tool we use to provide timely and fair disclosure to shareholders and other investors. Information on our website includes news releases, financial results, the status of our development pipeline, presentation materials, annual reports and an IR event calendar. We work to provide comprehensive information to our stakeholders. We focus on convenience for individual investors by offering the option of receiving e-mail notices whenever news releases and other updates are posted on the IR section of our website, and other initiatives include posting webcasts of IR events on the website. Chugai emphasizes fair information disclosure for domestic and overseas investors alike. As a rule, we post presentation materials and other information on our website and send out information by e-mail simultaneously in Japanese and English.

Board of Directors/Audit & Supervisory Board

(As of April 1, 2015)

Representative Directors

Osamu Nagayama

Motoo Ueno

Tatsuro Kosaka

Directors

Yoshio Itaya

Yutaka Tanaka

Yasuo Ikeda

Vice-Chairman of the Board of Directors, Musashi Academy of the Nezu Foundation, University Professor of Waseda University, Professor Emeritus of Keio University

Outside **Independent**

Masayuki Oku

Chairman of Sumitomo Mitsui Financial Group, Inc.

Outside **Independent**

Franz B. Humer

Non-executive Chairman of Diageo Plc. (U.K.)
Former Chairman, ROCHE HOLDING LTD

Outside

Daniel O'Day

Chief Operating Officer of Roche Pharmaceuticals Division, Member of the Roche Corporate Executive Committee, Member of the Genentech Board of Directors

Outside

Sophie Kornowski-Bonnet

Head of Roche Partnering and Member of the Roche Enlarged Corporate Executive Committee

Outside

Audit & Supervisory Board Members

Kunitoshi Watanabe
(full-time)

Shunji Yokoyama
(full-time)

Hisashi Hara

General Representative of the Asia-Pacific region, The Law Office of Nagashima Ohno & Tsunematsu

Outside

Michio Ishizuka

Ishizuka Certified Public Accountant Office

Outside **Independent**

Independent Independent officer pursuant to Article 436-2 of the regulations of Tokyo Stock Exchange, Inc.

Board of Directors (As of April 1, 2015)

Osamu Nagayama

1978 Entered the Company
1985 Deputy General Manager of Development and Planning Div. and Director
1987 Director & Senior Vice President
1989 Representative Director & Deputy President
1992 Representative Director, President & CEO
2010 Director, Sony Corporation (to present)
2012 Representative Director, Chairman & CEO (to present)

Motoo Ueno

1984 Entered the Company
1991 General Manager of London Representative Office
1993 Director
1994 Director and General Manager of Medical Information Div.
1995 Director and General Manager of Clinical Research & Development Division
1996 Director and Deputy General Manager of Research and Development Division
1997 Director & Senior Vice President
1998 Senior Vice President
2000 Director & Senior Vice President
2002 Director & Deputy President
2003 Director & Deputy President, Vice President
2004 Representative Director & Deputy President
2006 Representative Director & President, Chugai Pharma Manufacturing Co., Ltd.
2012 Representative Director & Deputy Chairman (to present)

Tatsuro Kosaka

1976 Entered the Company
1995 Deputy President of Chugai Pharma Europe Ltd. (U.K.)
2000 General Manager of Business Strategy Planning Office
2002 Vice President & General Manager of Corporate Planning Dept.
2004 Senior Vice President & General Manager of Corporate Planning Dept.
2005 Senior Vice President & Deputy Managing Director of Sales & Marketing Group
Senior Vice President & Head of Strategic Marketing Unit
2008 Senior Vice President & Head of Lifecycle Management & Marketing Unit
2010 Director & Executive Vice President, Head of Lifecycle Management & Marketing Unit
2011 Director & Executive Vice President
2012 Representative Director, President & COO (to present)

Yoshio Itaya

2003 Entered the Company
Senior Specialist of Finance & Accounting Div.
2006 Vice President and General Manager of Finance & Accounting Div.
2007 Vice President and General Manager of Corporate Planning Dept.
2010 Senior Vice President and General Manager of Finance Supervisory Div. and Finance & Accounting Dept.
2011 Senior Vice President, CFO, General Manager of Finance Supervisory Div. (to present) and Finance & Accounting Dept.
2012 Director, Executive Vice President & CFO (to present)

Yutaka Tanaka

1984 Entered Nippon Roche K.K. (NR)
2001 Department Manager of Product Research Dept. of Nippon Roche Research Center
2002 Senior Specialist of Product Research Dept. of the Company
2004 Senior Specialist of Product Strategy Dept.
2005 General Manager of Renal Disease Area Dept.
2007 Vice President, General Manager of Clinical Research & Development Div.
2009 Senior Vice President, General Manager of Clinical Research & Development Div.
Senior Vice President, Head of Portfolio Management Unit
2011 Senior Vice President, Head of Lifecycle Management & Marketing Unit
2012 Senior Vice President, Head of Project & Lifecycle Management Unit
2014 Director, Executive Vice President (to present)

Yasuo Ikeda

1979 Director of Keio University Hospital Blood Center
1991 Professor of Internal Medicine of Keio University School of Medicine
2001 Director of Keio University Center for Integrated Medical Research
2005 Dean of Keio University School of Medicine
2009 Professor Emeritus of Keio University (to present)
Professor of Department of Life Science and Medical Bioscience of Graduate School of Advanced Science and Engineering of Faculty of Science and Engineering of Waseda University
2010 Director of the Company (to present)
2013 Vice-Chairman of the Board of Directors, Musashi Academy of the Nezu Foundation (to present)
2014 University Professor of Waseda University (to present)

Masayuki Oku

1968 Entered The Sumitomo Bank, Ltd. (SB)
1994 Director, SB
1998 Managing Director, SB
1999 Managing Director and Managing Executive Officer, SB
2001 Senior Managing Director and Senior Managing Executive Officer, SB
Senior Managing Director and Senior Managing Executive Officer of Sumitomo Mitsui Banking Corporation (SMBC)
2002 Senior Managing Director of Sumitomo Mitsui Financial Group, Inc. (SMFG)
2003 Deputy President, SMBC
2005 Chairman, SMFG (to present)
President and Chief Executive Officer, SMBC
2015 Director of the Company (to present)

Franz B. Humer

1971 Entered ICME Zurich
1973 Entered Schering Plough Corporation
1981 Entered Glaxo Holdings plc
1995 Member of the Board of Directors, Head of the Pharmaceuticals Division of F. Hoffmann-La Roche Ltd (FHLR)
1996 COO of FHLR
1998 CEO of ROCHE HOLDING LTD (RH)
2001 Chairman of the Board of Directors and CEO of RH
2002 Director of the Company
2008 Chairman of the Board of Directors of RH
Non-executive Chairman of Diageo Plc (U.K.) (to present)
2014 Director of the Company (to present)

Daniel O'Day

1987 Entered Roche Pharma USA
1995 Director Human Resources, Roche Pharma U.S.A.
1996 Director Product Marketing, Roche Pharma U.S.A.
1998 Business Unit Head, Arthritis and Respiratory, Roche Pharma Headquarters
1999 Lifecycle Leader Tamiflu, Roche Pharma Headquarters
2001 Head Corporate Planning, Roche Pharma Japan
2003 General Manager, Roche Pharma Denmark
2006 President & CEO of Roche Molecular Diagnostics
2010 COO Roche Diagnostics Division, Member of the Corporate Executive Committee
2012 COO Roche Pharmaceuticals Division, Member of the Roche Corporate Executive Committee, Member of the Genentech Board of Directors (to present)
2013 Director of the Company (to present)

Sophie Kornowski-Bonnet

1985 Abbott Diagnostic Division – Paris - France
Scientific Manager
1989 Abbott Pharmaceutical Products – Chicago, U.S.A.
Marketing Research Analyst
1990 Abbott Pharmaceutical Products – New York, U.S.A.
Neuroscience Sales Representative
1991 Sanofi Winthrop – New York, U.S.A.
Director, Strategic Marketing, Diagnostic Imaging
1994 Sanofi Winthrop – Paris, France
Director, Neuroscience Business Unit
1996 Merck Sharp & Dohme Paris, France
Director, Marketing Research and Strategic Planning
1997 Merck Sharp & Dohme Israel Managing Director
2000 Vice-President Arthritis and Analgesia Franchise, Merck & Co. Inc. U.S.A.
2002 Merck Sharp & Dohme Paris, France
Director, Rheumatology Division
2006 Merck Sharp & Dohme Paris, France
Director, Cardiovascular Division
2007 Roche Pharma, France
General Manager
2012 Head of Roche Partnering, Member of the Roche Enlarged Corporate Executive Committee (to present)
Director of the Company (to present)

Executive Officers (As of April 1, 2015)

Executive Committee Members

① Osamu Nagayama
Representative Director, Chairman
CEO

② Motoo Ueno
Representative Director, Deputy Chairman
Corporate Social Responsibility, Audit

③ Tatsuro Kosaka
Representative Director, President
COO

④ Yoshio Itaya
Director, Executive Vice President
CFO, General Manager of Finance Supervisory Div.

⑤ Yutaka Tanaka
Director, Executive Vice President

⑥ Kunitoshi Watanabe
Audit & Supervisory Board Member

⑦ Shunji Yokoyama
Audit & Supervisory Board Member

① Masaaki Tohaya
Executive Vice President
Marketing & Sales Strategy

② Hitoshi Kuboniwa
Senior Vice President
General Manager of Pharmaceutical Technology Div.

③ Susumu Kato
Senior Vice President
General Manager of Marketing & Sales Div.

④ Shinya Unno
Senior Vice President
General Affairs and Secretarial

⑤ Mitsuru Kikuchi
Senior Vice President
General Manager of External Affairs Dept.

⑥ Yasushi Ito
Vice President
Head of Project & Lifecycle Management Unit

⑦ Yoshiaki Ohhashi
Vice President
Head of Quality & Regulatory Compliance Unit and General Manager of Drug Safety Div.

Executive Officers (Non-Executive Committee Members)

Hisafumi Okabe
Vice President
General Manager of Research Div.

Toshihiko Komori
Vice President
General Manager of Translational Clinical Research Div. and Department Manager of TCR Study Management Dept.

Shinji Hidaka
Vice President
Deputy General Manager of Marketing & Sales Div. and Head of Primary Unit

Tadahiko Sato
Vice President
Supervisory Branch Manager of Tokyo Branch 1
Marketing & Sales Div.

Osamu Okuda
Vice President
General Manager of Corporate Planning Dept.

Toshiaki Itagaki
Vice President
General Manager of Finance & Accounting Dept.

Keiji Kono
Vice President
General Manager of IT Supervisory Div.

Mamoru Togashi
Vice President
General Manager of Human Resources Supervisory Div. and General Manager of Human Resources Management Dept.

Junichi Ebihara
Vice President
General Manager of Legal Dept.

Data Section

This section is intended to give readers a deeper understanding of Chugai's innovations and the value we want to create. In addition to an overview of Chugai's development pipeline and basic information, this section includes general information on topics such as pharmaceutical industry and healthcare trends and the newest treatments.

Development Pipeline..... 98
Basic Information..... 100
Glossary 114

Development Pipeline (As of January 28, 2015)

Development Code (*Additional Indication)	Indication	Status: Phase I	Phase II	Phase III	Filed	Approved	
Oncology							
AF802 (RG7853)	◆ Non-small cell lung cancer					●	July 2014
				●	(Overseas)		
RG7204	◆ Melanoma					●	Dec. 2014
RG340*	Gastric cancer (adjuvant)				●		
RG1273*	◆ Breast cancer (adjuvant)				(Multinational study)		
	◆ Gastric cancer				(Multinational study)		
RG3502*	◆ Breast cancer (adjuvant)			●	(Multinational study)		
	◆ Gastric cancer				(II/III) (Multinational study)		
GA101 (RG7159)	Aggressive non-Hodgkin's lymphoma				(Multinational study)		
	Indolent non-Hodgkin's lymphoma				(Multinational study)		
RG7446	◆ Non-small cell lung cancer			●	(Multinational study)		
	◆ Bladder cancer			●	(Multinational study)		
RG435*	Cervical cancer		●				
GC33 (RG7686)	◆ Hepatocellular carcinoma			(Multinational study)			
CKI27 (RG7304)	◆ Solid tumors						
		(Overseas)					
RG7321	Solid tumors						
RG7596	Non-Hodgkin's lymphoma	●					
RG7604	◆ Solid tumors	●					
Bone and Joint Diseases							
RG484	Osteoporosis						
Autoimmune Diseases							
MRA* (RG1569)	Rheumatoid arthritis (New formulation: subcutaneous)					●	(Overseas: E.U.) April 2014
	Large-vessel vasculitis			●			
	Giant cell arteritis				(Overseas)		
	Systemic sclerosis			(Overseas)			
SA237	Neuromyelitis optica			●	(Multinational study)**		
Central Nervous System							
RG1450	◆ Alzheimer's disease			●	(Multinational study)		
RG7090	Major depressive disorder			(Multinational study)			
RG1577	◆ Alzheimer's disease						
RG1662	Improvement of intellectual ability in individuals with Down syndrome	●					
Other Diseases							
RG3637	◆ Asthma				(Multinational study)		
	◆ Idiopathic pulmonary fibrosis			(Multinational study)			
CIM331	◆ Atopic dermatitis			(Multinational study)**			
URC102	Gout			(Overseas)			
ACE910 (RG6013)	Hemophilia A			(I/II)			

●●● Designates change in status in 2014 and thereafter ◆ PHC-based drug discovery

** Multinational study managed by Chugai Pharmaceutical

Generic Name / Product Name	Origin (Collaborator)	Mode of Action
alectinib/Alecensa	In-house (Roche)	ALK inhibitor (Oral)
vemurafenib/Zelboraf (Overseas name: Zelboraf)	Roche	BRAF inhibitor (Oral)
capecitabine/Xeloda (Overseas name: Xeloda)	Roche (Yakult Honsha)	Antimetabolite, 5-FU derivative (Oral)
pertuzumab/Perjeta (Overseas name: Perjeta)	Roche	HER2 dimerization inhibitory humanized monoclonal antibody (Injection)
trastuzumab emtansine/Kadcyla (Overseas name: Kadcyla)	Roche	Anti-HER2 antibody-tubulin polymerization inhibitor conjugate (Injection)
obinutuzumab/Product name undetermined (Overseas name: Gazyva/Gazyvaro (E.U.))	Roche (Nippon Shinyaku)	Glycoengineered type II anti-CD20 monoclonal antibody (Injection)
—	Roche	Engineered anti-PDL1 monoclonal antibody (Injection)
bevacizumab/Avastin (Overseas name: Avastin)	Roche	Anti-VEGF (Vascular Endothelial Growth Factor) humanized monoclonal antibody (Injection)
—	In-house (Roche)	Anti-Glypican-3 humanized monoclonal antibody (Injection)
—	In-house (Roche)	Raf and MEK dual inhibitor (Oral)
pictilisib/Product name undetermined	Roche	PI3K inhibitor (Oral)
polatuzumab vedotin/Product name undetermined	Roche	Anti-CD79b antibody-drug conjugate (Injection)
taselisib/Product name undetermined	Roche	PI3K inhibitor (Oral)
ibandronic acid/Bonviva (Overseas name: Bonviva/Boniva (U.S.))	Roche (Taisho Pharmaceutical)	Bisphosphonate (Oral)
tocilizumab/Actemra (Overseas name: Actemra/RoACTEMRA (E.U.))	In-house (Roche)	Humanized anti-human IL-6 receptor monoclonal antibody (Injection)
—	In-house	Anti-IL-6 receptor humanized monoclonal antibody (Injection)
gantenerumab/Product name undetermined	Roche/MorphoSys	Anti-amyloid-beta human monoclonal antibody (Injection)
basimglurant/Product name undetermined	Roche	mGluR5 antagonist (Oral)
—	Roche	MAO-B inhibitor (Oral)
—	Roche	$GABA_A\alpha5$ receptor antagonist (Oral)
lebrikizumab/Product name undetermined	Roche	Anti-IL-13 humanized monoclonal antibody (Injection)
—	In-house	Anti-IL-31 receptor humanized monoclonal antibody (Injection)
—	In-house/JW Pharmaceutical	URAT1 inhibitor (Oral)
—	In-house (Roche)	Anti-FIXa/FX bispecific antibody (Injection)

Basic Information on the Pharmaceutical Industry

Overview of Domestic Pharmaceutical Market and 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 3 to 4 percent going forward. In the year ended March 2013, national medical expenses[1] totaled ¥39,211.7 billion, a ¥626.7 billion or 1.6 percent increase from the previous year. The rapid aging of Japan's society presents serious challenges to efficiently managing the increase in medical expenses for the elderly.

1. Source: Overview of National Medical Expense (2012) by Ministry of Health, Labour and Welfare

Promotion of the Use of Generics

The Japanese government is promoting the use of generics[2] 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. The roadmap sets the goal of raising the volume market share of generics, which was 51.2 percent as of March 2014, to more than 60 percent by the end of March 2018.

2. Drugs approved after the expiry of the patents for original drugs with the same active ingredients and efficacy

National Health Insurance (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 prices of pharmaceuticals prescribed under the health insurance system approximate their actual market price. MHLW does this by investigating the prices and volumes of all prescription drug transactions during a given period. In fiscal 2014, drug reimbursement prices declined by 0.58 percent overall on a medical expense basis, or 2.65 percent on a reimbursement price basis.

NHI Drug Price Revision Rate (%)

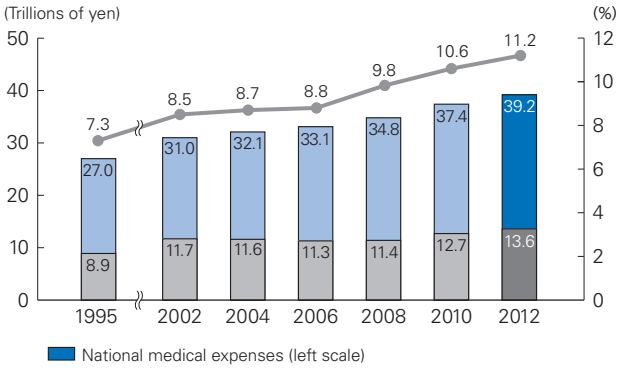
	2008	2010	2012	2014*
Industry Average	(5.2)	(6.5)	(6.25)	(2.65)
Chugai	(7.2)	(6.8)	(6.0)	0.8

Source: Chugai data
* Includes provision for increase in consumption tax

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

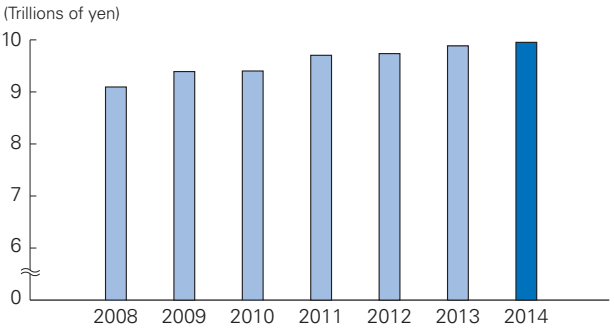
As part of the NHI drug pricing system reforms of fiscal 2010 (the year ended March 2011), a new pricing scheme was implemented on a trial basis to promote the creation of innovative medical products and solve the drug lag[3] problem. In this scheme, at the time of the NHI drug price revisions a premium (equal to the weighted-average percentage price

Trends in National and Elderly Medical Expenses



Source: Overview of National Medical Expense (2012) by Ministry of Health, Labour and Welfare
Note: National income is based on the actual results of the System of National Accounts (announced in December 2012 by the Cabinet office).

Prescription Drug Market



Copyright 2015 IMS Health Source: JPM 2008-2014.
Reprinted with permission. The scope of the market is defined by Chugai.

difference of all listed drugs minus 2 percent, multiplied by 0.8) is added to the price of 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.[4]

This premium pricing for new drugs was continued on a trial basis in the NHI drug pricing system reforms of fiscal 2012 and fiscal 2014. The fiscal 2014 reforms, however, added the condition that only companies that (1) conduct research and development of unapproved or off-label drugs as requested by a panel of MHLW, or (2) conduct research and development of drugs that clearly contribute to improving treatment quality[5] will be eligible to receive premium pricing for their products. In the year ended March 2014, 397 compounds and 758 products received premium pricing.

3. The inability of Japanese patients to gain access to global standard or most advanced treatments because the drugs are not developed in Japan
4. The percentage price difference between the current market price and the reimbursement price of the original drug must not exceed the weighted-average percentage price difference of all listed drugs.
5. Drugs for pediatric use, orphan drugs and drugs for diseases in which there are no adequate treatments with current therapies (e.g., drugs for intractable diseases or unmet medical need)

Solving the Drug Lag Problem

In January 2005, 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, 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. MHLW has also reinforced several functions of the Pharmaceutical and Medical Devices Agency, an independent administrative institution responsible for reviewing drugs and medical devices for approval. Measures have included increasing the number of staff involved in the reviewing process, introducing a project management system using a dedicated staff, providing guidelines on multinational clinical studies, clarifying reviewing criteria and offering an improved consultancy function. As a result, the median total review time for new drugs in the year ended March 2014 was 11.3 months.

Response to Requests from the MHLW Review Committee on Unapproved Drugs and Indications with High Medical Needs (As of January 28, 2015)

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	Awaiting evaluation by study panel regarding Chugai's view with respect to development request

Oncology

Overview of Diseases and Treatment Methods

Leading Cause of Death in Japan

Cancer has been the single most common cause of death in Japan since 1981. In 2013, 364,872 people* died of cancer, accounting for 28.8 percent* of all deaths in that year and the highest figure recorded since government surveys began in 1899.

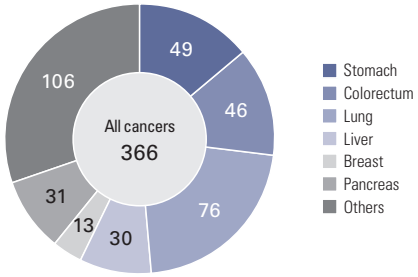
*Source: Outline of Vital Statistics (2013) by Ministry of Health, Labour and Welfare

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

In June 2006, the Diet enacted the Basic Act for Anticancer Measures, which stipulates the obligation of national and local governments to promote measures to fight cancer. The basic principle of the law is to develop cancer treatment systems in every region of the country so that patients can receive optimal treatment based on scientific knowledge and in accordance with their wishes ("the availability of optimal treatment" for cancer patients). The law includes provisions for (1) improvement of cancer prevention and treatment technologies, (2) development of oncologists and "hub" institutions that specialize in cancer, and (3) enhanced provision of information to patients. As a result of the enactment of this law, progress has been made in the training of oncologists and medical staff such as nurses and pharmacists. Other advances include greater efforts to establish networks among local medical institutions by designating interregional hub cancer centers. Moreover, an increasing percentage of medical institutions are adopting multidisciplinary team care in which oncologists, nurses, pharmacists and nutritionists work together to provide care tailored to the condition of each individual patient. In December 2013, the Cancer

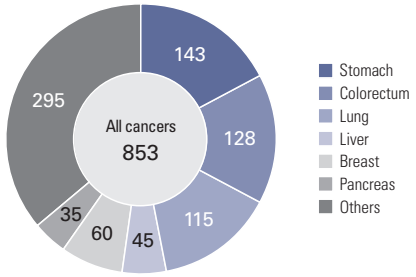
Cancer Mortality (Estimates for 2015)

(Thousands of cases)



Cancer Incidence (Estimates for 2015)

(Thousands of cases)

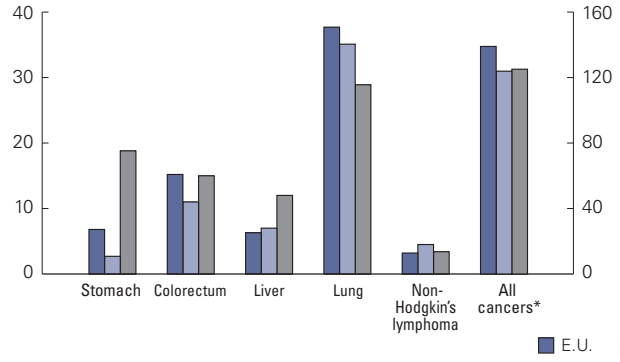


Source: White Paper on Cancer Statistics: Incidence/Death/Prognosis; 2012 (Shinoharashinsha Publishers Inc.)

International Comparison of Cancer Mortality Rates (2012)

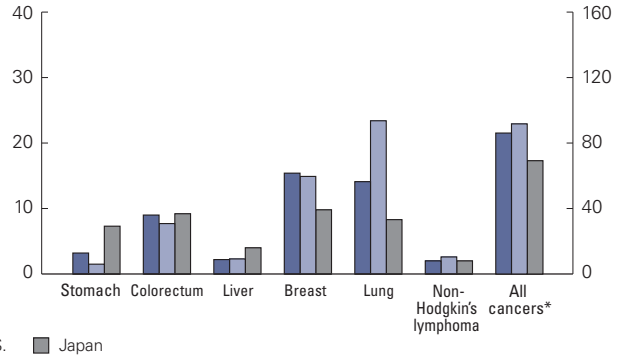
Male

Age-standardized rate per 100,000 population (persons)
(By cancer type) (All cancers)



Female

Age-standardized rate per 100,000 population (persons)
(By cancer type) (All cancers)



E.U. U.S. Japan

* Excluding non-melanoma skin cancer

Source: Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray, F. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available from: http://globocan.iarc.fr, accessed on 28/02/2015.

Registration Law was enacted requiring hospitals nationwide to provide information on each cancer patient. The law is aimed at shedding light on the current state of cancer treatment by centralizing patient information in a single database and using that resource to improve early detection and treatment.

Changes in Treatment Methods

Cancer treatment is increasingly being based on a multimodal approach that combines surgery, radiation therapy and anticancer agents. In particular, the field of anticancer agents is evolving, and highly innovative medications such as molecular targeted drugs have been introduced. This has brought a dramatic improvement in treatment outcomes in colorectal, lung and breast cancer, hematological malignancy and other forms of cancer.

It is recognized that the safety profiles of these drugs differ from those of conventional anticancer agents. Consequently, there is a need for cancer drug therapy specialists with a thorough knowledge of drug modes of action, pharmacokinetics and drug interactions. Furthermore, whereas many earlier drug therapies were administered in an inpatient setting, there has been an increase in drug therapies that can be administered on an outpatient basis, which allows patients to maintain normal lifestyles as much as possible during treatment. To ensure the medical safety of drug therapy for these patients, various medical staff in addition to oncologists must contribute their respective expertise. As a result, multidisciplinary team care is becoming increasingly important.

Overview of Products and Development Projects

Avastin

Avastin is a humanized monoclonal antibody targeting vascular endothelial growth factor (VEGF). It is the first therapeutic agent in the world that inhibits angiogenesis (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. Its primary modes of action are thought to be regression of tumor vessels, inhibition of tumor angiogenesis and improvement of VEGF-induced vascular permeability. In Japan, Avastin was launched in 2007 for the treatment of unresectable, advanced or recurrent colon and rectal cancer. Chugai obtained regulatory approval for the additional indications of advanced or recurrent non-squamous non-small cell lung cancer in 2009, and inoperable or recurrent breast cancer in 2011. Chugai also obtained approval for the additional indications of malignant glioma and ovarian cancer in June and November 2013, respectively. In January 2015, administration began in a phase II clinical trial for the potential treatment of cervical cancer in Japan.

Rituxan

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. Outside Japan, Rituxan is sold under the brand name MabThera/Rituxan by the Roche Group. In recent years, the usefulness of Rituxan in treating vasculitis and childhood-onset nephrotic syndrome has been recognized, and it has also become a valuable treatment option for patients with autoimmune diseases.

Herceptin

Herceptin is a humanized monoclonal antibody that targets human epidermal growth factor receptor type 2 (HER2), which contributes to tumor cell growth. Overexpression of HER2 is found in about 20 percent of breast cancers. These cancers are 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 regulatory approval for the additional indication of advanced or recurrent gastric cancer overexpressing HER2, not amenable to curative resection, bringing Personalized Healthcare to the field of gastric cancer.

Perjeta

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 additional indication of HER2-positive inoperable or recurrent breast cancer in September 2013, after obtaining regulatory approval in June 2013. Chugai is participating in phase III multinational studies that began in April 2012 for the indication of postoperative adjuvant chemotherapy in HER2-positive breast cancer and in July 2013 for the indication of HER2-positive gastric cancer.

Kadcyla

Kadcyla is an antibody-drug conjugate of the anti-HER2 humanized monoclonal antibody trastuzumab (the active ingredient of Herceptin) and the potent chemotherapeutic agent DM1, joined together with a stabilized linker. Chugai filed an application for regulatory approval for the treatment of 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. In addition, Chugai is participating in a phase II/III multinational study, which began in September 2012 for the potential treatment of HER2-positive metastatic gastric cancer. Chugai is also participating in a phase III multinational study, which began in January 2014, for the potential treatment of postoperative adjuvant chemotherapy in HER2-positive breast cancer.

Xeloda

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 the liver and tumor cells, and is eventually converted into active 5-FU within tumor tissue.

In Japan, Xeloda is currently used to treat inoperable or recurrent breast cancer and as a postoperative adjuvant chemotherapy for colon cancer. In addition, Xeloda has obtained regulatory approval for treating patients with advanced or recurrent colorectal cancer and for advanced or recurrent gastric cancer not amenable to curative resection. Phase II clinical trials started in Japan in July 2012 for the additional indication of postoperative adjuvant chemotherapy for gastric cancer, and Chugai filed an application for regulatory approval in December 2014 (co-development with Yakult Honsha Co., Ltd.).

Tarceva

Tarceva is an oral targeted small-molecule drug that inhibits the activation of human epidermal growth factor receptor (EGFR) tyrosine kinase, which is associated with the growth, progression and metastasis of cancer. In Japan, Tarceva had been used for second-line or later treatment of non-small cell lung cancer since its launch in 2007, but the approval of an additional indication in June 2013 allowed its use in first-line treatment of patients with *EGFR* mutations, in whom high efficacy is expected. About 10 percent of non-small cell lung cancer patients in Europe and about 30 percent in Asia test positive for *EGFR* mutations. In July 2011, Tarceva obtained regulatory approval for the additional indication of pancreatic cancer not amenable to curative resection.

Neutrogin

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 cell transplantation, which is performed for illnesses that affect production of normal blood cells, such as leukemia. Overseas, Neutrogin is sold under the name Granocyte.

Alecensa

Alecensa, an oral, small-molecule targeted molecular therapy created by Chugai, inhibits the activity of ALK kinase with *EML4-ALK* fusion gene expressed in about 2 to 5 percent of non-small cell lung cancers. It was designated as an orphan drug in Japan in September 2013 for the treatment of *ALK* fusion gene-positive unresectable, recurrent/advanced non-small cell lung cancer. In October 2013, Chugai filed an application for regulatory approval. Following approval in July 2014, Alecensa was launched first in Japan in September 2014.

Chugai has out-licensed the rights for Alecensa to Roche in Europe, North America and other markets outside Japan, and is co-developing it with Roche. A phase III clinical trial began overseas in August 2014. In June 2013, the drug was granted Breakthrough Therapy designation by the U.S. Food and Drug Administration (FDA).

Zelboraf

Zelboraf, in-licensed from Roche, is an oral, small-molecule drug that selectively inhibits a mutated form of the BRAF protein found in 30 to 40 percent of all malignant melanoma cases. Chugai filed an application for approval of Zelboraf as a treatment for unresectable melanoma with *BRAF* mutation in April 2014, obtained approval in December 2014 and launched the product in February 2015.

GA101 (RG7159) (generic name: obinutuzumab; overseas product name: Gazyva/Gazyvaro (E.U.))

GA101 is a type II glycoengineered humanized monoclonal antibody in-licensed from Roche. Like Rituxan, GA101 targets CD20. Phase III multinational studies for the potential treatment of low-grade non-Hodgkin's lymphoma and for intermediate- and high-grade non-Hodgkin's lymphoma are currently under way. In November 2012, Chugai entered into an agreement with Nippon Shinyaku Co., Ltd. to co-develop and co-market this compound in Japan.

RG7446

RG7446, an engineered anti-PDL1 monoclonal antibody in-licensed from Roche, is expected to become a treatment for various cancers. One way that tumor cells evade the immune system is by expressing a protein called programmed death-ligand 1 (PD-L1) on their surface, which is believed to shield them from immune system attacks. RG7446 maintains the immune response of T cells by binding to PD-L1, and is expected to demonstrate efficacy against cancer. Chugai began participating from Japan in phase III multinational studies for the potential treatment of non-small cell lung cancer and for the potential treatment of bladder cancer in February 2014 and January 2015, respectively.

GC33 (RG7686)

GC33, a humanized antibody from Chugai, targets glypican-3, which is specifically expressed in liver cancer. The project involves joint research between Chugai and Tokyo University, as well as clinical proteomics work by PharmaLogicals Research Pte. Ltd., a former subsidiary of Chugai. GC33 did not meet the primary endpoint in a phase II multinational monotherapy study started in March 2012. Future clinical trial plans, including combination therapy with other agents, are now under consideration.

CKI27 (RG7304)

CKI27 is a Raf and MEK dual inhibitor created by Chugai and out-licensed to Roche overseas. The two companies are co-developing CKI27, and phase I clinical trials in Japan and overseas for the treatment of solid tumors are currently under way.

RG7321 (generic name: pictilisib)

RG7321 is an oral PI3K inhibitor in-licensed from Roche. A phase I clinical trial started in Japan in June 2013 for the potential treatment of solid tumors.

RG7596 (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. A phase I clinical trial started in Japan in July 2014 for the potential treatment of non-Hodgkin's lymphoma.

RG7604 (generic name: taselisib)

RG7604 is a PI3K inhibitor in-licensed from Roche. A phase I clinical trial started in Japan in September 2014 for the potential 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 everyday activities. Among these, compression fractures of the spine and femoral neck fractures can decrease quality of life by leaving patients bed-ridden and can also increase mortality risk. About 13 million people in Japan suffer from osteoporosis, including one in every two women age 65 and older. However, the treatment rate stands at around only 20 percent of the estimated number of sufferers because there are virtually no noticeable 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 quality of life of patients.

Treatment Methods

Bone resorption inhibitors, bone formation stimulants and active vitamin D_3 derivatives are mainly used in the treatment of osteoporosis. Bisphosphonates, calcitonin preparations and selective estrogen receptor modulators (SERMs), which are bone resorption inhibitors, and active vitamin D_3 derivatives, which improve bone metabolism, have been the primary drug treatments used, but treatments such as human parathyroid hormone (PTH) therapy and a humanized anti-RANKL antibody are also approved.

Regulatory Trends

National guidelines for osteoporosis treatment 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 addition, Edirol and other medicines have recently been covered by insurance. Revised guidelines issued in December 2011 added preventive and diagnostic items from the standpoint of the importance of early treatment to broaden the overall scope of osteoporosis treatment. Since then, Bonviva and other medicines have been launched and covered by insurance, and the

guidelines are being updated. Revised management and treatment guidelines for steroid-induced osteoporosis were issued in 2014.

Overview of Products and Development Projects

Alfarol

Alfarol is an active vitamin D_3 derivative approved in 1981. It inhibits the decline of bone mass by adjusting calcium and bone metabolism, and therefore is effective in preventing vertebral fractures. The drug has also been shown to be effective in preventing falls, and attention has focused on this feature that sets Alfarol apart from other osteoporosis treatments.

Edirol

Edirol is a new vitamin D_3 preparation born out of Chugai's many years of research in vitamin D. 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 has been co-developed and is currently 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 2011 osteoporosis prevention and treatment guidelines published in December of that year, Edirol received a grade A recommendation, the first for an active vitamin D_3 preparation, for its effectiveness in increasing bone density and preventing vertebral fractures.

Bonviva

Bonviva is a bisphosphonate in-licensed from Roche. The injectable formulation was launched in August 2013. Under an agreement signed in September 2006, Bonviva is being co-developed and co-marketed with Taisho Pharmaceutical Co., Ltd. Bisphosphonates in Japan had previously been drip infusions that took 30 minutes or more to administer, but Bonviva IV Injection is given in a rapid intravenous injection once a month. This is expected to significantly reduce the burden on patients at the time of administration. In the results of a phase III clinical trial in September 2014, the oral formulation demonstrated non-inferiority to Bonviva IV Injection. Chugai filed an application for regulatory approval in Japan in February 2015.

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. It is estimated that there are about 700,000 patients in Japan suffering from RA, of whom some 330,000 are currently receiving drug treatment. The number of patients is increasing as the average age of the population rises. On the other hand, juvenile idiopathic arthritis (JIA), the form of RA suffered by children below 16 years of age, is associated with growth disorders, and is considered even more difficult to treat than adult forms of the disease, as few treatment options are available.

The most common joint disease is osteoarthritis. Degeneration of the cartilage in the joints and surrounding areas causes joint pain and reduced mobility in daily life. The prevalence of this disease increases with age, with knee osteoarthritis in particular affecting at least 80 percent of people 60 years of age or older, primarily women.

Treatment Methods and Market Conditions

Conventional RA treatment has been mainly symptomatic, using anti-rheumatic drugs, anti-inflammatory analgesics and steroids, but the introduction of biologics (anti-tumor necrosis factor (TNF) agents) targeting proteins involved in the process of inflammation has expanded the range of treatment choices. 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 reached U.S.$3.11 billion* in 2013, and continues to grow. The market is also changing. In 2013, a new oral formulation was launched in the United States and Japan, and a biosimilar was launched in Europe. In 2014, a biosimilar was also launched in Japan.

In addition to drip infusions, which were the only formulations previously available, subcutaneous formulations have been added, and new formulations that improve convenience, such as a dosage form that can be injected simply by pushing a button, are increasing. In Japan, Europe and the United States, the subcutaneous market is estimated to be larger than the intravenous market.

Systemic juvenile idiopathic arthritis (sJIA) is a serious and potentially fatal disease. While it is rare in Japan, with only a few hundred patients, effective treatments were limited. Steroid drugs, which had been the only treatment available, can cause growth impairment and other adverse reactions. Accordingly, the approval and launch of Actemra in April 2008 provided a significant advancement in therapy.

The main drug therapies for osteoarthritis include non-steroidal anti-inflammatory analgesics, steroids and hyaluronic acid preparations. However, as the joint fluid in osteoarthritis patients is known to have reduced hyaluronic acid content (density and molecular weight), intraarticular administration of hyaluronic acid preparations is used as a treatment in the early and

middle stages. Intraarticular administration of hyaluronic acid preparations has also demonstrated effectiveness in improving periarthritis of the shoulder and knee joint pain associated with rheumatoid arthritis.

* Copyright 2015 IMS Health
Source: IMS Health MIDAS, December 2013 DISEASE
Reprinted with permission.

Regulatory Trends

In October 2005, MHLW released the Report of the Rheumatism and Allergy Countermeasure Committee. The report calls for the following measures to prevent rheumatoid arthritis from becoming severe: (1) promotion of early diagnosis and the development of highly effective treatment methods; (2) establishment of medical service systems to provide appropriate care; and (3) improvement of the patient environment, including consultation opportunities and access to information. In the European Union, revised treatment recommendations in 2013 added Actemra and Orencia to the biologic drugs recommended in first-line therapy, which was previously limited to anti-TNF agents. In 2014, 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.

In recent years, academic societies and other players have been aggressively promoting research, diagnosis and treatment of osteoarthritis as an underlying cause of "locomotive syndrome," a term proposed in the field of orthopedics to designate the condition of individuals at high risk of suffering loss of motor function due to advanced age that leaves them requiring nursing care and bedridden.

Overview of Products and Development Projects

Actemra

Actemra, created by Chugai and the first therapeutic antibody originating in Japan, blocks the activity of interleukin-6 (IL-6), a type of cytokine. It was first launched in Japan in June 2005 as a treatment for Castleman's disease. In April 2008, Chugai obtained regulatory approval in Japan for the additional indications of rheumatoid arthritis (RA), polyarticular juvenile idiopathic arthritis (pJIA) and systemic juvenile idiopathic arthritis (sJIA). The requirement for post-marketing all-case registration surveillance as a condition of Actemra's approval in Japan was lifted in August 2010 for RA and pJIA, making Actemra an important option in treatment as a biological product. In May 2013, Chugai launched a new subcutaneous formulation that improves convenience for patients in addition to the existing drip infusion formulation. This subcutaneous formulation includes the first auto-injector in the Japanese RA market.

Actemra is marketed globally through Roche. In the European Union, where it is known as RoACTEMRA, sales of the drug started for the treatment of RA in 2009. Chugai's marketing subsidiary co-promotes RoACTEMRA with Roche in the U.K., France and Germany. In the United States, Actemra obtained regulatory 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 TNF antagonist therapies, 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 the European Union in April 2014, and has been launched in both markets. RoACTEMRA was also approved for early RA in the European Union in September 2014.

Actemra obtained approval for the additional indication of treatment of sJIA in the United States in April 2011 and in the European Union in August 2011.

In June 2014, Actemra was designated as an orphan drug in Japan for the additional indication of large-vessel vasculitis. A phase III clinical trial for Takayasu's arteritis, a type of large-vessel vasculitis, started in Japan in October 2014.

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's arteritis and giant cell arteritis (temporal arteritis).

Takayasu's 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 include reduced head and cerebral blood flow-related conditions such as 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.

Overview of Product

Suvenyl

Suvenyl, a drug that improves joint function through injection into the joint cavity, is a high molecular weight sodium hyaluronate drug that alleviates knee osteoarthritis, shoulder periarthritis and knee joint pain caused by RA. With physical and chemical properties close to that of hyaluronic acid found in the body, Suvenyl has been recognized for its superior performance, including its anti-inflammatory and analgesic effects.

Neuromyelitis Optica

Neuromyelitis optica (NMO), also known as Devic's disease, is an autoimmune disease of the central nervous system characterized by severe optic neuritis and transverse myelitis. The disease affects 0.3 to 4.4 in 100,000 people, and is more common in Asia than in Western countries, with 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 (blindness) and various impairments such as impairment of motor function and sensation. In some cases, the disease results in death. However, as there are no approved treatments available, NMO is an orphan disease with high unmet medical need. It is believed to occur when aquaporin-4 (AQP4) in the central nervous system is attacked by autoantibodies called anti-AQP4 antibodies.

Overview of Development Project

SA237

SA237, created by Chugai, is a next-generation therapeutic antibody that has shown success in blocking IL-6 receptors for an extended period of time. Chugai created SA237 by applying its novel antibody technology (recycling antibody technology) that enables a single antibody molecule to block the target antigen repeatedly. Preclinical studies have verified that this extends the duration of the blocking action on IL-6 receptors more than four times longer than Actemra, and an extension of serum half-life has been demonstrated in clinical trials. Because IL-6 promotes the production of the anti-AQP4 antibodies that cause NMO, this drug is expected to improve (reduce recurrence of) the symptoms of this disease as it inhibits the production of those antibodies by blocking the IL-6 signal. Chugai began a phase III multinational study in February 2014. In June 2014, SA237 was designated as an orphan drug in the United States.

Renal Diseases

Renal Anemia

Chronic Kidney Disease

Chronic kidney disease (CKD) is defined as the continuation for three months or more of "manifestations showing the existence of renal disease, such as positive proteinuria" or "presence of kidney damage (a glomerular filtration rate of less than 60ml/min)." Recently, reports containing ample evidence of the major risk posed by chronic kidney disease in end-stage renal disease and cardiovascular disease have prompted efforts to address this disease around the world. Also in Japan, measures are fully under way to deal with the problem. For example, the Japanese Society of Nephrology issued the CKD Clinical Practice Guidebook in 2007 and the Evidence-based Practice Guidelines for the Treatment of CKD in 2009, which were revised in 2012 and 2013, respectively. MHLW has started strategic research through The Kidney Foundation Japan with the objective of achieving a 15 percent reduction in five years of the number of dialysis patients compared with current forecasts.

CKD and Renal Anemia

CKD is a disease in which renal function is gradually reduced due to a variety of causes, including diabetes-related renal disease, chronic glomerulonephritis, nephrosclerosis and polycystic kidney disease. In recent years, the rise in the number of diabetes patients has led to a corresponding increase in CKD in patients with underlying diabetes-related renal disease; this has become the primary reason for dialysis use.

For dialysis patients and end-stage renal disease patients, the treatment of serious complications of advanced renal dysfunction, such as renal anemia, secondary hyperparathyroidism, and abnormal calcium and phosphorus metabolism, is a major issue. 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 renal disease patients. Renal anemia, in turn, is thought to be responsible for a wide range of further complications suffered by renal disease patients, including deterioration in heart functions. The importance of treating renal anemia and CKD - mineral and bone disorder (CKD-MBD) was

indicated in the Guideline for Renal Anemia in Chronic Kidney Disease (2008) and the Clinical Practice Guidelines for the Management of CKD-MBD (2012) issued by the Japan Society for Dialysis Therapy and in the Evidence-based Practice Guidelines for the Treatment of CKD (2013) issued by the Japanese Society of Nephrology.

Erythropoietin

Erythropoietin (EPO) is a hemopoietic factor produced mainly in the kidneys. It speeds up erythrocyte production by acting on normoblastic progenitor cells found in bone marrow. EPO preparations are effective in treating renal anemia caused primarily by the decline in erythropoietin production due to CKD. In addition to improving quality of life, the drug is also thought to help improve complications by correcting and controlling anemia. It is estimated that EPO preparations are currently used by approximately 80 percent of dialysis patients and the majority of pre-dialysis renal disease patients with renal anemia. Chugai's Epogin is thus an essential drug for the treatment of renal anemia.

A Flat-Sum Reimbursement System for Erythropoietin Preparations

The Japanese government decided in its 2006 revisions of medical fees that the administration of erythropoietin in dialysis treatment would be comprehensively incorporated as a flat-sum reimbursement within the medical fee points* for "artificial kidney" (dialysis treatment). The government changed the previous mechanism under which the number of fee points awarded depended on the amount of erythropoietin used. The new mechanism provides an integrated fee structure by adding the average amount of erythropoietin used per dialysis session to the medical fee points for one session.

* Formerly, the average amount of erythropoietin used per patient was approximately 4,500 international units per week, on the basis of three dialysis sessions per week. The new system adds points equivalent to 1,500 international units to the artificial kidney medical fee points and provides an integrated fee structure. The integrated fee points were reviewed in 2008, 2010, 2012 and 2014.

Overview of Products

Mircera

Mircera is a new type of anemia treatment with a very long serum half-life, enabling stable and sustained control of hemoglobin. It stimulates erythropoiesis by a different interaction with the erythropoietin receptor on progenitor cells in the bone marrow. Mircera was launched in Japan in July 2011 as a treatment for anemia. Outside Japan, Mircera obtained regulatory approval in the European Union in 2007 and is currently sold in more than 100 countries.

The serum half-life of Mircera is virtually the same for intravenous injection or subcutaneous administration, and the drug demonstrates effectiveness in relieving the symptoms of anemia when administered at four-week intervals during the maintenance period. Consequently, it may reduce the burden of hospital visits on patients with pre-dialysis renal disease and is expected to contribute to better treatment adherence. Furthermore, as a dialysis-related treatment, Mircera is expected to reduce medical costs such as drug administration costs and medical waste by dramatically reducing administration frequency. The product thus has the potential to expand the range of options for the treatment of renal anemia.

Epogin

Epogin is a human erythropoietin formulation that uses epoetin beta, produced through Chugai's unique gene recombinant technology, as its main active ingredient. Erythropoietin is effective in improving renal anemia primarily caused by the decline in erythropoietin production due to CKD. It also contributes to the improvement of a wide range of complications arising from anemia. Since its launch in 1990, Epogin has been widely used in the clinical setting for its approved indications of renal anemia under dialysis and before dialysis, anemia of prematurity and autologous blood transfusion of patients scheduled for surgery.

Oxarol

Synthesized by Chugai, Oxarol is the first intravenous active vitamin D_3 derivative agent in Japan. It treats secondary hyperparathyroidism, a result of prolonged dialysis, by acting directly on the parathyroid gland with high concentration to control parathyroid hormone synthesis and secretion, and by acting to improve osteitis fibrosa and excess remodeling. With its short serum half-life, Oxarol is proving to be effective in patients who could not be treated sufficiently with oral vitamin D_3 derivatives due to the onset of hypercalcemia.

Central Nervous System Diseases

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 disease progression by several months, they are unable to stop the neuron death, and a treatment for the underlying cause does not yet exist. Consequently, unmet medical need is high, and there is strong demand for a more effective drug.

Overview of Development Projects

RG1450 (generic name: gantenerumab)

RG1450 is an anti-amyloid-beta human monoclonal antibody in-licensed from Roche. A phase III multinational study of RG1450 as a potential treatment for Alzheimers' disease began in May 2014.

RG1577

RG1577, a monoamine-oxidase-B (MAO-B) inhibitor in-licensed from Roche, is an oral small-molecule compound that is expected to be effective in treating Alzheimer's disease. A phase I clinical trial started in Japan in May 2013.

Depression

Depression is a condition associated with brain dysfunction. It is classified by type, including exogenous, psychogenic, endogenous, reactive or situational, depending on the cause. Depression characterized by the presence of specific symptoms is called major depressive disorder. For treatment of depression, if the cause of the depressive state is clear, removal of the cause may be considered. However, if the cause is undetermined, or the depressive state is severe, drug therapy with an antidepressant is carried out. The number of patients in Japan with mood disorders including depression was estimated at 1.04 million in 2008, and has been trending upward year by year.

Overview of Development Project

RG7090 (generic name: basimglurant)

RG7090 is an oral metabotropic glutamate receptor subtype 5 (mGluR5) antagonist in-licensed from Roche as a potential treatment for major depressive disorder. Chugai has been participating in Roche's phase II multinational study since September 2012.

Down Syndrome

Down syndrome typically occurs as a result of the presence of an extra copy of chromosome 21 due to mutation. In addition to characteristic physical traits such as low muscle tone, most people with Down syndrome have delayed intellectual development. However, Down syndrome is viewed as an inborn characteristic (like personality and body type) rather than a disease. The syndrome is regarded as the most common chromosome anomaly, present in 1 of every 650 to 1,000 newborns. Because of improvements in dealing with complications, average life expectancy has increased in recent years, and the number of individuals with Down syndrome who play an active role in society is growing. The current lack of a drug therapy in Japan or overseas that improves the intellectual ability of individuals with Down syndrome is an obstacle to independent living.

Overview of Development Project

RG1662

RG1662 is an oral $GABA_A\alpha5$ receptor antagonist in-licensed from Roche as a potential treatment for improvement of intellectual ability in individuals with Down syndrome. Inhibitory neurotransmitters via GABA are dominant in Down syndrome. This is believed to hinder effective learning and memory. By selectively binding to the $GABA_A\alpha5$ subunit, RG1662 weakens the binding activity between the subunit and GABA and inhibits excessive activity of GABA. It is therefore expected to increase cognitive and memory ability. A phase I clinical trial started in Japan in May 2014.

Other Diseases

Chronic Hepatitis C

Chronic hepatitis C is a liver disease caused by persistent infection by the hepatitis C virus (HCV). In Japan, this disease has been designated a "21st century national health issue," as there are an estimated 2 million HCV carriers. Early detection and treatment of HCV is important because approximately 70 percent of those infected develop chronic hepatitis, which gradually progresses to liver cirrhosis and then liver cancer.

Treatment Methods and Market Conditions

There are two methods of treating chronic hepatitis C: antiviral therapy to eradicate HCV from the body, and liver-support therapy to improve liver function and prevent the hepatitis from worsening.

Interferon therapy is the main antiviral treatment. However, its efficacy was limited until about 2000, which led to an increase in the use of liver-support therapy in Japan. Since 2001, the introduction of interferon-ribavirin combination therapy and of peginterferon[1] has significantly improved treatment outcomes. Moreover, the approval in 2012 of a protease inhibitor that suppresses the growth of HCV now makes triple combination therapy with peginterferon and ribavirin possible. In 2014, the approval of an interferon-free treatment for patients who have not responded sufficiently to conventional therapies expanded the treatment options for chronic hepatitis C.

1. Interferon conjugated with polyethylene glycol, which makes the medication longer-acting

Regulatory Trends

In January 2010, a new law went into effect to promote comprehensive measures against hepatitis. This law establishes a new Hepatitis Countermeasures Promotion Council in MHLW to formulate basic policies for promoting measures against hepatitis, including prevention and medical treatment. The law also includes necessary provisions for the national and local governments to ease the financial burden on hepatitis patients to ensure that they can get appropriate treatment when necessary. In April 2011, pegylated interferon monotherapy for hepatitis B and three-drug combination therapy for hepatitis C were among the treatments that became eligible for medical expense subsidies.

Overview of Products

Pegasys/Copegus

Pegasys is a pegylated interferon-based drug that was improved to achieve a sustained antiviral effect with once-weekly[2] administration. The guidelines for chronic hepatitis C treatment published by the MHLW recommend Pegasys as monotherapy for patients with a low viral load or those who cannot use ribavirin. In 2011, Pegasys obtained approval for the additional indications of compensated liver cirrhosis caused by hepatitis C (in combination with Copegus) in July and chronic active hepatitis B (as a monotherapy) in September.

Copegus is a chronic hepatitis C treatment that synergistically strengthens the antiviral effect when used in combination with interferon. Chugai obtained regulatory approval for Copegus in January 2007 and launched it in March as a combination therapy with Pegasys for the treatment of patients with chronic hepatitis C serogroup 1 infection[3] and high viral load, or those who have either not responded to, or have relapsed following, interferon monotherapy.

2. Conventional interferon must be injected three or more times per week.
3. Genotypes I (1a) and II (1b), with which more than 70 percent of HCV patients in Japan are infected

Influenza

Influenza is an acute infectious disease characterized by the rapid onset of high fever (38 degrees centigrade or more) and severe systemic symptoms. It is highly infectious, and epidemics can develop quickly. In some cases, secondary infections can lead to very serious illness. 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.

Overview of Product

Tamiflu

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.

Since March 2007, restrictions on the use of Tamiflu in teenage patients with seasonal influenza have been 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. The report of an epidemiological survey with 10,000 flu patients conducted by a working group of MHLW suggested that there are no findings to date that point to a causal association between Tamiflu and the abnormal behavior of patients taking the drug. MHLW has concluded that it is appropriate to continue to take precautions and other measures, and is thus continuing the restriction on the use of Tamiflu. The shelf life of Tamiflu capsules was extended to 10 years from seven years for capsules manufactured after June 2013, and the shelf life of dry syrup was extended to seven years starting with the portion manufactured in the year ended March 2014.

Angina Pectoris

Hardening of the coronary artery or coronary spasms can cause constriction of the artery and lead to ischemia, a condition in which the heart does not receive sufficient blood flow. Clinical symptoms of angina pectoris include chest pain and pressure that accompany temporary ischemia. Vasodilators, such as nitric acid, that enlarge the coronary artery are used to control attacks. In addition, beta blocker agents are used to treat exertional angina pectoris, a symptom that appears during physical activity such as climbing stairs, and calcium blockers are used for coronary spasm-related angina pectoris.

Acute Heart Failure

Heart failure refers to the general condition that results from insufficient heart activity. When heart failure occurs suddenly in people with no previous history of heart disease, or when heart failure rapidly worsens in patients that had been stable, it is called acute heart failure. Treatments for acute heart failure include diuretics, vasodilators and inotropic drugs.

Overview of Product

Sigmart

Anti-anginal agent Sigmart is a drug that overcomes the flaws of nitrates such as nitroglycerin and is effective in treating various types of angina pectoris. Both oral and injectable forms are approved. Approval of the injectable formulation was obtained for treatment of unstable angina pectoris in 1993 and for acute heart failure in October 2007.

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 interleukin-6 (IL-6), one of the cytokines that causes inflammation. Castleman's disease is very rare, affecting approximately 1,500 people in Japan.

Overview of Product

Actemra

Actemra, an anti-human IL-6 receptor humanized monoclonal antibody produced using genetic recombination technology, is the first therapeutic antibody created in Japan. With a mode of action that inhibits the cytokine IL-6 from binding to its receptors, the drug improves Castleman's disease symptoms. It is estimated that hundreds of patients in Japan are eligible for Actemra treatment because they cannot be treated by surgery due to the presence of multiple enlarged lymph nodes and show resistance to traditional therapies.

Asthma

Asthma is a disease in which airways that have become sensitive due to inflammation narrow when exposed to irritants such as allergens, chemical substances or stress, causing attacks of breathing difficulty. It is accompanied by symptoms such as coughing, mucus production, wheezing and shortness of breath. In Japan, asthma affects approximately 4 million people, and about 10 percent of patients have symptoms that are not adequately controlled with existing treatments.

Overview of Development Project

RG3637 (generic name: lebrikizumab)

In-licensed from Roche, RG3637 is an anti-IL-13 humanized monoclonal antibody under development for the treatment of asthma. It is expected to improve symptoms and prevent attacks in patients with moderate to severe asthma who are unable to adequately control their symptoms with existing treatments. This agent has demonstrated particular efficacy in patients with high serum levels of the periostin protein induced by IL-13. Chugai joined Roche's phase III multinational study in July 2013. In addition, Chugai started a phase II multinational study of RG3637 for the potential indication of idiopathic pulmonary fibrosis in October 2014.

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 method is drug therapy using topical steroid preparations and/or topical immunosuppressants to control the inflammation and a skin care regimen to prevent the inflammation from recurring.

Overview of Development Project

CIM331

CIM331 is an anti-IL-31 receptor humanized monoclonal antibody originating from Chugai that is being developed as a potential treatment for atopic dermatitis. It is expected to suppress itching and improve skin inflammation. Chugai initiated a phase II multinational study in December 2013.

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 is centered on replacement therapy to supplement factor VIII or IX. However, since it involves intravenous injections three times a week, treatment is a significant burden, particularly on children. Moreover, patients must be watched for the development of autoantibodies, called inhibitors, to the supplemented factor. Patients with inhibitors are treated by other 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.

Overview of Development Project

ACE910

ACE910 is an anti-factor IXa/X bispecific antibody that employs Chugai's innovative antibody engineering technologies. Like factor VIII, ACE910 simultaneously binds to factor IXa and factor X, stimulating the activation of factor X by activated factor IX and promoting the blood coagulation that occurs as a result. Unaffected by inhibitors, ACE910 is expected to prevent bleeding with once-weekly (or less-frequent) subcutaneous injections. It was designated as an orphan drug in Europe in December 2013 and in the United States in January 2014. A phase I clinical trial started in Japan in August 2012, and an extension trial (phase I/II clinical trial) of the phase I trial on hemophilia A patients is currently under way. Chugai and Roche are co-developing ACE910 globally under an out-licensing agreement concluded in July 2014.

Gout

Gout occurs when uric acid crystals are deposited in the joints due to prolonged high levels of serum uric acid (hyperuricemia), causing inflammation. The peak age of onset is becoming younger, and has shifted from the 50s to the 30s. Hyperuricemia, the underlying cause of gout, has been increasing annually, and as many as 5 million people are estimated to be at risk for gout in Japan.

Overview of Development Project

URC102

URC102 is a URAT1 inhibitor discovered at C&C Research Laboratories, a joint venture between Chugai and JW Pharmaceutical Corporation of South Korea. It is an oral small-molecule uricosuric agent expected to be effective against gout. This compound is being co-developed with JW Pharmaceutical, and a phase II clinical trial started in South Korea in July 2014.

Glossary

Terms Related to Chugai's Business

Unmet medical need
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.

Development pipeline
At pharmaceutical companies, refers to drug candidates that are being developed as potential new drugs. It is important to have a well-stocked pipeline that has a high success rate and is expected to lead to differentiation from other companies' products.

Clinical trial
A study to verify the safety, efficacy and other characteristics of a drug in human subjects. Studies conducted for new drug development are called clinical trials. Clinical trials consist of phase I to phase III studies, which are conducted before filing for regulatory approval, and phase IV studies, which are conducted after obtaining approval.

Phase I: Performed on a small number of healthy volunteers (or, for certain therapeutic fields 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 confirm 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 efficacy of a new drug and gather information on any side effects or adverse reactions not identified in phase III.

Application for regulatory approval
An application submitted by a pharmaceutical company to a regulatory agency to obtain approval for manufacturing and marketing of a new drug after its efficacy and safety have been verified in clinical trials. In Japan, the Ministry of Health, Labour and Welfare (MHLW) grants manufacturing and marketing approval to substances deemed appropriate as pharmaceuticals based on reviews by the Pharmaceutical Affairs and Medical Devices Agency as well as academic and other experts in the Pharmaceutical Affairs and Food Sanitation Council.

NHI drug price
In Japan, the price paid by the National Health Insurance (NHI) system to hospitals and insurance pharmacies for the drugs they use for insured medical treatments. Drug prices are determined by the MHLW, and are revised based on prevailing market prices once every two years in principle.

All-case registration surveillance
A survey conducted on all patients using a particular drug to verify the efficacy and safety of the drug in actual use and to gather and analyze information on the occurrence of side effects and appropriate use. Required as a condition of approval for certain drugs.

Additional indication
A new indication added to the indication(s) already approved for a drug.

Lifecycle management
The various measures taken to maximize the potential value of a drug, including shortening development time, expanding sales, extending the product's life, and conducting appropriate cost control. Competitiveness can be strengthened further by using earnings from sales of established drugs to strategically reinvest in new drug development, marketing or other areas.

Drug lag
The time difference between the approval of drugs overseas and their approval in Japan. Progress has been made in eliminating the drug lag in recent years as the Japanese government and the pharmaceutical industry have taken various measures to make drugs available to patients in Japan as early as possible.

Consulting-based promotion
Chugai's approach to promoting the appropriate use of its products. Medical representatives (MRs) provide evidence-based information and proposals for treatment and side-effect management in line with the doctor's treatment plan and the patient's condition.

Multidisciplinary team care
A collaborative approach in which a team of healthcare professionals is formed according to the patient's medical condition. As medicine has become more specialized with advances in medical technology, this approach brings together doctors with different medical specialties as well as pharmacists, nurses, therapists, nutritionists, medical social workers and other professionals to provide patient-centered care as one team.

Terms Related to Drug Discovery

Molecular targeted therapy
A drug developed to treat illnesses more safely and effectively by targeting specific molecules in the body and suppressing their activity. Since these drugs target only specific molecules, they do less damage to normal cells, and are therefore expected to ease the burden on patients in comparison with conventional therapies.

Biopharmaceuticals
Drugs created by applying biotechnology such as genetic recombination and cell fusion. Chugai built its expertise in biopharmaceuticals through research and development of Epogin and Neutrogin.

Antibody
A molecule that selectively binds to a specific antigen (target) on a foreign substance and helps to remove the foreign substance from the body. When a foreign substance enters the body, it stimulates the production of antibodies that selectively bind to the antigen on the foreign substance and act to remove the substance.

Therapeutic antibody
A drug that is used to prevent or treat illness by creating an antibody against the substance that causes the illness. Therapeutic antibodies precisely target only specific antigens on the surface of cancer cells or other cells, and therefore can be expected to provide high therapeutic efficacy and reduce side effects.

Open innovation
Generating innovative, new value by utilizing the technologies and development capabilities of external research networks such as with universities, research institutions and other organizations, in addition to in-house capabilities.

Terms Related to the Roche Group

Roche
A pharmaceutical company established in 1896 and headquartered in Basel, Switzerland. With business operations in more than 150 countries, the Roche Group contributes to medicine in a wide range of fields through its two business segments: pharmaceuticals and diagnostics. Central to the Roche Group's strategy is Personalized Healthcare, the approach of selecting the most appropriate treatment by using biomarkers and diagnostic tests to identify patients most likely to show a significant response to a particular drug. The Roche Group's sales in 2014 were 47.5 billion Swiss francs.

Roche Diagnostics K.K.
The Japanese subsidiary of the Roche Group's diagnostics and equipment division. Established in 1998, Roche Diagnostics K.K. provides a wide range of innovative diagnostic solutions, from in-vitro diagnostics and diagnostic equipment and research reagents and related equipment to blood glucose meters for people with diabetes.

Genentech
A leading biotechnology company headquartered in South San Francisco, California. Genentech has been a member of the Roche Group since 1990.

Terms Related to Human Resources

Work-life balance/Work-life synergy
Work-life balance is the concept of creating harmony between work and personal life (family, hobbies, recreation and community activities) and achieving satisfaction in both realms.

The aim of work-life synergy is to generate synergy between each employee's job and lifestyle while improving the quality of both, as well as raising Chugai's productivity as an organization to become a top pharmaceutical company.

Diversity
At Chugai, diversity refers to a diversity of traits such as gender, age and nationality as well as ways of thinking and values. When people with various backgrounds work together, they become aware of diverse perspectives and ideas. Using this awareness for business innovation, companies promote diversity to create better-quality products and services. Also called "diversity and inclusion," this term refers to receptivity to diversity and incorporating diverse opinions and ideas rather than the simple pursuit of variety, and also encompasses the concept of raising organizational value.

Talent management
A human resource strategy to support the development of the next generation of leaders and core human resources and to improve the skills and enhance the motivation of employees throughout the Company, with the aim of realizing our goal of becoming a top pharmaceutical company. Each organization at Chugai has formulated a long-term human resource development plan and is building a talent pool of next-generation leader candidates.

Financial Section

Message from the CFO 116
11-Year Financial Summary 118
Management's Discussion and Analysis..... 120
Consolidated Financial Statements..... 128
Independent Auditor's Report 173

Network..... 174
Organization..... 176
Shareholder Information 177
Corporate Data..... 178

Message from the CFO

Chugai continues to transform its financial and capital strategies. We will evolve into an even stronger company by pursuing constant innovation with a focus on speed.

In its current mid-term business plan, ACCEL 15, Chugai is aiming to become a top pharmaceutical company by evolving and linking its unique strengths, and accelerating innovation. By further strengthening our management infrastructure, one of the four strategic policies of ACCEL 15, we have made progress in transforming our financial and capital strategies, including our earnings structure, cash management and shareholder returns, and will continue to evolve.

Evolution of Our Earnings Structure

Chugai today is highly profitable, with an operating profit margin in the top tier among Japanese pharmaceutical companies. Although our cost of sales to sales ratio has risen with the expansion of in-licensed products since entering the alliance with Roche, we have reduced the operating expense ratio, including marketing and distribution expenses and R&D expenditures, through a number of measures. In ACCEL 15, we have transformed our cost structure through an overhaul of IT systems and a global purchasing strategy, in addition to improving efficiency across our operations. Due to these initiatives, along with Company-wide efforts to promote the Productivity Improvement Project launched in 2013, we have established an earnings structure in which our operating expense ratio has decreased steadily to 37.2 percent and 36.2 percent for 2013 and 2014, respectively. This is an improvement of about 17 percentage points since the year ended March 2003, before the alliance with Roche, and comparable with the top global pharmaceutical companies.

The goal of the Productivity Improvement Project is to connect productivity gains with diversity and work-life synergy from a medium-to-long-term perspective in order to become a top pharmaceutical company. The basic concept is to continuously increase the efficiency of resource input while raising both the quality and quantity of output by using our strengths to pursue innovation and speed.

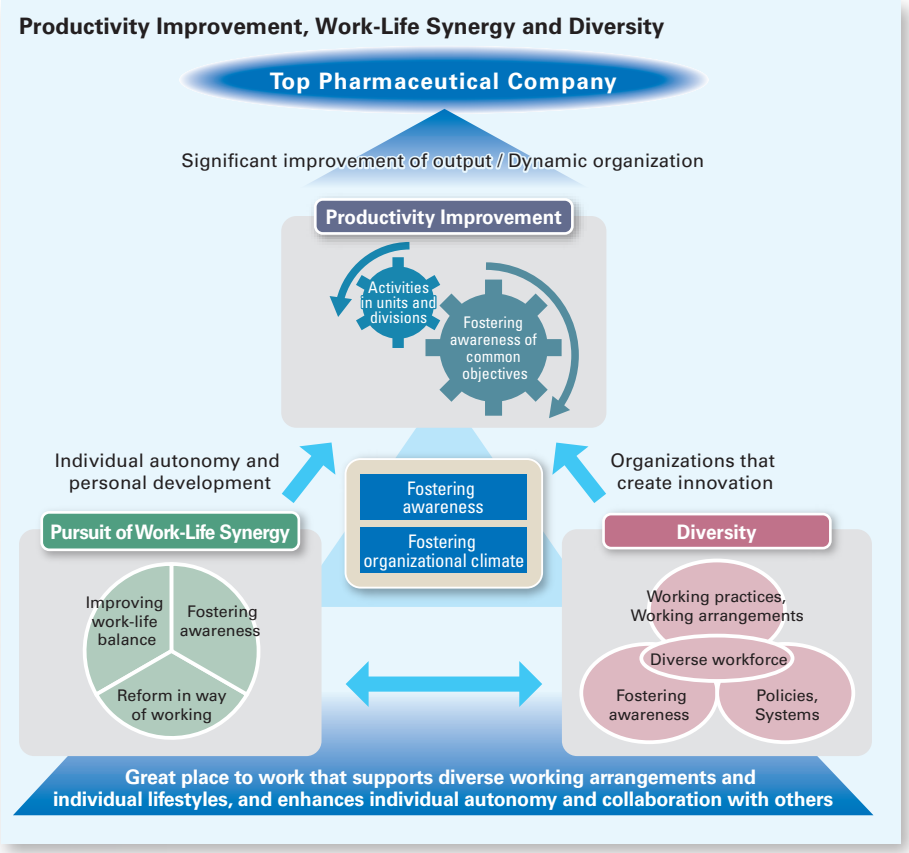
At the outset of the Productivity Improvement Project, we made a surprise discovery: Upon re-examining conditions in each department, we found that since implementing our Business Process Reengineering (BPR) initiatives and other activities from 2006 through 2010, many departments had continued to identify new issues on their own and proactively carried out productivity improvement measures. At that moment I was convinced that Chugai would become even stronger, because it was evident that the steps we had been taking to improve our earnings structure had become deeply embedded throughout the Company. In the Productivity Improvement Project, we use the Company intranet to share and visualize the efforts of each unit and division, and incorporated their respective productivity improvement measures into the yearly assignments of individual employees. This is raising the effectiveness of unit and division activities. We regularly conduct surveys to gauge the level of employees' awareness and activities, and both have steadily improved. In March 2015, Chugai was selected as a "Nadeshiko Brand"* in acknowledgement of its promotion of diversity, work-life synergy and measures to raise productivity, among other factors. I view this as evidence that our activities in these areas have begun to have an effect. I would like these measures to take root as a natural and enduring part of our corporate culture.

Strengthening Cash Flow Management

Strategic investment and cash management are key issues for Chugai's medium-to-long-term growth. We have ample net cash flow that amounts to roughly half of annual revenues, and in view of current growth potential, we will generate net cash of more than ¥20 billion each year on average. To manage this cash flow effectively, we will make proactive investments under ACCEL 15 to explore future business opportunities while maintaining appropriate returns to shareholders.

Our investment targets include in-licensing opportunities, plant and equipment, expansion of therapeutic fields and markets, incorporation of external research results and business development in regenerative medicine and other areas peripheral to our existing businesses. In addition, we need to prepare for the steady creation of therapeutic antibody candidates from our Singapore subsidiary (CPR), which is utilizing our proprietary innovative technologies. Therefore, our capital investment plans include investments in manufacturing improvements to enable simultaneous development of multiple antibodies and high-mix, low-volume production that will enable quick launches. To explore business opportunities, we will consider making diverse investments in scientifically and technologically promising projects and enhance our evaluation system with an emphasis on greater speed and quality.

For shareholder returns, our basic policy in ACCEL 15 is to raise the level of shareholder returns while maintaining stable dividends, with a Core earnings per share (EPS) basis payout ratio of 50 percent on average. We increased cash dividends per share by ¥3 to ¥48 in 2014, and plan to pay cash dividends of ¥52 per share for 2015 (a five-year average Core EPS payout ratio of 50.3 percent). We remain committed to delivering stable and substantial returns to shareholders in line with expansion of profits.



Further Value Creation

In addition to the changes I described in our financial and capital strategies, we are working to create value by promoting further evolution in our communications with investors. In 2013, we adopted an integrated reporting format for our annual report, and began applying International Financial Reporting Standards (IFRS). We are also disclosing Core basis results aligned with internal management performance indicators. These changes are aimed at improving convenience for investors and facilitating accurate analysis of Chugai's performance. Our emphasis is on using Core basis results as common indicators both internally and externally to provide a shared framework for dialogue with investors. We will continue to carry out IR activities from a medium-to-long-term perspective together with our investors.

Chugai will pursue even greater speed as it continues to innovate. On December 1, 2014, we unveiled a new slogan, "INNOVATION BEYOND IMAGINATION," and are promoting corporate branding activities based on our business philosophy, "Innovation all for the patients." I am confident that with constant innovation, Chugai will evolve into an even stronger company that can create its own future. I look forward to the continued guidance and support of our investors as we move forward.

* A joint program of the Ministry of Economy, Trade and Industry and the Tokyo Stock Exchange to select and publicly acknowledge listed companies that are exceptional in promoting the success of women in the workplace as "Nadeshiko Brand" companies.

Yoshio Itaya
Director, Executive Vice President & CFO

11-Year Financial Summary

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

(Billions of yen)

International Financial Reporting Standards (IFRS)	2014		2013		2012	
	IFRS	Core[1]	IFRS	Core[1]	IFRS	Core[1]
Results						
Revenues[2]	461.1		423.7		386.6	
Sales	436.9		401.3		375.2	
Royalties and other operating income	24.2		22.4		11.3	
Cost of sales	(218.1)	(217.0)	(187.0)	(186.1)	(168.2)	(167.3)
Operating expenses	(167.2)	(166.8)	(157.9)	(157.7)	(143.7)	(143.7)
Marketing and distribution	(71.7)	(71.7)	(71.6)	(71.5)	(67.9)	(67.9)
Research and development	(80.8)	(80.6)	(74.3)	(74.1)	(66.6)	(66.6)
General and administration	(14.6)	(14.6)	(12.1)	(12.1)	(9.2)	(9.2)
Operating profit	75.9	77.3	78.7	79.9	74.7	75.6
Profit before taxes	76.2	77.6	76.9	78.1	72.7	73.6
Net income	52.1	53.0	51.9	52.6	46.8	47.4
Attributable to Chugai shareholders	51.0	51.9	50.9	51.6	46.1	46.6
Core EPS (Yen)	—	95.04	—	94.69	—	85.64
Cash dividends per share (Yen)	48		45		40	
Core payout ratio	—	50.5%	—	47.5%	—	46.7%
Financial Position						
Net operating assets	357.7		325.2		307.9	
Total assets	739.5		697.2		645.3	
Total liabilities	(141.8)		(124.0)		(116.2)	
Total net assets	597.8		573.2		529.2	
Investment on property, plant and equipment	16.3		13.0		14.2	
Depreciation	13.7		13.5		13.3	
Main Indicators						
Cost of sales to sales	49.9%	49.7%	46.6%	46.4%	44.8%	44.6%
Operating profit to revenues	16.5%	16.8%	18.6%	18.9%	19.3%	19.6%
Research and development expenditures to revenues	17.5%	17.5%	17.5%	17.5%	17.2%	17.2%
Ratio of net income to equity attributable to Chugai shareholders (ROE)[3]	8.7%	—	9.3%	—	9.0%	—
Ratio of profit before taxes to total assets (ROA)[4]	10.6%	—	11.5%	—	11.8%	—
Equity per share attributable to Chugai shareholders (BPS) (Yen)	1,092.90	—	1,049.47	—	970.08	—
Ratio of equity attributable to Chugai shareholders	80.6%	—	82.0%	—	81.8%	—
Number of employees	7,023		6,872		6,836	

1. Core basis results are the results after adjusting non-Core items to IFRS basis results. Core basis results are used by Chugai as an internal performance indicator, 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. 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)
4. Ratio of profit before taxes to total assets (ROA) = Profit before taxes/Total assets (average of beginning and end of fiscal year)

(Billions of yen)

Japanese GAAP	2012	2011	2010	2009	2008	2007	2006	2005	2004
Results									
Revenues[1]	391.2	373.5	379.5	428.9	326.9	344.8	326.1	327.2	294.7
Sales	375.2	363.6	375.6	419.1	321.8	332.9	—	—	—
Other operating revenues	16.0	9.9	3.9	9.8	5.1	11.9	—	—	—
Cost of sales	167.7	157.5	162.4	192.9	127.0	137.3	133.1	119.4	115.4
Selling, general and administrative expenses	147.1	153.6	150.9	153.5	148.3	140.8	134.7	128.6	132.1
Marketing and distribution expenses	92.0	97.7	96.2	98.2	95.1	86.6	80.1	78.5	83.9
Research and development expenditures	55.1	55.9	54.7	55.3	53.2	54.2	54.6	50.1	48.2
Operating income	76.4	62.4	66.2	82.6	51.6	66.7	58.3	79.2	51.5
Net income (loss)	48.2	35.2	41.4	56.6	39.3	40.1	38.4	53.6	34.1
Net income per share (basic) (Yen)	88.58	64.75	76.14	104.00	72.07	73.23	69.35	97.00	62.27
Net income per share (diluted) (Yen)	88.54	64.72	76.12	103.98	72.04	73.16	69.26	96.33	61.34
Cash dividends per share (Yen)[2]	40	40	40	40	34	30	30	34	18
Payout ratio	45.2%	61.8%	52.5%	38.5%	47.2%	41.0%	43.3%	35.1%	28.9%
Financial Position									
Total assets	587.7	533.5	508.0	540.5	478.5	458.9	462.1	456.4	411.4
Total net assets[3]	490.1	459.1	449.4	434.7	397.1	385.8	391.6	368.3	320.8
Capital investments	14.2	11.9	12.7	14.6	26.6	19.6	16.3	16.1	9.9
Depreciation and amortization	15.3	15.9	18.0	19.5	20.1	14.9	13.8	17.0	14.4
Main Indicators									
Cost of sales to revenues	42.9%	42.2%	42.8%	45.0%	38.8%	39.8%	40.8%	36.5%	39.2%
Operating income to revenues	19.5%	16.7%	17.4%	19.3%	15.8%	19.3%	17.9%	24.2%	17.5%
Research and development expenditures to revenues	14.1%	15.0%	14.4%	12.9%	16.3%	15.7%	16.7%	15.3%	16.4%
Return on equity[4]	10.2%	7.8%	9.4%	13.7%	10.1%	10.4%	10.1%	15.6%	11.0%
Return on assets[5]	8.6%	6.8%	7.9%	11.1%	8.4%	17.4%	8.4%	12.4%	8.4%
Net assets per share (Yen)	896.02	839.50	821.87	794.51	725.18	703.80	703.08	665.29	583.61
Shareholders' equity to total assets	83.0%	85.6%	88.0%	80.0%	82.6%	83.5%	84.3%	80.7%	78.0%
Number of employees	6,836	6,779	6,709	6,485	6,383	6,257	5,905	5,280	5,313

1. Revenues do not include consumption tax.
2. Cash dividends per share for 2009 include a special year-end dividend of ¥6 per share. Cash dividends per share for 2005 include a special year-end dividend of ¥10 per share.
3. Net assets include minority interests from 2006 in accordance with a revision to regulations for consolidated financial statements in Japan.
4. Return on equity = Net income/Shareholders' equity (average of beginning and end of fiscal year)
5. Return on assets = Net income/Total assets (average of beginning and end of fiscal year)

Management's Discussion and Analysis

Operating Environment

The pharmaceutical industry continued to face numerous issues and intense competition in 2014. In addition to an emphasis on cost-containment measures in healthcare and health technology assessment (HTA)[1] stemming from the worsening of government finances in various countries, other factors included declining R&D productivity, stricter regulations on safety and quality, and changes in marketing activities. On the other hand, continued expansion is forecast in pharmaceutical markets that address unmet medical need, with expectations for ongoing growth of biopharmaceuticals and oncology drugs.

1. A multidisciplinary process of transparently summarizing information on the clinical efficacy, cost effectiveness, social impact and other issues related to new health technologies. HTA provides information to assist in the formulation of safe and effective healthcare policies centered on patients.

Management Policies

Based on its strategic alliance with Roche, a leading global pharmaceutical company, Chugai's mission is to dedicate itself to adding exceptional value through the creation of innovative medical products and services for the benefit of the medical community and human health around the world. Our primary management goal is to become a top pharmaceutical company capable of continuously delivering innovative drugs in Japan and internationally. We have been working to fulfill this mission and achieve our goal by building systems capable of efficiently and continuously developing and marketing new drugs, leveraging our close relationship with Roche to cooperate in areas such as in-licensing products from Roche's rich development pipeline, advancing Personalized Healthcare (PHC) and promoting global development and sales. We have also been working to refine our own strengths, and have achieved leading-edge drug discovery technology, represented by our next-generation antibody technologies, and captured the top share of the domestic oncology field by practicing consulting-based promotion.

ACCEL 15, our mid-term business plan for the years 2013 to 2015, positions this period as a turning point for accelerating our progress toward becoming a top pharmaceutical company. To further augment the competitive advantages we have established and to promote sustained growth in corporate value, we implement four strategic policies: increase of marketing productivity; acceleration of global development; continuous generation of innovative projects; and further strengthening of management infrastructure. As quantitative guidance, Chugai will aim for a Core EPS[2] compound annual growth rate in the mid to high single digits based on constant exchange rates (average for 2012), and will work to deliver shareholder returns with a target Core EPS payout ratio of 50 percent on average.

Chugai will unceasingly pursue innovation based on its business philosophy of "Innovation all for the patients" and its slogan "INNOVATION BEYOND IMAGINATION."

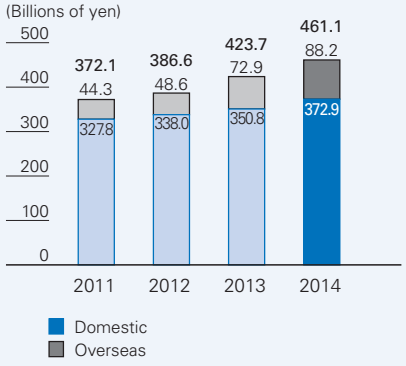
2. Fully diluted net income per share attributable to shareholders of Chugai after deducting items that Chugai defines as non-Core items

Overview of Results

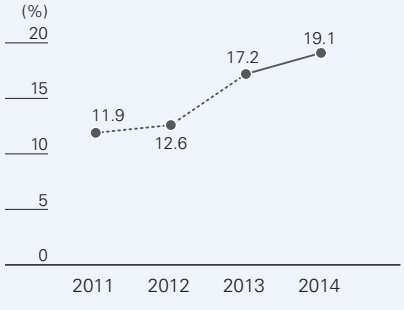
Chugai reports its results on a Core basis from 2013 in conjunction with its decision to apply IFRS. Core basis results are IFRS basis results adjusted to exclude non-Core items, and are consistent with the Core basis results disclosed by Roche. Chugai uses Core basis results as an internal performance indicator for explaining the status of recurring profit trends both internally and externally, and as indices for establishing profit distributions such as returns to shareholders.

Core basis results for 2014 were revenues of ¥461.1 billion, an 8.8 percent increase from the previous year, operating profit of ¥77.3 billion, a 3.3 percent decrease, and net income of ¥53.0 billion, a 0.8 percent increase, driven mainly by solid growth in

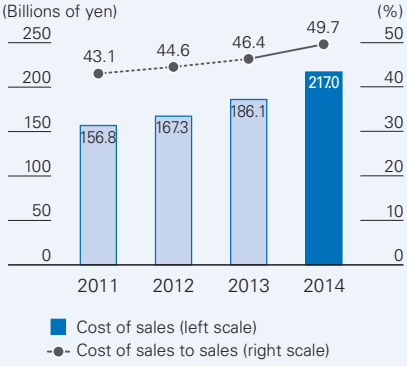
Revenues



Overseas Sales Ratio



Cost of Sales/ Cost of Sales to Sales



sales of major products and steady uptake of new products. IFRS basis results, before adjustment to Core basis results, were operating profit of ¥75.9 billion, a 3.6 percent decrease, and net income of ¥52.1 billion, a 0.4 percent increase. These results include amortization of intangible assets of ¥1.2 billion, impairment of intangible assets of ¥0.2 billion, restructuring costs of ¥0.1 billion and other items excluded from the Core basis results managed by Chugai.

Revenues

In 2014, revenues increased 8.8 percent compared with the previous year to ¥461.1 billion, with growth in sales, royalties and other operating revenues. Excluding sales of Tamiflu, which are seasonal, sales increased 8.6 percent to ¥423.8 billion.

Domestic Sales by Field

Domestic sales excluding Tamiflu increased 6.2 percent compared with the previous year to ¥349.5 billion. Sales in the oncology field continued to grow, rising 9.6 percent to ¥188.9 billion as Chugai maintained its number-one share (22.0 percent)[3] in the domestic oncology market. The increase was due to the steady expansion in sales of major anticancer agents such as Avastin, an anti-vascular endothelial growth factor (VEGF) humanized monoclonal antibody, and Tarceva, an epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor, in addition to contributions from two new products for the indication of HER2-positive breast cancer: Perjeta, an HER2 dimerization inhibitory humanized monoclonal antibody launched in September 2013, and Kadcyla, an anti-HER2 antibody-tubulin polymerization inhibitor conjugate launched in April 2014. Sales of Alecensa, an ALK inhibitor anticancer agent launched in September 2014, were ¥1.4 billion.

In the bone and joint diseases field, sales increased a substantial 14.9 percent compared with the previous year to ¥69.6 billion. The increase was driven by strong sales of Edirol, an active vitamin D_3 derivative that has become a top brand in the domestic market for oral therapeutic agents for osteoporosis, with contributions from Actemra, which was launched in a subcutaneous injection formulation in May 2013 and for which the restriction to two-week prescriptions was lifted in June 2014, and Bonviva (ibandronate sodium hydrate), an osteoporosis treatment launched in August 2013.

Sales in the renal diseases field decreased 8.6 percent compared with the previous year to ¥44.7 billion due to a substantial decline in sales of Epogin, a recombinant human erythropoietin agent, resulting from the effects of the NHI drug price revisions, among other factors.

In the transplant, immunology and infectious diseases field, sales excluding Tamiflu increased 10.6 percent compared with the previous year to ¥20.8 billion due to higher sales of peginterferon alfa-2a agent Pegasys and anti-viral agent Copegus, which are concurrently used in combination with a newly launched third-party product.

Sales of anti-influenza agent Tamiflu increased 18.2 percent to ¥13.0 billion. Seasonal sales were ¥12.9 billion and sales to the government for pandemic stockpiles totaled ¥0.2 billion.

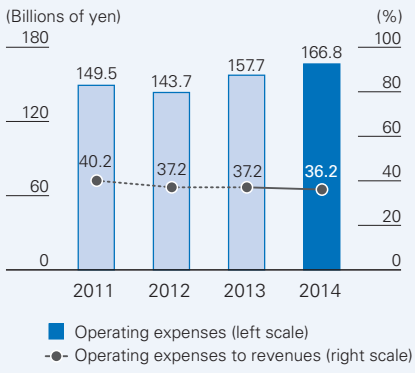
3. Copyright 2015 IMS Health Source: JPM 2014. Reprinted with permission. The scope of the market is defined by Chugai.

Overseas Product Sales, Royalties and Other Operating Revenues

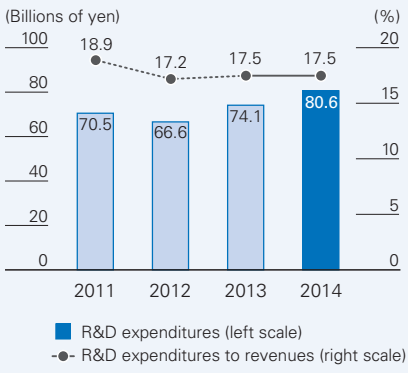
Overseas sales increased a substantial 21.6 percent compared with the previous year to ¥74.3 billion. Sales growth was driven by increased exports of Actemra to Roche on a volume basis in addition to the impact of the weaker yen.

Royalties and other operating revenues increased 8.0 percent to ¥24.2 billion, reflecting an increase in milestone revenues and an increase in revenues from the Roche Group for co-promotion and royalties in connection with the overseas sales growth of Actemra, an anti-IL-6 humanized monoclonal antibody.

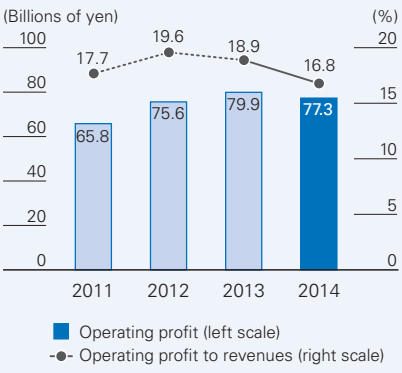
Operating Expenses/ Operating Expenses to Revenues



R&D Expenditures/ R&D Expenditures to Revenues



Operating Profit/ Operating Profit to Revenues



Cost of Sales and Gross Profit (Core Basis)

Cost of sales increased 16.6 percent to ¥217.0 billion compared with the previous year due to factors including the impact of the substantial depreciation of the yen. The cost of sales to sales ratio increased 3.3 percentage points to 49.7 percent.

As a result of the above, gross profit increased 2.8 percent compared with the previous year to ¥244.2 billion.

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

Operating expenses increased 5.8 percent to ¥166.8 billion. A breakdown of these expenses follows below.

Marketing and distribution expenses increased 0.3 percent to ¥71.7 billion, basically the same level as the previous year, mainly due to an increase in promotional activities associated with the launch of new products, as in 2013. R&D expenditures increased 8.8 percent to ¥80.6 billion due to the impact of the weaker yen, the progress of development projects originating from Chugai and increased activities at Chugai Pharmabody Research Pte. Ltd. (CPR). General and administrative expenses increased 20.7 percent to ¥14.6 billion due to increased expenditures for purposes including the renewal of buildings and PR activities to enhance corporate brand recognition.

As a result of the above, operating profit decreased 3.3 percent compared with the previous year to ¥77.3 billion, and the ratio of operating profit to revenues decreased 2.1 percentage points to 16.8 percent.

Net Income (Core Basis)

Other financial income was ¥0.3 billion, a substantial improvement from other financial expense of ¥1 8 billion in the previous year, and income taxes decreased 3.5 percent to ¥24.6 billion due to a reduction in the tax rate resulting from changes to the taxation system. As a result, net income increased 0.8 percent to ¥53.0 billion. Net income attributable to Chugai shareholders was ¥51.9 billion, an increase of 0.6 percent.

Profitability Indicators (Consolidated)

	2014	2013	2012
Gross profit to revenues (%) (Core)	53.0	56.1	56.7
Operating profit to revenues (%) (Core)	16.8	18.9	19.6
Ratio of profit before taxes to total assets (ROA) (%) (IFRS)	10.6	11.5	11.8
Ratio of net income attributable to Chugai shareholders (ROE) (%) (IFRS)	8.7	9.3	9.0

Notes:
1. ROA = Profit before taxes/Total assets (average of beginning and end of fiscal year)
2. ROE = Net income attributable to Chugai shareholders/Capital and reserves attributable to Chugai shareholders (average of beginning and end of fiscal year)

Financial Position

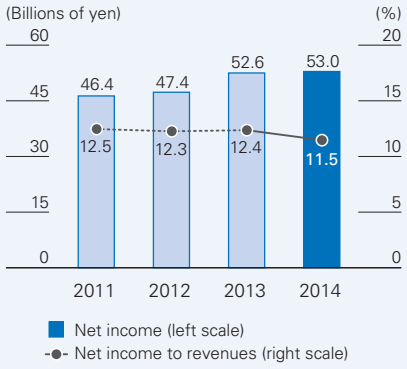
Assets, Liabilities and Net Assets

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 sheets, as the Core basis results concept only applies to the income statement

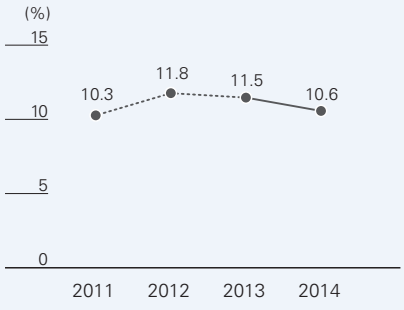
Net Operating Assets

Net working capital, which is composed of accounts receivable, inventories, accounts payable and other payables and receivables, was ¥209.4 billion as of December 31, 2014, an increase of ¥32.3 billion, or 18.2 percent, from a year earlier. Accounts receivable increased ¥30.2 billion from a year earlier, mainly due to differences in the timing of collection caused by accelerated payments in the previous year Inventories increased ¥11.1 billion from a year earlier due to expanded sales of major products, initial laying-in of new products and an increase in safety stock to ensure stable supply.

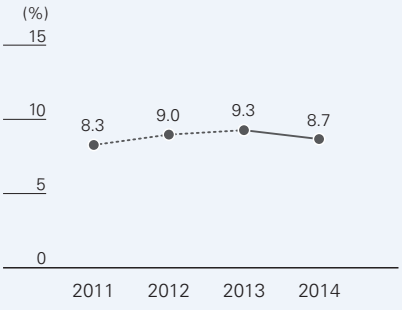
Net Income/Net Income to Revenues



ROA



ROE



Long-term net operating assets, consisting of property, plant and equipment, intangible assets and other items, were basically unchanged from the end of the previous year at ¥148.4 billion, an increase of ¥0.3 billion, or 0.2 percent. Intangible assets increased ¥1.8 billion due to product in-licensing lump-sum payments, while property, plant and equipment decreased ¥0.2 billion as a result of depreciation and amortization. Other long-term net operating assets decreased ¥1.4 billion due to deferral of income related to product out-licensing.

As a result, net operating assets – the total of net working capital and long-term net operating assets – increased ¥32.5 billion, or 10.0 percent, from a year earlier to ¥357.7 billion.

Total Net Assets

Net cash, including marketable securities and interest-bearing debt, decreased ¥4.5 billion, or 1.9 percent, to ¥229.9 billion.

"Other non-operating assets – net" decreased ¥3.4 billion, or 25.0 percent, from a year earlier to ¥10.2 billion, mainly due to a decrease in foreign exchange forward contracts and an increase in current income tax liabilities, which offset an increase in deferred tax assets.

As a result, total net assets, which is the total of net operating assets, net cash and "other non-operating assets – net," increased ¥24.6 billion, or 4.3 percent, to ¥597.8 billion.

The ratio of equity attributable to Chugai shareholders was 80.6 percent, a decrease of 1.4 percentage points from a year earlier.

Total Assets and Total Liabilities

Total assets on the consolidated balance sheet increased ¥42.3 billion, or 6.1 percent, from the end of the previous year to ¥739.5 billion, while total liabilities increased ¥17.8 billion, or 14 4 percent, to ¥141 8 billion.

Current assets minus current liabilities totaled ¥424.6 billion, and the current ratio was 471.3 percent, as Chugai maintained a highly sound financial position.

Financial Position (Billions of yen)

	2014	2013	2012
Movements of assets and liabilities			
Net working capital	209.4	177.1	157.9
Long-term net operating assets	148.4	148.1	150.0
Net operating assets	357.7	325.2	307.9
Net cash	229.9	234.4	211.7
Other non-operating assets – net	10.2	13.6	9.6
Total net assets	597.8	573.2	529.2
Consolidated Balance Sheet			
Total assets	739.5	697.2	645.3
Total liabilities	(141.8)	(124.0)	(116.2)
Total net assets	597.8	573.2	529.2

Financial Position Indicators

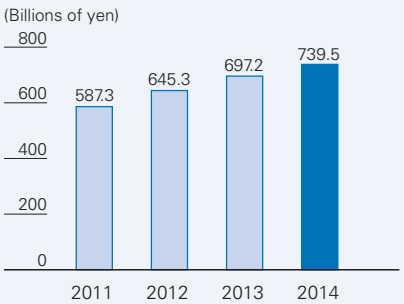
	2014	2013	2012
Ratio of equity attributable to Chugai shareholders (%)	80.6	82.0	81.8
Core return on net operating assets (%)	14.8	16.2	15.4
Cash conversion cycle (months)	9.6	9.3	8.5
Net cash turnover period (months)	6.0	6.6	6.6
Current ratio (%)	471.3	516.3	480.5
Debt-to-equity ratio (%)	0.0	0.0	0.0

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

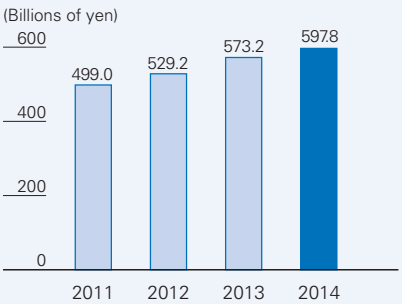
Cash Flows

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 an internal performance indicator (Roche discloses the same indicator). No items are excluded from cash flows, as the Core basis results concept only applies to the income statement.

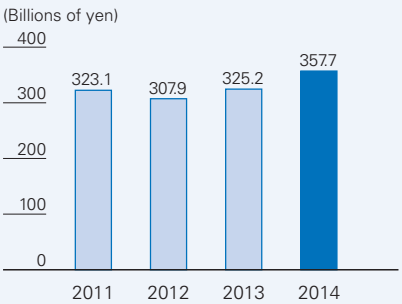
Total Assets



Total Net Assets



Net Operating Assets



Operating Free Cash Flows

Operating profit, net of operating cash adjustments (calculated by adjusting operating profit for depreciation and all other non-cash items included in operating profit and all cash inflows and outflows related to net operating assets that are not accompanied by profit and loss), amounted to a net cash inflow of ¥96.4 billion, compared with ¥97.3 billion for the previous year. The main adjustments were depreciation and impairment of property, plant and equipment totaling ¥15.5 billion.

Operating free cash flows, which are calculated by deducting the increase in net working capital of ¥33.3 billion and expenditures of ¥19.2 billion for the purchase of property, plant and equipment and intangible assets from operating profit, net of operating cash adjustments, amounted to ¥43.9 billion (compared with ¥63.0 billion for the previous year). Purchases of property, plant and equipment mainly consisted of purchases of research and plant equipment.

Cash Flows

(Billions of yen)

	2014	2013	2012
Movements of free cash flows			
Operating profit	75.9	78.7	74.7
Operating profit, net of operating cash adjustment	96.4	97.3	88.2
Operating free cash flow	43.9	63.0	91.0
Free cash flow	(6.5)	15.0	39.3
Net increase in net cash	(4.5)	22.7	42.2
Consolidated Statement of Cash Flows			
Cash flows from operating activities	37.0	53.5	77.5
Cash flows from investing activities	(14.4)	(13.2)	(54.9)
Cash flows from financing activities	(24.4)	(23.2)	(22.8)
Net increase in cash and cash equivalents	(1.0)	19.6	1.0
Cash and cash equivalents at end of year	114.0	115.1	95.4

Free Cash Flows (FCF)

Free cash flows, calculated by deducting the total of ¥50.4 billion comprising cash flows from financial asset management, income taxes paid and cash dividends paid from operating free cash flow, amounted to a net cash outflow of ¥6.5 billion, compared with an inflow of ¥15.0 billion for the previous year.

The result was a net decrease of ¥4.5 billion in net cash after foreign currency translation adjustments, and a decrease of ¥1.0 billion in cash and cash equivalents, excluding changes in marketable securities and interest-bearing debt, compared with a year earlier. The balance of cash and cash equivalents at the end of the year was ¥114.0 billion.

Cash Flows

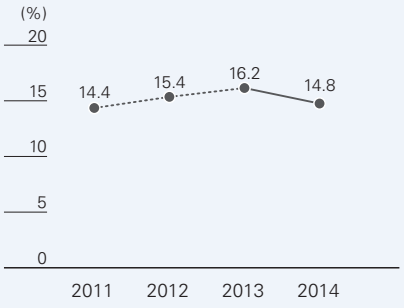
Cash flows in the consolidated statements of cash flows were net cash provided by operating activities of ¥37.0 billion, net cash used in investing activities of ¥14.4 billion and net cash used in financing activities of ¥24.4 billion.

Capital Investments

Capital investments increased 25.4 percent compared with the previous year to ¥16.3 billion. Significant capital investments included routine expenditures for research and plant equipment. Depreciation and amortization increased 1.2 percent to ¥13.7 billion.

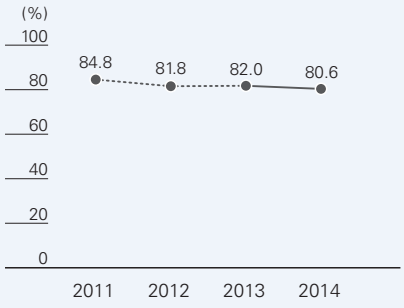
In 2015, Chugai is planning capital investments of ¥18.5 billion, including improvement of an investigational drug building for biologics at the Ukima site and improvement of a manufacturing building for biological drug substances and enhancement of high-mix, low-volume production capability for pre-filled syringe form products at the Utsunomiya site. Depreciation is projected to be ¥14.0 billion.

Core Return on Net Operating Assets (Core RONOA)*

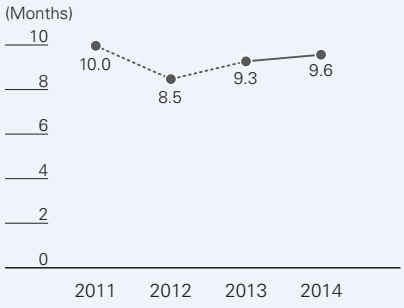


* Core RONOA = Core net income/ Net operating assets

Ratio of Equity Attributable to Chugai Shareholders



Cash Conversion Cycle*



* Cash conversion cycle = [Trade accounts receivable/ Sales + (Inventories – Trade accounts payable)/ Cost of sales] x Months passed

Plans for New Construction and Renovation of Facilities

(Chugai Pharmaceutical Co., Ltd.)

Site name (Location)	Description	Planned investment (Billions of yen) Total amount	Planned investment (Billions of yen) Investment to date	Funding method	Start of construction	Planned completion
Ukima site (Kita-ku, Tokyo)	Renovation of investigational drug building No. 2 for biologics (Doubling of manufacturing capacity for investigational biologics to enable simultaneous development of multiple drugs)	2.9	2.8	Self-financing	June 2013	August 2015
Utsunomiya site (Utsunomiya City, Tochigi Prefecture)	Installment of tray filler (Enhancement of high-mix, low-volume production capability for pre-filled syringe form products)	4.8	0.9	Self-financing	September 2013	March 2017

(Domestic subsidiary: Chugai Pharma Manufacturing Co., Ltd.)

(Billions of yen)

Site name (Location)	Description	Planned investment (Billions of yen) Total amount	Planned investment (Billions of yen) Investment to date	Funding method	Start of construction	Planned completion
Utsunomiya plant (Utsunomiya City, Tochigi Prefecture)	Renovation of manufacturing building No. 1 for biological APIs (UT1) (Improving production yield for Actemra subcutaneous formulation and stabilizing supply by having two manufacturing sites)	4.6	2.2	Self-financing	July 2013	September 2015

Per Share Data

Net income per share (basic) for 2014 increased ¥0.06 compared with the previous year to ¥93.53, and Core EPS was ¥95.04. Equity per share attributable to Chugai shareholders (BPS) as of December 31, 2014 increased ¥43.43 compared with a year earlier to ¥1,092.90.

Per Share Data (Consolidated)

(Yen)

	2014	2013	2012
Net income per share (basic)	93.53	93.47	84.62
Core EPS	95.04	94.69	85.64
Equity per share attributable to Chugai shareholders (BPS)	1,092.90	1,049.47	970.08
Dividends per share	48	45	40
Core payout ratio (%)	50.5	47.5	46.7

Note: Core EPS = Core net income attributable to Chugai shareholders/Diluted weighted average shares outstanding

Outlook for 2015

Forecast Assumptions

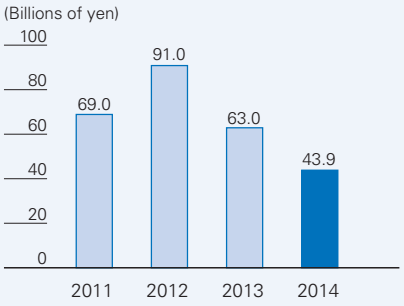
For 2015, Chugai assumes exchange rates of ¥116/CHF, ¥142/EUR, ¥119/USD and ¥91/SGD, and that the scale of seasonal influenza will be about the same as the average since 2007, excluding the influenza pandemic in the 2009/2010 season.

Results Forecast

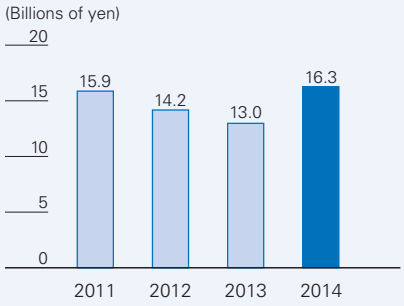
Chugai forecasts revenues of ¥486.5 billion, an increase of 5.5 percent compared with 2014.

Domestic sales excluding Tamiflu are forecast to rise steadily to ¥360.9 billion, an increase of 3.3 percent year on year. Chugai expects continued growth in sales of Avastin, Tarceva and other drugs in the oncology field as well as Edirol, Actemra and Mircera. New products Kadcyla, Alecensa, Perjeta and Bonviva are

Operating Free Cash Flows



Capital Investments on Property, Plant and Equipment



Core EPS

also expected to contribute to sales growth. Chugai plans to launch a number of new products in 2015, and has factored sales from these products into the forecast based on certain assumptions.

Exports to Roche are expected to increase steadily to ¥74.7 billion, a 35.6 percent increase year on year, reflecting growth in sales of Actemra outside Japan. On the other hand, sales outside Japan of other products are forecast to decrease 7.8 to ¥17.8 billion due to a decline in sales of Neutrogin caused by competition from follow-on biologics.

Royalties and other operating revenues are forecast to increase 5.8 percent year on year to ¥25.6 billion as a result of higher revenues from Roche for co-promotion and royalties for Actemra.

As a result of the growth in revenues, gross profit is forecast to increase 5.0 percent year on year to ¥256.3 billion. In expenses, budgeted costs have been increased, as in the previous year, to reflect higher expenses arising from the progress of in-house development projects and the increase in activities at CPR. However, Chugai forecasts Core operating profit of ¥85 0 billion an increase of 10.0 percent year on year, as the increase in gross profit is expected to exceed the increase in expenses. Core EPS is forecast to be ¥104.42, an increase of 9.9 percent year on year.

Fundamental Profit Distribution Policy and Dividends

After taking strategic funding needs and the results forecast into account, Chugai aims for a consolidated payout ratio of approximately 50 percent of Core EPS on average to provide for stable allocation of profit to all shareholders. Internal reserves will be used to increase corporate value through investments for further growth in existing strategic fields and to explore future business opportunities.

Total dividends for 2014 were ¥48 per share, and the Core payout ratio was 50.5 percent, with an average of 50.8 percent over the past five years.

Based on its dividend policy and the performance forecast for the year, Chugai forecasts total dividends for 2015 of ¥52 per share, including an interim dividend of ¥26 per share, which will be an increase in total dividends of ¥4 per share compared with 2014. This estimate assumes a forecast for the payout ratio of 49.8 percent of Core EPS in 2015, which will bring the five-year average Core payout ratio to 50.3 percent.

Business Risks

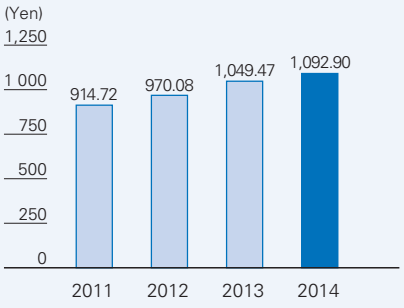
Chugai's corporate performance is subject to material impact from a range of possible future events. Below, we list what we consider the principal sources of risk to the development of our business. We recognize the possibility of these risk events actually occurring, and have prepared policies to forestall such events and take appropriate measures when they do occur.

The categories of risk identified in this section are based on assessments made by Chugai Pharmaceutical as of December 31, 2014.

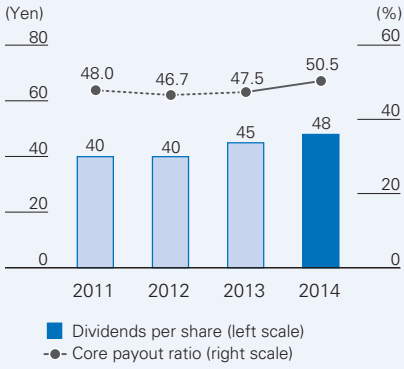
New Product Research and Development

With the goal of becoming a top pharmaceutical company capable of continuously delivering innovative new drugs, Chugai aggressively pursues research and development in Japan and overseas. Our development pipeline is well stocked, especially in the field of oncology. However, bringing all drug candidates smoothly through to the market from the development stage may not be possible, and we expect to have to abandon development in some cases. When such a situation occurs, there is a possibility of a material impact on Chugai's business performance and financial position, depending on the product under development.

Equity per Share Attributable to Chugai Shareholders (BPS)



Dividends per Share/ Core Payout Ratio



Changes in Product Environments

In recent years, there have been rapid technological advancements in the pharmaceutical industry, and Chugai faces fierce competition from pharmaceutical companies in Japan and overseas. Chugai's business performance and financial position may be materially affected by changes in product environments caused by the sale of competitor products and generics and also by changes in marketing and technology license contracts concluded by Chugai.

Side Effects

Pharmaceutical products are approved in Japan by the Ministry of Health, Labour and Welfare after stringent screening. However, because of the characteristics of these products, it is difficult to completely prevent side effects from their use even if all possible safety measures are taken. In cases where side effects occur, in particular newly discovered serious side effects, there is a risk of a material impact on Chugai's business performance and financial position.

Reform of Japan's Medical System

Japan's health insurance system is being reformed against a backdrop of rapid demographic change, with a falling birthrate and an increasing number of elderly people. As part of this process, measures are being taken to curb medical expenses. Revisions have been made to the system of reimbursement of medical fees, and debate is continuing in such areas as NHI drug price reform. Chugai's business performance could be materially affected by future developments in medical system reform, including NHI drug price reform.

Intellectual Property Rights

Chugai recognizes that it applies intellectual property rights in pursuing its business activities, and takes care to distinguish its own proprietary intellectual property rights and licensing arrangements recognized under law. However, the possibility remains of unintentional infringement on third-party intellectual property rights. Major disputes related to intellectual property rights relating to our business could have a material impact on Chugai's business performance and financial position.

Strategic Alliance with Roche

In line with 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 its 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 its business performance and financial position.

International Business Activities

Chugai actively conducts international operations including overseas marketing and research and development, and export and import of bulk drug products. These international business activities expose Chugai to risks associated with legal and regulatory changes, political instability, economic uncertainty, local labor-management relations, changes in and interpretations of systems of taxation, changes in foreign currency markets, differences in commercial practices and other issues that could have a material impact on Chugai's business performance and financial position.

Information Technology Security and Information Control

Chugai makes full use of a wide range of information technology systems in its business activities. Consequently, it is subject to the risk of its operations being disrupted due to system malfunctions, computer viruses or other external factors. In addition, an accident or other incident resulting in the leakage of confidential information could have a material impact on Chugai's business performance and financial position.

Impact from Large-Scale Disasters and Other Contingencies

In the event of natural disasters such as earthquakes or typhoons, or accidents such as fires or other contingencies, damage to Chugai's business sites or sales locations, or those of its business partners, could interrupt its operations. In addition, Chugai could incur significant expenses for the repair of damaged buildings and facilities. Such circumstances could therefore have a material impact on Chugai's business performance and financial position.

Litigation

There is a possibility that litigation may be brought against Chugai over side effects of pharmaceuticals, product liability, labor issues, fair trade or other issues associated with its business activities, which could have a material impact on Chugai's business performance and financial position.

Environmental Issues

In addition to complying with laws and regulations related to environmental issues, Chugai has established a set of even higher voluntary standards and has been making efforts to achieve them. In the course of Chugai's business activities, violations of relevant laws or regulations may occur as a result of an accident or other incident. Any related expenses could have a material impact on Chugai's business performance and financial position.

Consolidated Financial Statements

1. Consolidated income statement and consolidated statement of comprehensive income

1) Consolidated income statement in millions of yen

	Year ended December 31	
	2014	2013
Revenues	**461,109**	**423,652**
Sales (Note 2)	436,883	401,298
Royalties and other operating income (Note 2)	24,226	22,354
Cost of sales	(218,076)	(186,977)
Gross profit	**243,033**	**236,675**
Marketing and distribution	(71,742)	(71,588)
Research and development	(80,800)	(74,280)
General and administration	(14,632)	(12,069)
Operating profit	**75,859**	**78,738**
Financing costs (Note 3)	(11)	(12)
Other financial income (expense) (Note 3)	315	(1,782)
Profit before taxes	**76,164**	**76,944**
Income taxes (Note 4)	(24,087)	(25,058)
Net income	**52,077**	**51,886**
Attributable to :		
Chugai shareholders (Note 19)	50,980	50,895
Non-controlling interests (Note 20)	1,097	991
Earnings per share (Note 24)		
Basic (yen)	93.53	93.47
Diluted (yen)	93.38	93.35

2) Consolidated statement of comprehensive income in millions of yen

	Year ended December 31	
	2014	2013
Net income recognized in income statement	**52,077**	**51,886**
Other comprehensive income		
Remeasurements of defined benefit plans (Notes 4 and 19)	(1,452)	964
Items that will not be reclassified to the income statement	**(1,452)**	**964**
Available-for-sale investments (Notes 4 and 19)	1,050	1,834
Cash flow hedges (Notes 4 and 19)	(4,052)	4,090
Currency translation of foreign operations (Notes 4 and 19)	862	8,019
Items that may be reclassified subsequently to the income statement	**(2,140)**	**13,942**
Other comprehensive income, net of tax (Note 4)	**(3,592)**	**14,907**
Total comprehensive income	**48,485**	**66,793**
Attributable to:		
Chugai shareholders (Note 19)	47,379	65,497
Non-controlling interests (Note 20)	1,107	1,296

2. **Consolidated balance sheet** in millions of yen

	December 31, 2014	December 31, 2013
Assets		
Non-current assets:		
Property, plant and equipment (Note 5)	140,245	140,445
Intangible assets (Note 6)	11,286	9,514
Financial non-current assets (Note 7)	10,755	9,066
Deferred tax assets (Note 4)	25,673	19,244
Defined benefit plan assets (Note 22)	1,946	3,862
Other non-current assets (Note 8)	10,728	10,846
Total non-current assets	**200,635**	**192,977**
Current assets:		
Inventories (Note 9)	139,571	128,536
Accounts receivable (Note 10)	159,773	128,182
Current income tax assets (Note 4)	114	205
Marketable securities (Note 11)	116,030	119,573
Cash and cash equivalents (Note 12)	114,037	115,070
Other current assets (Note 13)	9,379	12,669
Total current assets	**538,904**	**504,235**
Total assets	**739,538**	**697,212**
Liabilities		
Non-current liabilities:		
Long-term debt (Note 14)	(185)	(195)
Deferred tax liabilities (Note 4)	(10,722)	(12,211)
Defined benefit plan liabilities (Note 22)	(2,616)	(1,269)
Long-term provisions (Note 15)	(2,110)	(2,082)
Other non-current liabilities (Note 16)	(11,799)	(10,584)
Total non-current liabilities	**(27,432)**	**(26,341)**
Current liabilities:		
Short-term debt (Note 14)	(29)	(38)
Current income tax liabilities (Note 4)	(16,619)	(12,673)
Short-term provisions (Note 15)	(987)	(105)
Accounts payable (Note 17)	(62,694)	(59,544)
Other current liabilities (Note 18)	(34,021)	(25,307)
Total current liabilities	**(114,350)**	**(97,667)**
Total liabilities	**(141,782)**	**(124,008)**
Total net assets	**597,756**	**573,204**
Equity:		
Capital and reserves attributable to Chugai shareholders (Note 19)	596,099	571,692
Equity attributable to non-controlling interests (Note 20)	1,657	1,512
Total equity	**597,756**	**573,204**

3. Consolidated statement of cash flows in millions of yen

	Year ended December 31	
	2014	2013
Cash flows from operating activities		
Cash generated from operations (Note 25)	99,050	100,959
(Increase) decrease in working capital	(33,302)	(19,660)
Payments made for defined benefit plans	(2,254)	(2,327)
Utilization of provisions (Note 15)	(122)	(163)
Other operating cash flows	(1,115)	(1,461)
Cash flows from operating activities, before income taxes paid	**62,256**	**77,348**
Income taxes paid	(25,222)	(23,827)
Total cash flows from operating activities	**37,034**	**53,521**
Cash flows from investing activities		
Purchase of property, plant and equipment	(16,232)	(11,287)
Purchase of intangible assets	(2,935)	(3,377)
Disposal of property, plant and equipment	794	(300)
Interest and dividends received (Note 25)	490	419
Purchases of marketable securities	(228,292)	(240,860)
Sales of marketable securities	231,873	242,198
Other investing cash flows	(49)	(6)
Total cash flows from investing activities	**(14,351)**	**(13,213)**
Cash flows from financing activities		
Interest paid	(6)	(11)
Dividends paid to Chugai shareholders	(24,520)	(22,874)
Dividends paid to non-controlling shareholders	(962)	(983)
Exercise of equity compensation plans (Note 23)	1,226	820
(Increase) decrease in own equity instruments	(19)	(12)
Other financing cash flows	(109)	(109)
Total cash flows from financing activities	**(24,388)**	**(23,169)**
Net effect of currency translation on cash and cash equivalents	673	2,486
Increase (decrease) in cash and cash equivalents	**(1,032)**	**19,625**
Cash and cash equivalents at January 1	115,070	95,445
Cash and cash equivalents at December 31 (Note 12)	**114,037**	**115,070**

4. Consolidated statement of changes in equity in 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, 2013							
At January 1, 2013	**72,967**	**64,668**	**397,221**	**(6,895)**	**527,961**	**1,200**	**529,161**
Net income recognized in income statement	–	–	50,895	–	50,895	991	51,886
Available-for-sale investments (Notes 4 and 19)	–	–	–	1,834	1,834	–	1,834
Cash flow hedges (Notes 4 and 19)	–	–	–	4,090	4,090	–	4,090
Currency translation of foreign operations (Notes 4, 19 and 20)	–	–	–	7,716	7,716	303	8,019
Remeasurements of defined benefit plans (Notes 4, 19 and 20)	–	–	963	–	963	2	964
Total comprehensive income	**–**	**–**	**51,858**	**13,639**	**65,497**	**1,296**	**66,793**
Dividends (Notes 19 and 20)	–	–	(22,866)	–	(22,866)	(983)	(23,850)
Equity compensation plans (Note 19)	–	138	–	–	138	–	138
Own equity instruments (Note 19)	–	962	–	–	962	–	962
At December 31, 2013	**72,967**	**65,768**	**426,213**	**6,744**	**571,692**	**1,512**	**573,204**
Year ended December 31, 2014							
At January 1, 2014	**72,967**	**65,768**	**426,213**	**6,744**	**571,692**	**1,512**	**573,204**
Net income recognized in income statement	–	–	50,980	–	50,980	1,097	52,077
Available-for-sale investments (Notes 4 and 19)	–	–	–	1,050	1,050	–	1,050
Cash flow hedges (Notes 4 and 19)	–	–	–	(4,052)	(4,052)	–	(4,052)
Currency translation of foreign operations (Notes 4, 19 and 20)	–	–	–	851	851	10	862
Remeasurements of defined benefit plans (Notes 4, 19 and 20)	–	–	(1,451)	–	(1,451)	(1)	(1,452)
Total comprehensive income	**–**	**–**	**49,529**	**(2,150)**	**47,379**	**1,107**	**48,485**
Dividends (Notes 19 and 20)	–	–	(24,521)	–	(24,521)	(962)	(25,483)
Equity compensation plans (Note 19)	–	(73)	–	–	(73)	–	(73)
Own equity instruments (Note 19)	–	1,623	–	–	1,623	–	1,623
At December 31, 2014	**72,967**	**67,317**	**451,220**	**4,594**	**596,099**	**1,657**	**597,756**

Notes to Consolidated Financial Statements

1. General accounting principles and significant accounting policies

1) Basis of preparation of the consolidated financial statements

These financial statements are the annual consolidated financial statements of Chugai Pharmaceutical Co., Ltd., ("Chugai") a company registered in Japan, and its subsidiaries ("the Group"). The common stock of Chugai is publicly traded and is listed on the Tokyo Stock Exchange under the stock code "TSE: 4519". The consolidated financial statements were approved by Osamu Nagayama, representative director, Chairman of the Board & CEO, and Yoshio Itaya, Board Director & CFO on March 26, 2015.

Roche Holding Ltd. is a public company registered in Switzerland and the parent company of the Roche Group, which discloses its results in accordance with International Financial Reporting Standards ("IFRS"). The shareholding percentage of Roche Holding Ltd. in Chugai is 59.89% and the percentage ownership interest is 61.46%. Chugai and its subsidiaries became principal members of the Roche Group after entering into a strategic alliance in October 2002.

The Group meets all of the requirements for a "Specified Company" as stipulated under Article 1-2 of the "Regulations Concerning Terminology, Forms, and Preparation Methods of Consolidated Financial Statements" (Ministry of Finance of Japan Regulation No. 28, 1976, "the regulation"). Hence, in accordance with Article 93 of the regulation, the consolidated financial statements have been prepared in accordance with IFRS.

The consolidated financial statements are presented in Japanese yen, which is Chugai's functional currency and amounts are rounded to the nearest ¥1 million. As a result, the totals shown in the accompanying consolidated financial statements do not necessarily agree with the sum of the individual amounts. They have been prepared using the historical cost convention except for items that are required to be accounted for at fair value.

2) Key accounting judgments, estimates and assumptions

The preparation of the consolidated financial statements requires management to make judgments, estimates and assumptions that affect the reported amounts of revenues, expenses, assets, liabilities and contingent amounts. Actual outcomes could differ from those management estimates. The estimates and underlying assumptions are reviewed on an ongoing basis and are based on historical experience and various other factors. Revisions to estimates are recognized in the period in which the estimate is revised. The following are considered to be the key accounting judgments, estimates and assumptions made and are believed to be appropriate based upon currently available information.

Revenues. Revenues are only recognized when, in management's judgment, the significant risks and rewards of ownership have been transferred and when the Group does not retain continuing managerial involvement or effective control over the goods sold or when the obligation has been fulfilled. The Group is party to out-licensing agreements which involve upfront and milestone payments occurring over several years and which may also involve certain future obligations. Therefore, for some transactions this can result in cash receipts being initially recognized as deferred income and then released to income over subsequent periods on the basis of the performance of the conditions specified in the agreement.

Sales allowances. The Group makes accruals for expected sales rebates, which are estimated based on analyses of existing contractual or legislatively-mandated obligations, historical trends and the Group's experience. As these deductions are based on management estimates, they may be subject to change as better information becomes available. Such changes that arise could impact the accruals recognized in the balance sheet in future periods and consequently the level of sales recognized in the income statement in future periods.

Impairment. Intangible assets not yet available for use are reviewed annually for impairment. Property, plant and equipment and intangible assets in use are assessed for impairment when there is a triggering event that provides evidence that an asset may be impaired. To assess whether any impairment exists estimates of expected future cash flows are used. Actual outcomes could vary significantly from such estimates of discounted future cash flows. Factors such as changes in discount rates, the planned use of buildings, machinery or equipment, closure of facilities, the presence or absence of competition, technical obsolescence and lower than anticipated product sales could lead to shorter useful lives or impairment.

Post-employment benefits. The Group operates defined benefit plans and the fair value of the recognized plan assets and liabilities are based upon statistical and actuarial calculations. The measurement of the net defined benefit obligation is particularly sensitive to changes in the discount rate and expected mortality. The actuarial assumptions used may differ materially from actual results due to changes in market and economic conditions, longer or shorter life spans of participants, and other changes in the factors being assessed. These differences could impact on the assets or liabilities recognized in the balance sheet in future periods.

Legal. The Group provides for anticipated legal settlement costs when there is a probable outflow of resources that can be reasonably estimated. These estimates consider the specific circumstances of each legal case and relevant legal advice, and are inherently judgmental due to the highly complex nature of legal cases. The estimates could change substantially over time as new facts emerge and each legal case progresses. Where no reliable estimate can be made, no provision is recorded and contingent liabilities are disclosed where material.

Environmental. The Group provides for anticipated environmental remediation costs when there is a probable outflow of resources that can be reasonably estimated. Environmental provisions consist primarily of costs to fully clean and refurbish contaminated sites, including landfills, and to treat and contain contamination at certain other sites. These estimates are inherently judgmental due to uncertainties related to the detection of previously unknown contaminated sites, the method and extent of remediation, the percentage of the problematic materials attributable to the Group at the remediation sites, and the financial capabilities of the other potentially responsible parties. The estimates could change substantially over time as new facts emerge and each environmental remediation progresses.

Income taxes. Significant estimates are required to determine the current and deferred tax assets and liabilities. Some of these estimates are based on interpretations of existing tax laws or regulations. Factors that may impact on current and deferred taxes include changes in tax laws, regulations or rates, changing interpretations of existing tax laws or regulations, future levels of research and development spending and changes in pre-tax earnings.

Leases. The treatment of leasing transactions is mainly determined by whether the lease is considered to be an operating or finance lease. In making this assessment, management looks at the substance of the lease, as well as the legal form, and makes a judgment about whether substantially all of the risks and rewards of ownership are transferred. Arrangements which do not take the legal form of a lease but that nevertheless convey the right to use an asset are also covered by such assessments.

3) Significant accounting policies

Consolidation policy

Subsidiaries are all companies over which the Group has control. Chugai controls an entity when the Group is exposed to, or has rights to, variable returns from its involvement with the entity and has the ability to affect those returns through its power over the entity. Companies acquired during the year are consolidated from the date on which control is transferred to the Group, and subsidiaries to be divested are included up to the date on which control passes from the Group. Inter-company balances, transactions and resulting unrealized income are eliminated in full. Changes in ownership interests in subsidiaries are accounted for as equity transactions if they occur after control has already been obtained and if they do not result in a loss of control. Associates are companies over which the Group exercises, or has the power to exercise, significant influence, but which it does not control and they are accounted for using the equity method.

Foreign currency translation

Most foreign subsidiaries of the Group use their local currency as their functional currency. Certain foreign subsidiaries use other currencies (such as the euro) as their functional currency where this is the currency of the primary economic environment in which the entity operates. Local transactions in other currencies are initially reported using the exchange rate at the date of the transaction. Gains and losses from the settlement of such transactions and gains and losses on translation of monetary assets and liabilities denominated in other currencies are included in income, except when they are qualifying cash flow hedges. In such cases the gains and losses are deferred into other comprehensive income.

Upon consolidation, assets and liabilities of foreign subsidiaries using functional currencies other than the Japanese yen are translated into Japanese yen using year-end rates of exchange. The income statement and statement of cash flows are translated at the average rates of exchange for the year. Translation differences due to the changes in exchange rates between the beginning and the end of the year and the difference between net income translated at the average and year-end exchange rates are taken directly to other comprehensive income.

Revenue recognition

Sales represent amounts received and receivable for goods supplied to customers after deducting trade discounts, cash discounts and volume rebates, and exclude consumption taxes and other taxes directly linked to sales. Revenues from the sale of products are recognized upon transfer to the customer of significant risks and rewards. Trade discounts, cash discounts and volume rebates are recorded on an accrual basis consistent with the recognition of the related sales. Sales returns, charge-backs and other rebates are also deducted from sales and recorded as accrued liabilities or as a deduction from accounts receivable.

Royalties and other operating income are recorded as earned or as the services are performed. Single transactions are split into separately identifiable components to reflect the substance of the transaction, where necessary. Conversely, two or more transactions may be considered together for revenue recognition purposes, where the commercial effect cannot be understood without reference to the series of transactions as a whole.

Cost of sales

Cost of sales includes the corresponding direct production costs and related production overheads of goods sold and services rendered. Royalties, alliance and collaboration expenses, including all collaboration profit-sharing arrangements are also reported as part of cost of sales. Start-up costs between validation and the achievement of normal production capacity are expensed as incurred.

Research and development
Internal research and development activities are expensed as incurred for the following:

- Internal research costs incurred for the purpose of gaining new scientific or technical knowledge and understanding.
- Internal development costs incurred for the application of research findings or other knowledge to plan and develop new products for commercial production. The development projects undertaken by the Group are subject to technical, regulatory and other uncertainties, such that, in the opinion of management, the criteria for capitalization as intangible assets are not met prior to obtaining marketing approval by the regulatory authorities in major markets.
- Post-marketing studies after regulatory approval, such as phase IV costs in the pharmaceuticals business, generally involve safety surveillance and on-going technical support of a drug after it receives marketing approval to be sold. They may be required by regulatory authorities or may be undertaken for safety or commercial reasons. The costs of such post-marketing studies are not capitalized as intangible assets, as in the opinion of management, they do not generate separately identifiable incremental future economic benefits that can be reliably measured.

Acquired in-process research and development resources obtained through in-licensing arrangements, business combinations or separate asset purchases are capitalized as intangible assets. The acquired asset must be controlled by the Group, be separately identifiable and expected to generate future economic benefits, even if uncertainty exists as to whether the research and development will ultimately result in a marketable product. Consequently, upfront and milestone payments to third parties for pharmaceutical products or compounds before regulatory marketing approval are recognized as intangible assets. Assets acquired through such arrangements are measured on the basis set out in the “Intangible assets” policy. Subsequent internal research and development costs incurred post-acquisition are treated in the same way as other internal research and development costs. If research and development are embedded in contracts for strategic alliances, the Group carefully assesses whether upfront or milestone payments constitute funding of research and development work or acquisition of an asset.

Licensing, milestone, and other upfront receipts
Royalty income is recognized on an accrual basis in accordance with the substance of the respective licensing agreements. If the collectability of a royalty amount is not reasonably assured, those royalties are recognized as revenues when the cash is received. The Group receives upfront, milestone and other similar payments from third parties relating to the sale or licensing of products or technology. Revenues associated with performance milestones are recognized based on achievement of the deliverables as defined in the respective agreements. Upfront payments and license fees for which there are subsequent deliverables are initially reported as deferred income and are recognized in income as earned over the period of the development collaboration or the manufacturing obligation.

Employee benefits
Short-term employee benefits include wages, salaries, social security contributions, paid annual leave and sick leave, profit sharing and bonuses, and non-monetary benefits for current employees. The costs are recognized within the operating results when the employee has rendered the associated service. The Group recognizes a liability for profit sharing and bonuses where contractually obliged or where there is a past practice that has created a constructive obligation.

Termination benefits are payable when employment is terminated by the Group before the normal retirement date, or whenever an employee accepts voluntary redundancy in exchange for these benefits. Termination costs are recognized at the earlier of when the Group can no longer withdraw the offer of the benefits or when the Group recognizes any related restructuring costs.

Post-employment benefits
For defined contribution plans, the Group contributions are recognized within the operating results when the employee has rendered the associated service.

For defined benefit plans the liability or asset recognized in the balance sheet is net amount of the present value of the defined benefit obligation and the fair value of the plan assets. All changes in the net defined benefit liability (asset) are recognized as they occur as follows:

Recognized in the income statement:
- Current service costs are charged to the appropriate income statement heading within the operating results.
- Past service costs, including curtailment gains or losses, are recognized immediately in general and administration within the operating results.
- Settlement gains or losses are recognized in general and administration within the operating results.
- Net interest on the net defined benefit liability (asset) is recognized in financing costs.

Recognized in other comprehensive income:
- Actuarial gains and losses arising from experience adjustments (the difference between previous assumptions and what has actually occurred) and changes in actuarial assumptions.
- The return on plan assets, excluding amounts included in net interest on the net defined benefit liability (asset).

Net interest on the net defined benefit liability (asset) comprises interest income on plan assets and interest costs on the defined benefit obligation. The net interest is calculated using the same discount rate that is used in calculating the defined benefit obligation, applied to the net defined benefit liability (asset) at the start of the period, taking account of any changes from contribution or benefit payments.

Pension assets and liabilities in different defined benefit plans are not offset unless the Group has a legally enforceable right to use the surplus in one plan to settle obligations in the other plan.

Equity compensation plans
The fair value of all equity compensation awards granted to directors and certain employees is estimated at the grant date and recorded as an expense over the vesting period. The expense is charged to the appropriate income statement heading within the operating results. For equity-settled plans, an increase in equity is recorded for this expense and any subsequent cash flows from exercises of vested awards are recorded as changes in equity.

Property, plant and equipment
Property, plant and equipment are initially recorded at cost of purchase or construction, and include all costs directly attributable to bringing the asset to the location and condition necessary for it to be capable of operating in the manner intended by management. These include items such as costs of site preparation, installation and assembly costs and professional fees. The net costs of testing whether the asset is functioning properly, including validation costs, are also included in the initially recorded cost of construction. Property, plant and equipment are depreciated on a straight-line basis, except for land, which is not depreciated. The estimated useful lives of major classes of depreciable assets are as follows:
- Land improvements: 40 years
- Buildings: 10-50 years
- Machinery and equipment: 3-15 years

Where parts of an item of property, plant and equipment have different useful lives, they are accounted for as separate components. The estimated useful lives of the assets are regularly reviewed, and, if necessary, the future depreciation charges are accelerated. Repairs and maintenance costs are expensed as incurred.

Leases
Where the Group is the lessee, finance leases exist when substantially all of the risks and rewards of ownership of leased assets are transferred to the Group. Finance lease assets are capitalized at the start of the lease at fair value, or the present value of the minimum lease payments, if lower. The rental obligation, net of finance charges, is reported within debt. Finance lease assets are depreciated over the shorter of the lease term and its useful life. The interest element of the lease payment is charged against income over the lease term based on the effective interest rate method. Operating leases are when substantially all of the risks and rewards of ownership are not transferred to the Group. Payments made under operating leases are charged against income on a straight-line basis over the period of the lease.

Intangible assets
Purchased patents, trademarks, licenses and other intangible assets are initially recorded at cost. Assets that have been acquired through a business combination are initially recorded at fair value. Once available for use, intangible assets are amortized on a straight-line basis over their useful lives. The estimated useful life is the lower of the legal duration and the economic useful life. The estimated useful lives of intangible assets are regularly reviewed. Estimated useful lives of major classes of amortizable intangible assets are as follows:

- Product intangibles in use: 5–12 years
- Marketing intangibles in use: 5 years
- Technology intangibles in use: 3–9 years

Impairment of property, plant and equipment and intangible assets
An impairment assessment is carried out at each reporting date when there is evidence that an item of property, plant and equipment or intangible asset in use may be impaired. In addition intangible assets that are not yet available for use are tested for impairment annually. When the recoverable amount of an asset, being the higher of its fair value less costs to sell and its value in use, is less than its carrying value, then the carrying value is reduced to its recoverable amount. This reduction is reported in the income statement as an impairment loss. Value in use is calculated using estimated cash flows. These are discounted using an appropriate long-term interest rate. When an impairment loss arises, the useful life of the asset is reviewed and, if necessary, the future depreciation/amortization charge is accelerated. If the amount of impairment loss subsequently decreases and the decrease can be related objectively to an event occurring after the impairment was recognized, then the previously recognized impairment loss is reversed through the income statement as an impairment reversal.

Inventories
Inventories are stated at the lower of cost and net realizable value. The cost of finished goods and work in process includes raw materials, direct labor and other directly attributable costs and overheads based upon the normal capacity of production facilities. Cost is determined using the weighted average method. Net realizable value is the estimated selling price less cost to completion and selling expenses.

Accounts receivable
Accounts receivable are carried at the original invoice amount less allowances made for doubtful accounts, trade discounts, cash discounts, volume rebates and similar allowances. An allowance for doubtful accounts is recorded where there is objective evidence that the Group will not be able to collect all amounts due. These estimates are based on specific indicators, such as the aging of customer balances, specific credit circumstances and the Group's historical experience, taking also into account economic conditions. Expenses for doubtful trade receivables are recognized within marketing and distribution expenses. Trade discounts, cash discounts, volume rebates and similar allowances are recorded on an accrual basis consistent with the recognition of the related sales, using estimates based on existing contractual obligations, historical trends and the Group's experience.

Cash and cash equivalents
Cash and cash equivalents include cash on hand and time, call and current balances with banks and similar institutions. Such balances are only reported as cash equivalents if they are readily convertible to known amounts of cash, are subject to insignificant risk of changes in their fair value and have a maturity of three months or less from the date of acquisition.

Provisions and contingencies
Provisions are recognized where a legal or constructive obligation has been incurred which will probably lead to an outflow of resources that can be reliably estimated. In particular, restructuring provisions are recognized when the Group has a detailed formal plan that has either commenced implementation or has been announced. Provisions are recorded for the estimated ultimate liability that is expected to arise and are discounted when the time value of money is material. A contingent liability is disclosed where the existence of the obligation will only be confirmed by future events or where the amount of the obligation cannot be measured with reasonable reliability. Contingent assets are not recognized, but are disclosed where an inflow of economic benefits is probable.

Fair values
Fair value is the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. It is determined by reference to quoted market prices or by the use of established valuation techniques such as option pricing models and the discounted cash flow method if quoted prices in an active market are not available.

Financial instruments
Financial instruments are classified into the following categories:

Available-for-sale. These are non-derivative financial assets that are either designated as such or are not classified in any other financial asset category. Available-for-sale financial assets are initially recorded and subsequently carried at fair value. Changes in fair value are recorded in other comprehensive income, except for impairments, interest and foreign exchange components. When an investment is derecognized the cumulative gains and losses in equity are reclassified to other financial income (expense). Available-for-sale assets are mainly comprised of marketable securities and most of financial non-current assets.

Fair value – hedging instruments. These are derivative financial instruments that are used to manage the exposures to foreign currency risk. Derivative financial instruments are initially recorded and subsequently carried at fair value. Apart from those derivatives designated as qualifying cash flow hedging instruments, all changes in fair value are recorded as other financial income (expense).

Fair value – designated. These are non-derivative financial instruments that are designated as fair value through profit or loss on initial recognition. Designated fair value instruments are initially recorded and subsequently carried at fair value. Changes in fair value are recorded in the income statement. Designated fair value instruments mainly comprise of financial assets held for trading.

Loans and receivables. These are non-derivative financial assets with fixed or determinable payments that are not quoted in an active market. Loans and receivables are initially recorded at fair value and subsequently carried at amortized cost using the effective interest rate method, less any impairment losses. Loans and receivables are mainly comprised of accounts receivable, cash and cash equivalents and a part of financial non-current assets.

Other financial liabilities. These are non-derivative financial liabilities. Other financial liabilities are initially recorded at fair value and subsequently carried at amortized cost using the effective interest rate method. Other financial liabilities are mainly comprised of accounts payable and debt.

Derecognition of financial instruments
A financial asset is derecognized when the contractual cash flows from the asset expire or when the Group transfers the rights to receive the contractual cash flows from the financial assets in a transaction in which substantially all the risks and rewards of ownership of the financial asset are transferred. A financial liability is derecognized when the contractual obligations are discharged, cancelled or expire.

Impairment of financial assets
Financial assets are individually assessed for possible impairment at each reporting date. An impairment charge is recorded where there is objective evidence of impairment, such as where the issuer is in bankruptcy, default or other significant financial difficulty. Available-for-sale equity securities that have a market value of more than 25% below their original cost, or have a market value below their original cost for a sustained six-month period will be considered as impaired.

For financial assets carried at amortized cost, any impairment charge is the difference between the carrying value and the recoverable amount, calculated using estimated future cash flows discounted using the original effective interest rate. For available-for-sale financial assets, any impairment charge is the amount currently carried in other comprehensive income for the difference between the original cost, net of any previous impairment, and the fair value.

An impairment loss is reversed if the reversal can be related objectively to an event occurring after the impairment loss was recognized. For equity securities held as available-for-sale, the reversal is recognized directly in other comprehensive income. For debt securities measured at amortized cost or available-for-sale, the reversal is recognized in other financial income (expense).

Hedge accounting
The Group uses derivatives to manage its exposures to foreign currency risk. The instruments used may include forwards contracts and options. The Group generally limits the use of hedge accounting to certain significant transactions. To qualify for hedge accounting the hedging relationship must meet several strict conditions on documentation, probability of occurrence, hedge effectiveness and reliability of measurement. While many of these transactions can be considered as hedges in economic terms, if the required conditions are not met, then the relationship does not qualify for hedge accounting. In this case the hedging instrument and the hedged item are reported independently as if there were no hedging relationship, which means that any derivatives are reported at fair value, with changes in fair value included in other financial income (expense).

Cash flow hedge. Is a hedge of the exposure to variability in cash flows that is attributable to a particular risk associated with a recognized asset or liability or a highly probable forecast transaction and could affect profit or loss. The hedging instrument is recorded at fair value. The effective portion of the hedge is included in other comprehensive income and any ineffective portion is reported in other financial income (expense). If the hedging relationship is the hedge of the foreign currency risk of a firm commitment or highly probable forecasted transaction that results in the recognition of a non-financial item, the cumulative changes in the fair value of the hedging instrument that have been recorded in other comprehensive income are included in the initial carrying value of the non-financial item at the date of recognition. For all other cash flow hedges, the cumulative changes in the fair value of the hedging instrument that have been recorded in other comprehensive income are included in other financial income (expense) when the forecasted transaction affects net income.

Fair value hedge. Is a hedge of the exposure to changes in fair value of a recognized asset or liability, or an unrecognized firm commitment, or an identified portion of such an asset, liability or firm commitment, that is attributable to a particular risk and could affect profit or loss. The hedging instrument is recorded at fair value and the hedged item is recorded at its previous carrying value, adjusted for any changes in fair value that are attributable to the hedged risk. Changes in the fair values are reported in other financial income (expense).

Taxation
Income taxes include all taxes based upon the taxable profits of the Group. Other taxes not based on income, such as property and capital taxes, are included in the appropriate heading within the operating results.

Liabilities for income taxes, which could arise on the remittance of retained earnings, principally relating to subsidiaries, are only recognized where it is probable that such earnings will be remitted in the foreseeable future.

Deferred tax assets and liabilities are recognized on temporary differences between the tax bases of assets and liabilities and their carrying values. Deferred tax assets are recognized to the extent that it is probable that future taxable profit will be available against which the unused tax losses can be utilized.

Current and deferred tax assets and liabilities are offset when the income taxes are levied by the same taxation authority and when there is a legally enforceable right to offset them. Deferred taxes are determined based on the currently enacted tax rates applicable in each tax jurisdiction where the Group operates.

Own equity instruments
The Group's holdings in its own equity instruments are recorded as a deduction from equity. The original purchase cost, consideration received for subsequent resale of these equity instruments and other movements are reported as changes in equity. The exercise of stock acquisition rights granted to directors and certain employees will result in the allotment from own equity instruments.

4) Changes in accounting policies
The Group has adopted the following new standards and amendments to standards, including any consequential amendments to other standards, with a date of initial application of 1 January 2014.

IFRS		Description of new and revised standards
IFRS 10	Consolidated Financial Statements	
IFRS 12	Disclosure of Interests in Other Entities	Accounting for investments held by investment entities
IAS 27	Separate Financial Statements	
IAS 32	Financial Instruments: Presentation	Offsetting of financial instruments and financial liabilities
IAS 36	Impairment of Assets	Recoverable amount disclosures for non-financial assets
IAS 39	Financial Instruments: Recognition and Measurement	Revision of accounting for derivative contract renewals
IFRIC 21	Levies	Clarification of accounting for levies

The above standards do not materially impact the Group's performance or financial status.

5) Future new and revised standards

The Group is currently assessing the potential impacts of new standards and interpretations that will be effective from January 1, 2015 and beyond. Based on the analysis to date, the Group does not anticipate that these will have a material impact on the Group's overall results and financial position.

By the date of approval of the consolidated financial statements, the following new and revised standards have been issued by the International Accounting Standards Board (IASB) and have not been implemented by the Group yet.

	IFRS	Mandatory adoption (from the year beginning)	To be adopted by the Group	Description of new and revised standards
IFRS 15	Revenue from Contracts with Customers	January 1, 2017	To be determined	Revision of accounting relating to revenue recognition
IFRS 9	Financial Instruments	January 1, 2018	To be determined	Classification, measurement and recognition of financial instruments

2. Operating segment information

The Group has a single business of pharmaceuticals and does not have multiple operating segments. The Group's pharmaceuticals business consists of the research and development of new prescription medicines and the subsequent manufacturing, marketing and distribution activities. These functional activities are integrated and managed effectively.

Information on revenues by geographical area in millions of yen

	2014		2013	
	Sales	Royalties and other operating income	Sales	Royalties and other operating income
Japan	362,574	10,300	340,241	10,512
Overseas	74,309	13,926	61,057	11,842
of which Switzerland	55,051	13,884	42,909	11,729
Total	**436,883**	**24,226**	**401,298**	**22,354**

Information on revenues by major customers in millions of yen

	2014		2013	
	Revenues	%	Revenues	%
Alfresa Corporation	94,483	20.5	94,288	22.3
Mediceo Corporation	72,767	15.8	75,240	17.8
F. Hoffmann-La Roche Ltd	68,784	14.9	54,638	12.9
Suzuken Co., Ltd.	47,658	10.3	49,728	11.7

3. Financing costs and other financial income (expense)

Financing costs in millions of yen

	2014	2013
Interest expense	(6)	(11)
Net interest cost of defined benefit plans	63	66
Net other financing costs	(68)	(68)
Total financing costs	**(11)**	**(12)**

Other financial income (expense) in millions of yen

	2014	2013
Dividend income	287	148
Gains on sale of equity securities	-	-
Losses on sale of equity securities	-	-
Write-downs and impairments of equity securities	(0)	(3)
Net income from equity securities	**287**	**145**
Interest income	205	243
Gains on sale of debt securities	-	-
Losses on sale of debt securities	-	-
Net interest income and income from debt securities	**205**	**243**
Foreign exchange gains (losses)	(672)	(5,730)
Gains (losses) on foreign currency derivatives	495	3,560
Net foreign exchange gains (losses)	**(177)**	**(2,170)**
Total other financial income (expense)	**315**	**(1,782)**

4. Income taxes

Income tax expenses in millions of yen

	2014	2013
Current income taxes	(29,244)	(25,260)
Deferred taxes	5,158	202
Total income tax (expense)	**(24,087)**	**(25,058)**

Reconciliation of the Group's effective tax rate

	2014	2013
Expected tax rate	38.0 %	38.0 %
Tax effect of		
- Non-taxable income/non-deductible expenses	+1.1 %	+1.2 %
- Effect of changes in applicable tax rates on deferred tax balances	+2.4 %	+0.1 %
- Research and development tax credits	(7.7) %	(4.9) %
- Other differences	(2.2) %	(1.9) %
Group's effective tax rate	**31.6 %**	**32.5 %**

Tax effects of other comprehensive income in millions of yen

	2014			2013		
	Pre-tax amount	Tax benefit	After-tax amount	Pre-tax amount	Tax benefit	After-tax Amount
Remeasurements of defined benefit plans	(2,256)	804	(1,452)	1,496	(532)	964
Available-for-sale investments	1,632	(582)	1,050	2,760	(926)	1,834
Cash flow hedges	(6,543)	2,491	(4,052)	6,597	(2,508)	4,090
Currency translation of foreign operations	862	-	862	8,019	-	8,019
Other comprehensive income	**(6,305)**	**2,713**	**(3,592)**	**18,873**	**(3,966)**	**14,907**

Income tax assets (liabilities) in millions of yen

	December 31, 2014	December 31, 2013
Current income taxes		
- Assets	114	205
- Liabilities	(16,619)	(12,673)
Net current income tax assets (liabilities)	**(16,505)**	**(12,468)**
Deferred taxes		
- Assets	25,673	19,244
- Liabilities	(10,722)	(12,211)
Net deferred tax assets (liabilities)	**14,950**	**7,033**

Current income taxes: movements in recognized net assets (liabilities) in millions of yen

	2014	2013
Net current income tax assets (liabilities) at January 1	(12,468)	(11,093)
Income taxes paid	25,222	23,827
(Charged) credited to the income statement	(29,244)	(25,260)
Currency translation effects and other	(15)	58
Net current income tax assets (liabilities) at December 31	**(16,505)**	**(12,468)**

Deferred taxes: movements in recognized net assets (liabilities) in millions of yen

	Property, plant and equipment	Intangible assets	Provisions	Employee benefits	Other temporary differences	Total
Year ended December 31, 2013						
At January 1, 2013	(20,938)	528	185	3,192	27,805	10,772
(Charged) credited to the income statement	797	(1,237)	139	202	302	202
(Charged) credited to other comprehensive income	–	–	–	(532)	(3,434)	(3,966)
(Charged) credited to equity	–	–	–	–	–	–
Currency translation effects and other	–	–	–	–	25	25
At December 31, 2013	**(20,142)**	**(709)**	**324**	**2,862**	**24,698**	**7,033**
Year ended December 31, 2014						
At January 1, 2014	(20,142)	(709)	324	2,862	24,698	7,033
(Charged) credited to the income statement	1,334	(232)	304	(52)	3,804	5,158
(Charged) credited to other comprehensive income	–	–	–	804	1,909	2,713
(Charged) credited to equity	–	–	–	–	–	–
Currency translation effects and other	–	–	–	–	46	46
At December 31, 2014	**(18,808)**	**(940)**	**628**	**3,613**	**30,457**	**14,950**

Other temporary differences mainly relate to prepaid expenses and amortization of deferred assets.

Deferred tax assets are not recognized for deductible temporary differences of ¥1,530 million at December 31, 2014 (2013: ¥1,882 million).
Deferred tax assets are recognized for tax losses carried forward only to the extent that realization of the related tax benefit is probable.

Unrecognized tax losses: expiry in millions of yen

	2014	2013
Less than one year	–	–
Over one year and less than five years	–	–
Over five years	2,617	3,212
Tax losses not recognized in deferred tax assets	**2,617**	**3,212**

Deferred tax assets for unused tax credits are recognized only to the extent that realization of the related tax benefit is probable.

Unrecognized unused tax credits: expiry in millions of yen

	2014	2013
Less than one year	–	–
Over one year and less than five years	–	2,358
Over five years	121	106
Unused tax credits not recognized in deferred tax assets	**121**	**2,464**

Deferred tax liabilities have not been established for the withholding tax and other taxes that would be payable on the unremitted earnings of wholly-owned foreign subsidiaries of the Group, where such amounts are currently regarded as permanently reinvested. The temporary differences relating to the unremitted earnings were ¥1,857 million (2013: ¥1,690 million).

5. Property, plant and equipment

Property, plant and equipment: movements in carrying value of assets in millions of yen

	Land	Buildings and land improvements	Machinery and equipment	Construction in progress	Total
At January 1, 2013					
Cost	10,388	110,947	156,452	516	278,304
Accumulated depreciation and impairment	(274)	(50,607)	(84,323)	(44)	(135,248)
Net book value	**10,114**	**60,340**	**72,129**	**472**	**143,056**
Year ended December 31, 2013					
At January 1, 2013	10,114	60,340	72,129	472	143,056
Additions	-	4	304	12,691	12,999
Disposals	-	(209)	(416)	(51)	(675)
Transfers	-	4,267	5,788	(10,055)	-
Depreciation charge	-	(3,621)	(9,899)	-	(13,520)
Impairment charge	(1)	(771)	(882)	(44)	(1,697)
Other	-	(28)	0	-	(28)
Currency translation effects	-	16	290	4	310
At December 31, 2013	**10,114**	**59,998**	**67,315**	**3,019**	**140,445**
Cost	10,388	114,000	158,239	3,019	285,646
Accumulated depreciation and impairment	(275)	(54,003)	(90,924)	-	(145,201)
Net book value	**10,114**	**59,998**	**67,315**	**3,019**	**140,445**
Year ended December 31, 2014					
At January 1, 2014	10,114	59,998	67,315	3,019	140,445
Additions	-	338	391	15,689	16,418
Disposals	(169)	(756)	(438)	-	(1,362)
Transfers	-	5,283	9,188	(14,471)	-
Depreciation charge	-	(3,777)	(9,911)	-	(13,688)
Impairment charge	(580)	(813)	(382)	-	(1,775)
Other	-	0	1	-	1
Currency translation effects	-	47	135	26	207
At December 31, 2014	**9,365**	**60,320**	**66,298**	**4,262**	**140,245**
Cost	9,973	117,796	160,610	4,262	292,642
Accumulated depreciation and impairment	(608)	(57,476)	(94,312)	-	(152,396)
Net book value	**9,365**	**60,320**	**66,298**	**4,262**	**140,245**

In 2014 no borrowing costs were capitalized as property, plant and equipment (2013: none).

Impairment charge

During 2014 the impairment charge was mainly related to unused buildings at Ukima plant. During 2013 the impairment charge was mainly related to unused buildings at Kamakura research laboratories. The carrying value was reduced to the value in use as the recoverable amount of the assets was less than the carrying value.

Classification of impairment of property, plant and equipment in millions of yen

	2014	2013
Cost of sales	1,116	188
Marketing and distribution	-	24
Research and development	4	1,485
General and administration	656	1
Total impairment charge	**1,775**	**1,697**

Finance leases
The capitalized cost of property, plant and equipment under finance leases was ¥191 million (2013: ¥202 million) and the net book value of these assets was ¥50 million (2013: ¥67 million). The carrying value of the leasing obligation was ¥53 million (2013: ¥71 million), which is reported as part of Debt (see Note 14).

Operating leases
Group companies are party to a number of operating leases, mainly for machinery and equipment, motor vehicles and property rentals. The arrangements do not impose any significant restrictions on the Group. Total operating lease rental expense was ¥6,763 million (2013: ¥6,819 million).

Operating leases: future minimum lease payments under non-cancellable leases in millions of yen

	December 31, 2014	December 31, 2013
Within one year	4,400	4,632
Between one and five years	6,541	9,530
More than five years	598	749
Total minimum payments	**11,539**	**14,912**

Capital commitments
The Group has non-cancellable capital commitments for the purchase or construction of property, plant and equipment totaling ¥6,272 million (2013: ¥3,446 million).

6. Intangible assets

Intangible assets: movements in carrying value of assets in millions of yen

	Product intangibles: in use	Product intangibles: not available for use	Marketing intangibles: in use	Technology intangibles: in use	Total
At January 1, 2013					
Cost	12,369	2,181	169	45	14,765
Accumulated amortization and impairment	(8,254)	-	(10)	(0)	(8,265)
Net book value	**4,116**	**2,181**	**159**	**45**	**6,500**
Year ended December 31, 2013					
At January 1, 2013	4,116	2,181	159	45	6,500
Additions	-	3,909	56	30	3,995
Disposals	-	-	-	-	-
Transfers	994	(994)	-	-	-
Amortization charge	(924)	-	(39)	(6)	(970)
Impairment charge	-	(89)	-	-	(89)
Currency translation effects	-	78	-	-	78
At December 31, 2013	**4,185**	**5,085**	**175**	**68**	**9,514**
Cost	14,055	5,174	225	75	19,529
Accumulated amortization and impairment	(9,870)	(89)	(49)	(7)	(10,014)
Net book value	**4,185**	**5,085**	**175**	**68**	**9,514**
Year ended December 31, 2014					
At January 1, 2014	4,185	5,085	175	68	9,514
Additions	38	2,576	492	28	3,134
Disposals	-	-	-	-	-
Transfers	2,479	(2,479)	-	-	-
Amortization charge	(1,123)	-	(58)	(11)	(1,192)
Impairment charge	-	(171)	-	-	(171)
Currency translation effects	-	0	-	-	0
At December 31, 2014	**5,580**	**5,012**	**609**	**85**	**11,286**
Cost	16,577	5,271	717	103	22,668
Accumulated amortization and impairment	(10,997)	(259)	(107)	(17)	(11,381)
Net book value	**5,580**	**5,012**	**609**	**85**	**11,286**

Significant intangible assets

The product intangibles in use and not available for use are mainly acquired through in-licensing agreements of products with related parties. The remaining amortization periods for product intangibles in use are from 1 to 12 years.

Classification of amortization and impairment expenses in millions of yen

	2014		2013	
	Amortization	Impairment	Amortization	Impairment
Cost of sales	1,123	-	924	-
Marketing and distribution	58	-	39	-
Research and development	11	171	6	89
General and administration	-	-	-	-
Total	**1,192**	**171**	**970**	**89**

Internally generated intangible assets
The Group currently has no internally generated intangible assets from development as the criteria for the recognition as an asset are not met.

Intangible assets with indefinite useful lives
The Group currently has no intangible assets with indefinite useful lives.

Product intangibles not available for use
These mostly represent in-process research and development assets acquired either through in-licensing arrangements or separate purchases. Due to the inherent uncertainties in the research and development processes, intangible assets not available for use are particularly at risk of impairment if the project is not expected to result in a commercialized product.

Impairment of intangible assets
Impairment charges arise from changes in the estimates of the future cash flows expected to result from the use of the asset and its eventual disposal. Factors such as the presence or absence of competition, technical obsolescence or lower than anticipated sales for products with capitalized rights could result in shortened useful lives or impairment.

Potential commitments from alliance collaborations
The Group is party to in-licensing and similar arrangements with its alliance partners. These arrangements may require the Group to make certain milestone or other similar payments dependent upon the achievement of agreed objectives or performance targets as defined in the collaboration agreements.

The Group's current estimate of future commitments for such payments is set out in the table below. These figures are undiscounted and are not risk adjusted, meaning that they include all such potential payments that can arise assuming all projects currently in development are successful. The timing is based on the Group's current best estimate.

Potential future collaboration payments at December 31, 2014 in millions of yen

	Third party	Related party	Total
Within one year	1,598	964	2,562
Between one and two years	3,281	1,037	4,318
Between two and three years	450	1,892	2,342
Total	**5,329**	**3,893**	**9,222**

7. Financial non-current assets

Financial non-current assets in millions of yen

	December 31, 2014	December 31, 2013
Available-for-sale investments	10,755	8,966
Other financial non-current assets	-	100
Total financial non-current assets	**10,755**	**9,066**

Financial non-current assets are held for the Group's business purposes to strengthen and maintain the relationship with business partners. The available-for-sale investments are mainly equity investments in Japanese listed companies.

8. Other non-current assets

Other non-current assets in millions of yen

	December 31, 2014	December 31, 2013
Long-term prepaid expenses	6,177	5,823
Other assets	4,552	5,023
Total other non-current assets	**10,728**	**10,846**

Long-term prepaid expenses are mainly payments to related parties for start-up and validation costs at plants used for outsourcing to the related parties.

9. Inventories

Inventories in millions of yen

	December 31, 2014	December 31, 2013
Raw materials and supplies	34,668	36,054
Work in process	145	101
Intermediates	33,023	34,770
Finished goods	72,228	58,249
Less: Provision for slow-moving and obsolete inventory	(493)	(639)
Total inventories	**139,571**	**128,536**

Inventories expensed through cost of sales totaled ¥204,275 million (2013: ¥179,077 million). Expenses relating to inventory write-down totaled ¥1,182 million (2013: ¥1,013 million).

10. Accounts receivable

Accounts receivable in millions of yen

	December 31, 2014	December 31, 2013
Trade receivables – third party	124,697	99,076
Trade receivables – related party	16,630	12,017
Notes receivables	17	15
Other receivables – third party	6,818	6,640
Other receivables – related party	11,616	10,442
Allowances for doubtful accounts	(5)	(7)
Total accounts receivable	**159,773**	**128,182**

11. Marketable securities

Marketable securities in millions of yen

	December 31, 2014	December 31, 2013
Available-for-sale financial assets		
Money market instruments and time accounts over three months	116,030	119,573
Total marketable securities	**116,030**	**119,573**

Marketable securities are held for fund management purposes. The money market instruments are mainly certificates of deposit and commercial papers.

12. Cash and cash equivalents

Cash and cash equivalents in millions of yen

	December 31, 2014	December 31, 2013
Cash - cash in hand and in current or call accounts	105,435	110,810
Cash equivalents - time accounts with a maturity of three months or less	8,602	4,259
Total cash and cash equivalents	**114,037**	**115,070**

13. Other current assets

Other current assets in millions of yen

	December 31, 2014	December 31, 2013
Derivative financial instruments	1,911	7,367
Total financial current assets	**1,911**	**7,367**
Prepaid expenses	7,468	5,302
Total non-financial current assets	**7,468**	**5,302**
Total other current assets	**9,379**	**12,669**

14. Debt

Debt: movements in carrying value of recognized liabilities in millions of yen

	2014	2013
At January 1	233	257
Increase in debt	27	22
Decrease in debt	(46)	(47)
At December 31	**214**	**233**
Finance lease obligations	53	71
Other debt	161	162
Total debt	**214**	**233**
Long-term debt	185	195
Short-term debt	29	38
Total debt	**214**	**233**

15. Provisions and contingent liabilities

Provisions: movements in recognized liabilities in millions of yen

	Environmental provisions	Restructuring provisions	Other provisions	Total
Year ended December 31, 2013				
At January 1, 2013	515	13	1,370	1,898
Additional provisions created	1	211	390	601
Unused amounts reversed	(70)	-	(10)	(80)
Utilized	(1)	(161)	(76)	(239)
Other	-	7	-	7
At December 31, 2013	**444**	**69**	**1,674**	**2,187**
Long-term provisions	444	36	1,601	2,082
Short-term provisions	-	33	72	105
At December 31, 2013	**444**	**69**	**1,674**	**2,187**
Year ended December 31, 2014				
At January 1, 2013	444	69	1,674	2,187
Additional provisions created	83	63	1,070	1,215
Unused amounts reversed	(47)	-	(55)	(102)
Utilized	(28)	(95)	(89)	(212)
Other	-	5	3	8
At December 31, 2014	**453**	**42**	**2,602**	**3,097**
Long-term provisions	235	7	1,868	2,110
Short-term provisions	218	35	734	987
At December 31, 2014	**453**	**42**	**2,602**	**3,097**
Expected outflow of resources				
Within one year	218	35	734	987
Between one to two years	-	7	-	7
Between two to three years	-	-	-	-
More than three years	235	-	1,868	2,102
At December 31, 2014	**453**	**42**	**2,602**	**3,097**

Environmental provisions

Provisions for environmental matters include various separate environmental issues. By their nature the amounts and timings of any outflows are difficult to predict. Significant provisions are discounted where the time value of money is material.

Restructuring provisions

These arise from planned programs that materially change the scope of business undertaken by the Group or the manner in which business is conducted. Such provisions include only the costs necessarily entailed by the restructuring which are not associated with the recurring activities of the Group. The timings of these cash outflows are reasonably certain. These provisions are not discounted as the time value of money is not material in these matters.

Other provisions

Other provisions arise mainly from expected decommissioning and removal costs with respect to property, plant and equipment. The timings of cash outflows are by their nature uncertain. Significant provisions are discounted where the time value of money is material.

Contingent liabilities
The operations and earnings of the Group continue, from time to time and in varying degrees, to be affected by political, legislative, fiscal and regulatory developments, including those relating to environmental protection. The industries in which the Group operates are also subject to other risks of various kinds. The nature and frequency of these developments and events, not all of which are covered by insurance, as well as their effect on future operations and earnings, are not predictable.

The Group has entered into strategic alliances with various companies in order to gain access to potential new products or to utilize other companies to help develop the Group's own potential new products. Potential future payments may become due to certain collaboration partners achieving certain milestones as defined in the collaboration agreements. The Group's best estimates for future commitment payments are given in Note 6.

16. Other non-current liabilities

Other non-current liabilities in millions of yen

	December 31, 2014	December 31, 2013
Deferred income	10,755	9,462
Other long-term liabilities	1,044	1,122
Total other non-current liabilities	**11,799**	**10,584**

17. Accounts payable

Accounts payable in millions of yen

	December 31, 2014	December 31, 2013
Trade payables – third party	7,267	7,128
Trade payables – related party	28,119	28,811
Other taxes payable	4,621	2,420
Accounts payable - purchase of property, plant and equipment	6,560	6,459
Other payables – third party	3,429	3,008
Other payables – related party	12,697	11,719
Total accounts payable	**62,694**	**59,544**

18. Other current liabilities

Other current liabilities in millions of yen

	December 31, 2014	December 31, 2013
Deferred income	701	555
Accrued bonus and related items	9,985	9,595
Derivative financial instruments	199	-
Other accrued liabilities	23,135	15,158
Total other current liabilities	**34,021**	**25,307**

19. Equity attributable to Chugai shareholders

Changes in equity attributable to Chugai shareholders in millions of yen

	Share capital	Capital surplus	Retained earnings	Other reserves			Total
				Fair value reserve	Hedging reserve	Translation reserve	
Year ended December 31, 2013							
At January 1, 2013	72,967	64,668	397,221	1,871	73	(8,839)	527,961
Net income attributable to Chugai shareholders	-	-	50,895	-	-	-	50,895
Available-for-sale investments							
- Fair value gains (losses) taken to equity	-	-	-	2,757	-	-	2,757
- Transferred to income statement on sale or impairment	-	-	-	3	-	-	3
- Income taxes	-	-	-	(926)	-	-	(926)
Cash flow hedges							
- Effective portion of fair value gains (losses) taken to equity	-	-	-	-	7,327	-	7,327
- Transferred to income statement	-	-	-	-	(72)	-	(72)
- Transferred to initial carrying amount of hedged items	-	-	-	-	(657)	-	(657)
- Income taxes	-	-	-	-	(2,508)	-	(2,508)
Currency translation of foreign operations							
- Exchange differences	-	-	-	-	-	8,019	8,019
- Non-controlling interests	-	-	-	-	-	(303)	(303)
Defined benefit plans							
- Remeasurement gains (losses)	-	-	1,496	-	-	-	1,496
- Income taxes	-	-	(532)	-	-	-	(532)
- Non-controlling interests	-	-	(2)	-	-	-	(2)
Other comprehensive income, net of tax	**-**	**-**	**963**	**1,834**	**4,090**	**7,716**	**14,602**
Total comprehensive income	**-**	**-**	**51,858**	**1,834**	**4,090**	**7,716**	**65,497**
Dividends	-	-	(22,866)	-	-	-	(22,866)
Equity compensation plans	-	138	-	-	-	-	138
Own equity instruments	-	962	-	-	-	-	962
At December 31, 2013	**72,967**	**65,768**	**426,213**	**3,704**	**4,163**	**(1,123)**	**571,692**

Changes in equity attributable to Chugai shareholders in millions of yen

	Share capital	Capital surplus	Retained earnings	Other reserves			Total
				Fair value reserve	Hedging reserve	Translation reserve	
Year ended December 31, 2014							
At January 1, 2014	72,967	65,768	426,213	3,704	4,163	(1,123)	571,692
Net income attributable to Chugai shareholders	-	-	50,980	-	-	-	50,980
Available-for-sale investments							
- Fair value gains (losses) taken to equity	-	-	-	1,632	-	-	1,632
- Transferred to income statement on sale or impairment	-	-	-	0	-	-	0
- Income taxes	-	-	-	(582)	-	-	(582)
Cash flow hedges							
- Effective portion of fair value gains (losses) taken to equity	-	-	-	-	(803)	-	(803)
- Transferred to income statement	-	-	-	-	(337)	-	(337)
- Transferred to initial carrying amount of hedged items	-	-	-	-	(5,403)	-	(5,403)
- Income taxes	-	-	-	-	2,491	-	2,491
Currency translation of foreign operations							
- Exchange differences	-	-	-	-	-	862	862
- Non-controlling interests	-	-	-	-	-	(10)	(10)
Defined benefit plans							
- Remeasurement gains (losses)	-	-	(2,256)	-	-	-	(2,256)
- Income taxes	-	-	804	-	-	-	804
- Non-controlling interests	-	-	1	-	-	-	1
Other comprehensive income, net of tax	**-**	**-**	**(1,451)**	**1,050**	**(4,052)**	**851**	**(3,601)**
Total comprehensive income	**-**	**-**	**49,529**	**1,050**	**(4,052)**	**851**	**47,379**
Dividends	-	-	(24,521)	-	-	-	(24,521)
Equity compensation plans	-	(73)	-	-	-	-	(73)
Own equity instruments	-	1,623	-	-	-	-	1,623
At December 31, 2014	**72,967**	**67,317**	**451,220**	**4,755**	**111**	**(271)**	**596,099**

Share capital (Number of shares)

	December 31, 2014	December 31, 2013
Authorized shares	799,805,050	799,805,050
Issued shares (Non-par value common stock)	559,685,889	559,685,889

Dividends

Date of resolution	Type of shares	Total dividends (millions of yen)	Dividend per share (yen)	Record date	Effective date
March 27, 2013 (Resolution of the Annual General Meeting of shareholders)	Common stock	10,885	20	December 31, 2012	March 28, 2013
July 25, 2013 (Board resolution)	Common stock	11,981	22	June 30, 2013	August 30, 2013
March 27, 2014 (Resolution of the Annual General Meeting of shareholders)	Common stock	12,529	23	December 31, 2013	March 28, 2014
July 24, 2014 (Board resolution)	Common stock	11,992	22	June 30, 2014	September 1, 2014
March 26, 2015 (Resolution of the Annual General Meeting of shareholders)	Common stock	14,181	26	December 31, 2014	March 27, 2015

Own equity instruments

	Number of shares	
	2014	2013
At January 1	14,944,320	15,440,438
Issue of common stocks	-	-
Exercises of equity compensation plans	(692,100)	(501,600)
Increase/decrease in own equity instruments	6,217	5,482
At December 31	**14,258,437**	**14,944,320**
Book value (millions of yen)	**33,370**	**34,970**

Other reserves

Fair value reserve: The fair value reserve represents the cumulative net change in the fair value of available-for-sale financial assets until the asset is sold, impaired or otherwise disposed of.

Hedging reserve: The hedging reserve represents the effective portion of the cumulative net change in the fair value of cash flow hedging instruments related to hedged transactions that have not yet occurred.

Translation reserve: The translation reserve represents the cumulative currency translation differences relating to the consolidation of foreign subsidiaries of the Group that use functional currencies other than the Japanese yen.

20. Non-controlling interests

Changes in equity attributable to non-controlling interests in millions of yen

	2014	2013
At January 1	1,512	1,200
Net income attributable to non-controlling interests	1,097	991
Currency translation of foreign operations	10	303
Remeasurements of defined benefit plans	(1)	2
Other comprehensive income, net of tax	**10**	**305**
Total comprehensive income	**1,107**	**1,296**
Dividends to non-controlling shareholders	(962)	(983)
Changes in non-controlling interests	-	-
At December 31	**1,657**	**1,512**

Non-controlling interests are attributable to the minority shareholders of Chugai sanofi-aventis S.N.C. and Chugai Pharma Taiwan Ltd.

21. Employee benefits

Employee benefits expense in millions of yen

	2014	2013
Wages and salaries	64,928	62,652
Social security costs	7,949	7,725
Defined contribution plans	912	867
Operating expenses for defined benefit plans	3,316	3,214
Equity compensation plans	342	292
Other employee benefits	3,386	3,201
Employee benefits expense included in operating results	**80,834**	**77,951**
Net interest cost of defined benefit plans	(63)	(66)
Total employee benefits expense	**80,771**	**77,885**

Other employee benefits consist mainly of welfare costs.

22. Post-employment benefits plans

Post-employment benefit plans are classified as “defined contribution plans” if the Group pays fixed contributions into third-party financial institutions and will have no further legal or constructive obligation to pay further contributions. All other plans are classified as “defined benefit plans”, even if Chugai’s potential obligation is relatively minor or has a relatively remote possibility of arising.

Employees are covered by defined contribution and defined benefit plans sponsored by Group companies, most of which are classified as defined benefit plans.

A resolution was passed in the 98th Annual General Meeting of shareholders held in March 2009 to abolish the retirement benefits system for directors. In addition, a resolution was passed in the 95th Annual General Meeting of shareholders held in March 2006 to abolish the retirement benefits system for outside directors and audit & supervisory board members (including outside audit & supervisory board members).

Defined contribution plans
Defined contribution plans are funded through payments by the Group to funds administered by third parties. The Group’s expenses for these plans were ¥912 million (2013: ¥867 million).

Defined benefit plans
The Group has defined benefit plans mainly comprising a corporate pension fund and a lump-sum retirement benefit plan. Under the corporate pension fund, employees can receive a lump-sum payment based on the number of accumulated points received during their years of service. Employees with over a certain period of service can receive part of or all of the payment as certain annuity or life annuity. Under the lump-sum retirement benefit plan, employees can receive a lump-sum payment based on the number of accumulated points received during their years of service. A retirement benefit trust has been established for the lump-sum retirement benefit plan. Certain employees may be entitled to additional special retirement benefits apart from the defined benefit plans based on the conditions under which termination occurs.

The corporate pension fund and retirement benefit plan trust are independent of the Group and are funded only by payments from the Group. These plan assets are invested in various financial instruments while taking into consideration long-term performance over the duration of the plan liabilities. The funding status is closely monitored at the corporate level and valuations at the balance sheet date are carried out annually.

The defined benefit obligation is calculated using the projected unit credit method. If potential assets arise since defined benefit plans are over-funded, the recognition of pension assets is limited to the present value of any economic benefits available from refunds from the plans or reductions in future contributions to the plan.

Defined benefit plans: income statement in millions of yen

	2014	2013
Current service cost	3,316	3,214
Past service (income) cost	-	-
Settlement (gain) loss	-	-
Total operating expenses	**3,316**	**3,214**
Net interest cost of defined benefit plans	(63)	(66)
Total expense recognized in income statement	**3,253**	**3,148**

Defined benefit plans: funding status in millions of yen

	December 31, 2014	December 31, 2013
Fair value of plan assets	74,897	71,029
Defined benefit obligation	(75,567)	(68,436)
Over (under) funding	**(670)**	**2,593**
Defined benefit plan assets	1,946	3,862
Defined benefit plan liabilities	(2,616)	(1,269)
Net recognized asset (liability)	**(670)**	**2,593**

Defined benefit plans: fair value of plan assets in millions of yen

	2014	2013
At January 1	71,029	66,267
Interest income on plan assets	1,083	1,165
Remeasurements on plan assets	3,340	3,883
Currency translation effects	105	14
Employer contributions	1,992	1,949
Benefits paid – funded plans	(2,652)	(2,250)
At December 31	**74,897**	**71,029**
Composition of plan assets		
- Equity securities	16,437	15,272
- Debt securities	42,237	39,088
- Cash and cash equivalents	9,517	10,182
- Other investments	6,706	6,486
Total plan assets	**74,897**	**71,029**

Equity securities and debt securities have quoted market prices (Level 1 of fair value hierarchy).

Defined benefit plans: present value of defined benefit obligation in millions of yen

	2014	2013
At January 1	68,436	64,334
Current service cost	3,316	3,214
Interest cost	1,021	1,099
Remeasurements – demographic assumption	683	1
Remeasurements – financial assumptions	4,865	2,239
Remeasurements – experience adjustments	48	147
Currency translation effects	113	27
Benefits paid – funded plans	(2,914)	(2,625)
At December 31	**75,567**	**68,436**
Duration in years	15.1	14.8

Actuarial assumptions

Actuarial assumptions are unbiased and mutually compatible estimates of variables that determine the ultimate cost of providing post-employment benefits. They are set on an annual basis by the responsible departments of the Group based on advice from actuaries. Actuarial assumptions consist of demographic assumptions on matters such as mortality and employee turnover, and financial assumptions on matters such as interest rates.

Demographic assumptions: Demographic assumptions relate to mortality and employee turnover rates. Mortality rates are based on the standard mortality rate stated in the Ordinance for Enforcement of the Defined-Benefit Corporate Pension Act. Rates of employee turnover are based on historical behavior within the Group companies.

Financial assumptions: Discount rates are determined mainly with reference to interest rates on high-quality corporate bonds and reflect the period over which the obligations are to be settled.

	December 31, 2014	December 31, 2013
Discount rates (%)	1.08	1.53
Expected inflation rates (%)	-	-

Defined benefit plans: sensitivity of defined benefit obligation to actuarial assumption in millions of yen
The impact resulting from changes of actuarial assumption on the defined benefit obligation is shown in the table below. It is based on the assumption that variables other than the stated assumption used for the calculation are held constant.

	2014
Discount rates	
- 0.25% increase	(2,755)
- 0.25% decrease	2,880
Expected inflation rates	
- 0.25% increase	-
- 0.25% decrease	-
Life expectancy	
- 1 year increase	1,185

Future cash flows
Based on the most recent actuarial valuations, the Group expects that employer contributions for defined benefit plans in 2015 will be approximately ¥2,005 million.

23. Equity compensation plans

The Group operates equity-settled equity compensation plans for directors and certain employees. IFRS 2 "Share-based Payment" requires that the value be estimated by fair value at grant date and recorded as an expense over the vesting period.

Expenses for equity compensation plans in millions of yen

	2014	2013
Cost of sales	2	2
Marketing and distribution	36	30
Research and development	43	32
General and administration	260	228
Total	**342**	**292**
Equity-settled plans		
- Chugai common stock options	225	173
- Chugai stock options as stock-based compensation	117	119

Cash inflow from equity compensation plans in millions of yen

	2014	2013
Equity-settled plans		
- Exercises of Chugai common stock options	1,226	820
- Exercises of Chugai stock options as stock-based compensation	0	-

Chugai common stock options

The Group has issued stock acquisition rights to directors and certain employees as common stock options. Each right entitles the holder to purchase 100 Chugai shares at a specified exercise price. The rights are non-tradable and have an exercise period of around ten years after receiving the rights under the condition of approximately two years of continuous service of the holder after the grant date.

Chugai common stock options – movement in number of rights outstanding

	2014		2013	
	Number of rights	Weighted average exercise price (yen)	Number of rights	Weighted average exercise price (yen)
Outstanding at January 1	23,025	204,917	25,113	190,214
Granted	3,100	267,400	3,270	250,000
Forfeited	-	-	(40)	201,400
Exercised	(6,511)	188,325	(5,016)	163,517
Expired	(413)	172,418	(302)	158,516
Outstanding at December 31	**19,201**	**221,330**	**23,025**	**204,917**
- of which exercisable	12,851	202,966	16,465	206,495

Chugai common stock options – terms of rights outstanding at December 31, 2014

Year of grant	Rights outstanding			Rights exercisable	
	Number outstanding	Weighted average years remaining contractual life	Weighted average exercise price (yen)	Number exercisable	Weighted average exercise price (yen)
2005	510	0.22	164,900	510	164,900
2006	2,101	1.23	224,500	2,101	224,500
2007	2,841	2.23	303,900	2,841	303,900
2008 – no awards	-	-	-	-	-
2009	1,410	4.23	169,600	1,410	169,600
2010	1,631	5.31	188,100	1,631	188,100
2011	1,730	6.40	139,700	1,730	139,700
2012	2,628	7.31	152,800	2,628	152,800
2013	3,250	8.32	250,000	-	-
2014	3,100	9.31	267,400	-	-
Total	**19,201**	**5.72**	**221,330**	**12,851**	**202,966**

Chugai stock options as stock-based compensation

The Group has issued stock acquisition rights to directors as stock options as stock-based compensation since 2009 in lieu of the retirement benefit system for directors which was abolished. Each right entitles the holder to purchase 100 Chugai shares at an exercise price of ¥100. The rights are non-tradable and have an exercise period of 30 years after receiving the rights, which may be vested upon the holder's retirement as a director of Chugai.

Chugai stock options as stock-based compensation – movement in number of rights outstanding

	2014		2013	
	Number of rights	Weighted average exercise price (yen)	Number of rights	Weighted average exercise price (yen)
Outstanding at January 1	3,360	100	2,838	100
Granted	461	100	522	100
Forfeited	-	-	-	-
Exercised	(410)	100	-	-
Expired	-	-	-	-
Outstanding at December 31	**3,411**	**100**	**3,360**	**100**
- of which exercisable	-	-	-	-

Chugai stock options as stock-based compensation – terms of rights outstanding at December 31, 2014

Year of grant	Rights outstanding			Rights exercisable	
	Number outstanding	Weighted average years remaining contractual life	Weighted average exercise price (yen)	Number exercisable	Weighted average exercise price (yen)
2009	519	24.31	100	-	-
2010	579	25.31	100	-	-
2011	672	26.40	100	-	-
2012	723	27.31	100	-	-
2013	457	28.32	100	-	-
2014	461	29.31	100	-	-
Total	**3,411**	**26.74**	**100**	**-**	**-**

Fair value measurement

The inputs used in the measurement of the fair values at grant date of the stock acquisition rights in 2014 are set out below. Expected volatility was determined primarily based on historically observed prices of the underlying equity (same as exercise period).

Chugai common stock option in 2014

Number of rights granted	3,100
Granted common stocks per right	100
Date of grant	May 12, 2014
Vesting period	May 12, 2014 – April 25, 2016
Contractual life(*)	May 12, 2014 – April 24, 2024
Fair value of rights at grant date	¥792
Model used	Binomial
Inputs to option pricing model	
- Share price at grant date	¥263,400
- Exercise price	¥267,400
- Expected volatility	30.49 %
- Expected dividend yield	1.71 %
- Risk-free rate	0.60 %

(*)A person granted the stock acquisition rights cannot exercise the rights during the first two years after the date of approval for issuance.

Chugai stock option as stock-based compensation in 2014

Number of rights granted	461
Granted common stocks per a right	100
Date of grant	May 12, 2014
Vesting period	-
Contractual life(*)	May 12, 2014 – April 24, 2044
Fair value of rights at grant date	¥2,506
Model used	Binomial
Inputs to option pricing model	
- Share price at grant date	¥263,400
- Exercise price	¥100
- Expected volatility	26.33 %
- Expected dividend yield	1.71 %
- Risk-free rate	0.10 %

(*) A person granted the stock acquisition rights can exercise all stock acquisition rights at one time within ten days from the day following the date on which he/she loses the position as a director.

Exercises of stock acquisition rights

	2014		2013	
	Number of rights	Weighted average share price (yen)	Number of rights	Weighted average share price (yen)
Chugai common stock options	6,511	2,951	5,016	2,128
Chugai stock options as stock-based compensation	410	2,577	-	-

24. Earnings per share

Basic earnings per share

	2014	2013
Net income attributable to Chugai shareholders (millions of yen)	**50,980**	**50,895**
Weighted average number of common stock	559,685,889	559,685,889
Weighted average number of treasury stock	(14,630,702)	(15,161,596)
Weighted average number of shares in issue	**545,055,187**	**544,524,293**
Basic earnings per share (yen)	**93.53**	**93.47**

Diluted earnings per share

	2014	2013
Net income attributable to Chugai shareholders (millions of yen)	**50,980**	**50,895**
Weighted average number of shares in issue	545,055,187	544,524,293
Adjustment for assumed exercise of equity compensation plans, where dilutive	892,848	659,346
Weighted average number of shares in issue used to calculate diluted earnings per share	**545,948,035**	**545,183,639**
Diluted earnings per share (yen)	**93.38**	**93.35**

There were 5,941 rights of equity compensation plans, which are anti-dilutive, and therefore excluded from the calculation of diluted earnings per share. (2013: 9,897 rights)

25. Statement of cash flows

Cash flows from operating activities

Cash flows from operating activities arise from the Group's primary activities including research and development, manufacturing and sales in the Pharmaceuticals business. These are calculated by the indirect method by adjusting the Group's operating profit for any operating income and expenses that are not cash flows (for example depreciation, amortization and impairment) in order to derive the cash generated from operations. Operating cash flows also include income taxes paid on all activities.

Cash generated from operations in millions of yen

	2014	2013
Net income	52,077	51,886
Financing costs	11	12
Other financial income (expense)	(315)	1,782
Income taxes	24,087	25,058
Operating profit	**75,859**	**78,738**
Depreciation of property, plant and equipment	13,688	13,520
Amortization of intangible assets	1,192	970
Impairment of property, plant and equipment	1,775	1,697
Impairment of intangible assets	171	89
Operating expense for defined benefit plans	3,316	3,214
Operating expense for equity-settled equity compensation plans	342	292
Net (income) expense for provisions	99	142
Inventories write-down	1,182	1,013
Other adjustments	1,426	1,283
Cash generated from operations	**99,050**	**100,959**

Cash flows from investing activities

Cash flows from investing activities are principally those arising from the Group's investments in property, plant and equipment and intangible assets. Cash flows connected with the Group's portfolio of marketable securities and other investments are also included, as are any interest and dividend payments received in respect of these securities and investments.

Interest and dividends received in millions of yen

	2014	2013
Interest received	203	271
Dividends received	287	148
Total	**490**	**419**

Cash flows from financing activities

Cash flows from financing activities are primarily dividend payments to Chugai shareholders.

Significant non-cash transactions

There were no significant non-cash transactions (2013: none).

26. Risk management

1) Financial risk management

The Group is exposed to various financial risks arising from its underlying operations and corporate finance activities. The Group's financial risk exposures are predominantly related to changes in foreign exchange rates, interest rates and equity prices as well as the creditworthiness and the solvency of the Group's counterparties.

Financial risk management within the Group is governed by policies reviewed by the board of directors of Chugai. These policies cover credit risk, liquidity risk and market risk. The policies provide guidance on risk limits, type of authorized financial instruments and monitoring procedures. The policies prohibit the use of derivative financial instruments for speculative trading purposes. Policy implementation and day-to-day risk management are carried out by the relevant functions and regular reporting on these risks is performed by the relevant finance & accounting and controlling functions within Chugai.

(i) Credit risk

Accounts receivable are exposed to customer credit risk. The main accounts receivable are trade receivables. The management of trade receivables is focused on the assessment of country risk, setting of credit limits, ongoing credit evaluation and account monitoring procedures. As part of the credit risk management, sales administration departments regularly monitor the financial position of major customers by checking payment term and balances of trade receivables for each customer according to the accounting manuals to ensure early identification and mitigation of overdue balances and potential bad debts associated with the deterioration of customers' financial position.

The objective of the management of trade receivables is to sustain the growth and profitability of the Group by optimizing asset utilization while maintaining risks at an acceptable level. The Group obtains credit insurance and similar enhancements when appropriate to protect the collection of trade receivables. No material collateral was held for trade receivables (2013: none).

Of the Group's accounts receivable, trade receivables from third parties are mainly to Japanese customers, of which major customers account for 72% as of December 31, 2014.

Trade receivables: major customers in millions of yen

	December 31, 2014	December 31, 2013
Alfresa Corporation	29,876	26,185
Mediceo Corporation	28,875	20,575
Suzuken Co., Ltd.	19,513	14,075
Toho Pharmaceutical Co., Ltd.	11,280	11,719
Total	**89,545**	**72,554**

Aging of accounts receivable that are not impaired in millions of yen

	December 31, 2014	December 31, 2013
Neither overdue nor impaired	159,698	128,043
Overdue less than 1 month	49	131
Overdue 1-3 months	12	0
Overdue 4-6 months	4	8
Overdue 7-12 months	-	-
Overdue more than 1 year	9	-
Total	**159,773**	**128,182**

Derivative transactions and money market instruments are restricted to financial institutions with high credit ratings in an effort to mitigate the counterparty risks.

The maximum exposure to credit risk resulting from financial activities, without taking into account any collateral held or other credit enhancements, is equal to the carrying value of the Group's financial assets.

Impairment losses by asset class

The Group's impairment loss on available-for-sale investments was not material (2013: ¥3 million).

(ii) Liquidity risk

Liquidity risk arises through a surplus of financial obligations over available financial assets due at any point in time. The Group's approach to liquidity risk is to maintain sufficient readily available reserves in order to meet its liquidity requirements at any point in time. The Group manages liquidity risks based on a cash management plan prepared and updated as appropriate by finance and accounting departments based on the reporting from each department.

Chugai is rated as highly creditable by more than one major credit rating agency. The ratings will permit efficient access to the international capital markets in the event of major financing requirements. Chugai has unused committed credit lines with various financial institutions totaling ¥40,000 million (2013: ¥40,000 million).

Contractual maturities of financial liabilities in millions of yen

	Total	0-3 months	4-6 months	7-12 months	Over 1 year
Year ended December 31, 2014					
Accounts payable	62,694	60,520	2,173	-	0
Other current liabilities					
- Derivative financial instruments	199	199	-	-	-
Total financial liabilities	**62,893**	**60,720**	**2,173**	**-**	**0**
Year ended December 31, 2013					
Accounts payable	59,544	55,680	3,864	-	-
Other current liabilities					
- Derivative financial instruments	-	-	-	-	-
Total financial liabilities	**59,544**	**55,680**	**3,864**	**-**	**-**

(iii) Market risk

Market risk arises from changing market prices, mainly due to foreign exchange rates and interest rates, of the Group's financial assets or financial liabilities which affect the Group's net income and equity.

Foreign exchange risk: Accounts receivable and accounts payable denominated in foreign currencies are exposed to foreign exchange risk. The objective of the Group's foreign exchange risk management activities is to preserve the economic value of its current and future assets and to minimize the volatility of the Group's financial result. The Group enters into derivative transactions such as foreign exchange forward contracts and currency options to reduce the risk of foreign currency exchange fluctuations related to assets and liabilities denominated in foreign currencies. Some of these transactions qualify as cash flow hedges at the point that the forecast transaction is expected.

When making use of derivatives for hedging foreign exchange risk on assets and liabilities denominated in foreign currencies, Chugai conducts such operations in accordance with its internal regulations and monthly reports are prepared on the balance of such transactions, valuation gains and losses, and other related matters at fair value. Consolidated subsidiaries do not utilize derivative transactions.

Sensitivity analysis: Chugai has financial instruments denominated in currencies other than its functional currency. The table below shows the impact to profit before taxes resulting from a 1% decrease of the Swiss franc, euro and U.S. dollar against the Japanese yen, which is Chugai's functional currency. The effective portion of derivative financial instruments for which hedge accounting is applied is excluded from the calculation. All calculations are based on the assumption that exchange rates for other currencies are constant and there are no changes in other variables such as interest rates.

Foreign currency sensitivity analysis

	2014	2013
Average exchange rate (yen per each currency)		
CHF	115.69	105.24
EUR	140.49	129.51
USD	105.84	97.54
Profit before taxes (millions of yen)		
CHF	(39)	39
EUR	15	(2)
USD	33	14

(Note) Positive numbers are the amount of positive impact on profit before taxes resulting from a 1% decrease of each currency against the Japanese yen. The amounts above do not reflect the impact on Chugai's cash flows or forecast result.

The impact resulting from a 1% decrease of each currency against the Japanese yen on the financial instruments denominated in foreign currency is shown in the tables below.

	2014			2013		
	Exposure (m CHF)	Exposure (m YEN)	Impact (m YEN)	Exposure (m CHF)	Exposure (m YEN)	Impact (m YEN)
CHF						
Accounts receivable	184	22,189	(222)	140	16,635	(166)
Accounts payable	(306)	(36,947)	369	(333)	(39,417)	394
Financial non-current assets	-	-	-	-	-	-
Cash and cash equivalents	69	8,336	(83)	69	8,196	(82)
Notional amounts of derivative financial instruments						
- Effective portion of hedge	(100)	(12,214)	-	426	50,405	-
- Other than above	85	10,362	(104)	90	10,645	(106)
Total	**(68)**	**(8,274)**	**(39)**	**393**	**46,464**	**39**
	Exposure (m EUR)	Exposure (m YEN)	Impact (m YEN)	Exposure (m EUR)	Exposure (m YEN)	Impact (m YEN)
EUR						
Accounts receivable	4	645	(6)	3	377	(4)
Accounts payable	(15)	(2,154)	22	(1)	(192)	2
Financial non-current assets	-	-	-	-	-	-
Cash and cash equivalents	-	-	-	-	-	-
Notional amounts of derivative financial instruments						
- Effective portion of hedge	-	-	-	-	-	-
- Other than above	-	-	-	-	-	-
Total	**(10)**	**(1,509)**	**15**	**1**	**185**	**(2)**
	Exposure (m USD)	Exposure (m YEN)	Impact (m YEN)	Exposure (m USD)	Exposure (m YEN)	Impact (m YEN)
USD						
Accounts receivable	6	683	(7)	3	342	(3)
Accounts payable	(33)	(3,953)	40	(16)	(1,714)	17
Financial non-current assets	-	-	-	-	-	-
Cash and cash equivalents	-	-	-	-	-	-
Notional amounts of derivative financial instruments						
- Effective portion of hedge	110	13,231	-	90	9,472	-
- Other than above	-	-	-	-	-	-
Total	**83**	**9,961**	**33**	**77**	**8,100**	**14**

Interest rate risk: The amounts of debt and loans were insignificant and therefore the Group is not exposed to material interest rate risk.

2) Financial instruments fair value

Carrying value and fair value of financial instruments

The Group's financial instruments are mainly comprised of financial non-current assets, accounts receivable, marketable securities, cash and cash equivalents, derivative financial instruments included in other current assets, accounts payable, derivative financial instruments included in other current liabilities and debt. The carrying values of these financial instruments are equal to or reasonably approximate fair values.

Fair value hierarchy

The table below analyses financial instruments carried at fair value, by valuation method. The different levels have been defined as follows:

- Level 1 – quoted prices (unadjusted) in active markets for identical assets and liabilities.
- Level 2 – observable inputs other than quoted prices in active markets for identical assets and liabilities.
- Level 3 – fair value determined using valuation method which includes unobservable inputs.

Fair value hierarchy of financial instruments in millions of yen

	Level 1	Level 2	Level 3	Total
At December 31, 2014				
Marketable securities:				
- Money market instruments and time accounts over 3 months	-	116,030	-	116,030
- Debt securities	-	-	-	-
Other current assets				
- Derivative financial instruments	-	1,911	-	1,911
Financial non-current assets				
- Available-for-sale investments	9,318	-	1,438	10,755
Financial assets recognized at fair value	**9,318**	**117,941**	**1,438**	**128,696**
Other current liabilities				
- Derivative financial instruments	-	(199)	-	(199)
Financial liabilities recognized at fair value	**-**	**(199)**	**-**	**(199)**
At December 31, 2013				
Marketable securities:				
- Money market instruments and time accounts over 3 months	-	119,573	-	119,573
- Debt securities	-	-	-	-
Other current assets				
- Derivative financial instruments	-	7,367	-	7,367
Financial non-current assets				
- Available-for-sale investments	8,506	-	461	8,966
Financial assets recognized at fair value	**8,506**	**126,940**	**461**	**135,906**
Other current liabilities				
- Derivative financial instruments	-	-	-	-
Financial liabilities recognized at fair value	**-**	**-**	**-**	**-**

Level 1 financial assets consist of government bonds, corporate bonds and quoted shares. Level 2 financial assets consist primarily of commercial paper, certificates of deposit and derivative financial instruments.

Level 2 fair value for marketable securities and derivative financial instruments is based on valuation models that use observable market data for interest rates, yield curves, foreign exchange rates and implied volatilities for similar instruments at the measurement date.

The Group recognizes transfers between levels of the fair value hierarchy as of the end of the reporting period during which the transfer has occurred. There were no significant transfers between Level 1 and Level 2 and vice versa.

Level 3 financial assets consist of unquoted shares.

Reconciliation of financial instruments classified into level 3 in millions of yen

	Fair value through other comprehensive income	Fair value through income statement	Total
At January 1, 2013	462	-	462
Gains or losses	(3)	-	(3)
Purchases	-	-	-
Disposals	-	-	-
Transfers	-	-	-
Currency translation effects	2	-	2
At December 31, 2013	**461**	**-**	**461**
At January 1, 2014	461	-	461
Gains or losses	826	-	826
Purchases	152	-	152
Disposals	(1)	-	(1)
Transfers	-	-	-
Currency translation effects	1	-	1
At December 31, 2014	**1,438**	**-**	**1,438**

3) Derivative financial instruments

Derivative financial instruments in millions of yen

Assets	December 31, 2014	December 31, 2013
Forward exchange contracts	1,911	7,367
Currency options	-	-
Total derivative financial instruments	**1,911**	**7,367**

Liabilities	December 31, 2014	December 31, 2013
Forward exchange contracts	(199)	-
Currency options	-	-
Total derivative financial instruments	**(199)**	**-**

Hedge accounting

The Group has the following cash flow hedges which are designated in a qualifying hedge relationship.

Cash flow hedges

The Group is exposed to foreign exchange risk from transactions for inventories and other materials in foreign currencies with foreign related parties. The Group has entered into foreign exchange forward contracts and currency options to hedge a part of foreign exchange risk. Such instruments are recorded as fair value assets of ¥172 million (2013: ¥6,715 million). There was no ineffective portion.

The present value of expected cash flows from qualifying cash flow hedges are shown in the table below.

Present value of expected cash flows of qualifying cash flow hedges in millions of yen

	Total	0-6 months	7-12 months	Over 1 year
Year ended December 31, 2014				
Cash inflows	25,483	10,298	15,185	-
Cash outflows	(25,310)	(10,215)	(15,095)	-
Total cash inflow (outflow)	**172**	**82**	**90**	**-**
Year ended December 31, 2013				
Cash inflows	59,877	18,802	31,015	10,059
Cash outflows	(53,162)	(16,872)	(27,467)	(8,823)
Total cash inflow (outflow)	**6,715**	**1,930**	**3,548**	**1,236**

4) Capital management

The Group defines the capital that it manages as the Group's total capitalization, being the sum of debt plus equity including non-controlling interests. The Group's objectives when managing capital are:

- To safeguard the Group's ability to continue as a going concern, so that it can continue to provide benefits for patients and returns to investors.
- To provide an adequate return to investors based on the level of risk undertaken.
- To have available the necessary financial resources to allow the Group to invest in areas that may deliver future benefits for patients and returns to investors.
- To maintain sufficient financial resources to mitigate against risks and unforeseen events.

Capitalization is monitored and reported to the Chief Financial Officer as part of the Group's regular internal management reporting.

The Group is not subject to regulatory capital adequacy requirements.

Capital in millions of yen

	December 31, 2014	December 31, 2013
Capital and reserves attributable to Chugai shareholders	596,099	571,692
Equity attributable to non-controlling interests	1,657	1,512
Total equity	**597,756**	**573,204**
Total debt	214	233
Capitalization	**597,970**	**573,437**

27. Related parties

1) Controlling shareholder

Effective October 1, 2002, Roche and Chugai completed an alliance to create a leading research-driven Japanese pharmaceutical company, which was formed by the merger of Chugai and Roche's Japanese pharmaceuticals subsidiary, Nippon Roche. Through the merger, Chugai become a principal member of the Roche Group as the surviving company.

Chugai has entered into certain agreements with Roche, which are discussed below:

Basic Alliance Agreement: As part of the Basic Alliance Agreement signed in December 2001, Roche and Chugai entered into certain arrangements covering the future operation and governance of Chugai. Amongst other matters these cover the following areas:

- The structuring of the alliance.
- Roche's rights as a shareholder.
- Roche's rights to nominate members of Chugai's Board of Directors.
- Certain limitations to Roche's ability to buy or sell Chugai's common stock.

Chugai issues additional shares of common stock in connection with its convertible debt and equity compensation plans, and may issue additional shares for other purposes, which affects Roche's percentage ownership interest. The Basic Alliance Agreement provides, amongst other matters, that Chugai will guarantee Roche's right to maintain its shareholding percentage in Chugai at not less than 50.1%.

Licensing Agreements: Under the Japan Umbrella Rights Agreement signed in December 2001, Chugai has exclusive rights to market Roche's pharmaceutical products in Japan. Chugai also has right of first refusal on the development and marketing in Japan of all development compounds advanced by Roche.

The Rest of the World Umbrella Rights Agreement (excluding Japan and South Korea) signed in May 2002 was revised and the Amended and Restated Rest of the World Umbrella Rights Agreement (excluding Japan, South Korea and Taiwan) was signed in August 2014. Under this Agreement, Roche has the right of first refusal on the development and marketing of Chugai's development compounds in markets outside Japan, excluding South Korea and Taiwan.

Further to these agreements, Roche and Chugai have signed a series of separate agreements for certain specific products. Depending on the specific circumstances and the terms of the agreement, this may result in payments on an arm's length basis between Roche and Chugai, for any or all of the following matters:

- Upfront payments, if a right of first refusal to license a product is exercised.
- Milestone payments, dependent upon the achievement of agreed performance targets.
- Royalties on future product sales.

These specific product agreements may also cover the manufacture and supply of the respective products to meet the other party's clinical and/or commercial requirements on an arm's length basis.

Research Collaboration Agreements: Roche and Chugai have entered into research collaboration agreements in the areas of small-molecule synthetic drug research and biotechnology-based drug discovery.

Dividends: The dividends distributed to Roche by Chugai in respect to its holdings of Chugai shares totaled ¥15,085 million (2013: ¥14,079 million).

2) Material transactions and balances with related parties

Transactions with F. Hoffmann-La Roche in millions of yen

	2014	2013
Sales	55,051	42,909
Purchases of inventory and other materials	122,189	112,799

Balances with F. Hoffmann-La Roche in millions of yen

	December 31, 2014	December 31, 2013
Accounts receivable	28,201	22,245
Accounts payable	(37,447)	(39,417)

3) Key management personnel

The operating functions of Chugai are retained by the members of the Board of Directors who act as the chief operating decision-maker. The term of office for directors expires at the conclusion of the Annual General Meeting of shareholders held with respect to the last business year ending within two years after election. The term of office for audit & supervisory board members expires at the conclusion of the Annual General Meeting of shareholders held with respect to the last business year ending within four years after election.

Remuneration of members of the board and audit & supervisory board members in millions of yen

	2014	2013
Board of directors		
- Regular remuneration	349	335
- Bonuses	220	186
- Chugai common stock options	104	78
- Chugai stock options as stock-based compensation	117	119
Total	**790**	**718**
Audit & supervisory board members		
- Regular remuneration	85	85
Total	**85**	**85**

28. Subsidiaries

Subsidiaries	Country of Incorporation	Equity interest %	
		2014	2013
Consolidated subsidiaries			
Chugai Research Institute for Medical Science, Inc.	Japan	100 %	100 %
Chugai Clinical Research Center Co., Ltd.	Japan	100 %	100 %
Chugai Business Support Co., Ltd.	Japan	100 %	100 %
Medical Culture, Inc.	Japan	100 %	100 %
Chugai Distribution Co., Ltd.	Japan	100 %	100 %
Chugai Pharma Manufacturing Co., Ltd.	Japan	100 %	100 %
Forerunner Pharma Research Co., Ltd.	Japan	100 %	100 %
Chugai U.S.A. Inc.	United States	100 %	100 %
Chugai Pharma U.S.A., LLC	United States	100 %	100 %
Chugai Pharma Europe Ltd.	United Kingdom	100 %	100 %
Chugai Pharma U.K. Ltd.	United Kingdom	100 %	100 %
Chugai Pharma Marketing Ltd.	United Kingdom	100 %	100 %
Chugai Pharma France S.A.S.	France	100 %	100 %
Chugai sanofi-aventis S.N.C.	France	55 %	55 %
Chugai Pharma Taiwan Ltd.	Taiwan	70 %	70 %
Chugai Pharma R&D Taiwan Ltd.	Taiwan	100 %	100 %
Chugai Pharma (Shanghai) Consulting Co., Ltd.	China	100 %	100 %
Chugai Pharma Science (Beijing) Co., Ltd.	China	100 %	100 %
Chugai Pharma China Co., Ltd.	China	100 %	-
Chugai Pharmabody Research Pte. Ltd.	Singapore	100 %	100 %

29. Subsequent events

There were no material subsequent events (2013: none).

Independent Auditor's Report

Independent Auditor's Report

To the Board of Directors of Chugai Pharmaceutical Co., Ltd.:

We have audited the accompanying consolidated financial statements of Chugai Pharmaceutical Co., Ltd. and its consolidated subsidiaries, which comprise the consolidated balance sheet as at December 31, 2014, and the consolidated income statement, statement of comprehensive income, statement of changes in equity and statement of cash flows for the year then ended, and notes, comprising a summary of significant accounting policies and other explanatory information.

Management's Responsibility for the Consolidated Financial Statements

Management is responsible for the preparation and fair presentation of these consolidated financial statements in accordance with International Financial Reporting Standards, and for such internal control as management determines is necessary to enable the preparation of consolidated financial statements that are free from material misstatement, whether due to fraud or error.

Auditor's Responsibility

Our responsibility is to express an opinion on these consolidated financial statements based on our audit. We conducted our audit in accordance with auditing standards generally accepted in Japan. Those standards require that we comply with ethical requirements and plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free from material misstatement.

An audit involves performing procedures to obtain audit evidence about the amounts and disclosures in the consolidated financial statements. The procedures selected depend on our judgement, including the assessment of the risks of material misstatement of the consolidated financial statements, whether due to fraud or error. In making those risk assessments, we consider internal control relevant to the entity's preparation and fair presentation of the consolidated financial statements in order to design audit procedures that are appropriate in the circumstances, while the objective of the financial statement audit is not for the purpose of expressing an opinion on the effectiveness of the entity's internal control. An audit also includes evaluating the appropriateness of accounting policies used and the reasonableness of accounting estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements.

We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinion.

Opinion

In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of Chugai Pharmaceutical Co., Ltd. and its consolidated subsidiaries as at December 31, 2014, and their financial performance and cash flows for the year then ended in accordance with International Financial Reporting Standards.

KPMG AZSA LLC

March 26, 2015
Tokyo, Japan

Network (As of June 25, 2015)

Chugai Pharmaceutical

Head Office

1-1 Nihonbashi-Muromachi 2-chome,
Chuo-ku, Tokyo 103-8324 Japan
Tel +81-(0)3-3281-6611
URL: http://www.chugai-pharm.co.jp/english

Research Laboratories

Fuji Gotemba Research Laboratories
1-135 Komakado, Gotemba City, Shizuoka Pref.
412-8513 Japan
Tel +81-(0)550-87-3411

Kamakura Research Laboratories
200 Kajiwara, Kamakura City, Kanagawa Pref.
247-8530 Japan
Tel +81-(0)467-47-2260

Ukima Research Laboratories
5-5-1 Ukima, Kita-ku, Tokyo 115-8543 Japan
Tel +81-(0)3-3968-6111

Plants (Chugai Pharma Manufacturing Co., Ltd.)

Ukima Plant
5-5-1 Ukima, Kita-ku, Tokyo 115-8543 Japan
Tel +81-(0)3-3968-6111

Fujieda Plant
2500 Takayanagi, Fujieda City, Shizuoka Pref.
426-0041 Japan
Tel +81-(0)54-635-2311

Utsunomiya Plant
16-3 Kiyohara-Kogyodanchi, Utsunomiya City,
Tochigi Pref. 321-3231 Japan
Tel +81-(0)28-667-7611

Branches

Domestic

Sapporo Branch
Nihon Seimei Sapporo Bldg., 4-1-1
Kita-sanjo-Nishi, Chuo-ku, Sapporo City,
Hokkaido 060-0003 Japan
Tel +81-(0)11-271-5311

Sendai Branch
Sankyo Sendai Bldg., 1-12-7 Honcho,
Aoba-ku, Sendai City, Miyagi Pref.
980-0014 Japan
Tel +81-(0)22-225-8551

Tokyo Branch 1
Shinjuku NS Bldg., 2-4-1 Nishi-Shinjuku,
Shinjuku-ku, Tokyo 163-0807 Japan
Tel +81-(0)3-3346-0211

Tokyo Branch 2
Omiya Center Bldg., 1-9-6 Sakuragicho,
Omiya-ku, Saitama City, Saitama Pref.
330-0854 Japan
Tel +81-(0)48-642-4771

Yokohama Branch
Yokohama East Square, 1-4 Kinkoucho,
Kanagawa-ku, Yokohama City,
Kanagawa Pref. 221-0056 Japan
Tel +81-(0)45-450-7670

Nagoya Branch
KDX Sakuradori Bldg., 3-20-17
Marunouchi, Naka-ku,
Nagoya City, Aichi Pref. 460-0002 Japan
Tel +81-(0)52-961-8511

Kyoto Branch
Karasuma Chuo Bldg., 659 Tearaimizu-cho,
Nishikikoji-agaru, Karasuma-dori,
Nakagyo-ku, Kyoto City, Kyoto
604-8152 Japan
Tel +81-(0)75-212-6090

Osaka Branch
Uemura Nissei Bldg., 3-3-31 Miyahara,
Yodogawa-ku, Osaka City, Osaka
532-0003 Japan
Tel +81-(0)6-6350-6355

Hiroshima Branch
Nissei Hiroshima Bldg., 7-32
Nakamachi, Naka-ku, Hiroshima City,
Hiroshima Pref. 730-0037 Japan
Tel +81-(0)82-543-6100

Takamatsu Branch
Ichigo Takamatsu Bldg., 2-2-7 Kotobuki-cho,
Takamatsu City, Kagawa Pref. 760-0023
Japan
Tel +81-(0)87-811-6988

Fukuoka Branch
Echo Bldg., 2-13-34 Hakataeki-higashi,
Hakata-ku, Fukuoka City, Fukuoka Pref.
812-0013 Japan
Tel +81-(0)92-451-8181

Domestic Subsidiaries

Chugai Clinical Research Center Co., Ltd.
1-1 Nihonbashi-Muromachi 2-chome,
Chuo-ku, Tokyo 103-8324 Japan
(within the Chugai Pharmaceutical Head Office)
Tel+81-(0)3-3273-1173

Chugai Research Institute for Medical Science, Inc. (Head Office)
1-135 Komakado, Gotemba City,
Shizuoka Pref. 412-8513 Japan
(within the Fuji Gotemba Research Laboratories)
Tel +81-(0)550-87-5425

Chugai Business Support Co., Ltd.
5-5-1 Ukima, Kita-ku, Tokyo
115-8543 Japan
(within the Ukima Representative Office)
Tel +81-(0)3-3968-8760

Medical Culture Inc.
Muromachi CS Bldg., 4-6-5
Nihonbashi-Muromachi,
Chuo-ku, Tokyo 103-0022 Japan
Tel +81-(0)3-5202-8270

Chugai Distribution Co., Ltd.
1-20, Okuwa, Kazo City, Saitama Pref.
347-0010 Japan
(within the Kazo Distribution Center)
Tel +81-(0)480-76-0381

Chugai Pharma Manufacturing Co., Ltd.
5-5-1 Ukima, Kita-ku, Tokyo
115-8543 Japan
(within the Ukima Representative Office)
Tel +81-(0)3-3968-6200

Forerunner Pharma Research Co., Ltd.
4-2-16 Komaba, Meguro-ku, Tokyo
153-0041 Japan
Tel +81-(0)3-5465-0871

Overseas Subsidiaries, Affiliates and R&D Partners

Chugai Pharma U.K. Ltd.
Mulliner House, Flanders Road,
Turnham Green, London W4 1 NN U.K.
Tel +44-(0)20-8987-5680

Chugai Pharma Marketing Ltd.
Mulliner House, Flanders Road,
Turnham Green, London W4 1 NN U.K.
Tel +44-(0)20-8987-5600

Germany Branch
Lyoner Straße 15 60528
Frankfurt/M, Germany
Tel +49-(0)69-663000-0

Chugai Pharma France SAS
Tour Franklin, Arche SUD,
100/101 Quartier Boieldieu
92042 Paris La Défense Cedex, France
Tel +33-(0)1-56-37-05-20

Chugai sanofi-aventis S.N.C.
9 rue du Président Allendé
94256 Gentilly Cedex, France
Tel +33-(0)1-41-24-66-69

Chugai USA, Inc.
300 Connell Drive, Suite 3100
Berkeley Heights, NJ 07922 U.S.A.
Tel +1-908-516-1350

Chugai Pharma USA, LLC
300 Connell Drive, Suite 3100
Berkeley Heights, NJ 07922 U.S.A.
Tel +1-908-516-1350

Chugai Pharma China Co., Ltd.
Bldg. G31, No. 801 Jiankang Dadao,
Medical City, Taizhou, Jiangsu 225300 China
Tel +86-(0)523-8681-9823

Shanghai Branch
Unit 2901, Central Plaza, No. 381
Central Huaihai Road,
Shanghai 200020 China
Tel +86-(0)21-6319-0388

Beijing Branch
2101 Beijing Fortune Bldg.
No. 5, Dong San Huan Bei Lu,
Chao Yang District,
Beijing 100004 China
Tel +86-(0)10-6590-8066

Guangzhou Branch
Unit 2508B, Yian Plaza,
No. 33 Jian She 6th Road,
Guangzhou 510060 China
Tel +86-(0)20-8363-3468

Chugai Pharma Science (Beijing) Co., Ltd.
2103 Beijing Fortune Bldg. No. 5,
Dong San Huan Bei Lu,
Chao Yang District, Beijing 100004 China
Tel +86-(0)10-6590-9556

Chugai Pharma Taiwan Ltd.
3 Fl., No. 73, ZhouZi Street,
Neihu District, Taipei 11493 Taiwan
Tel +886-(0)2-2658-8800

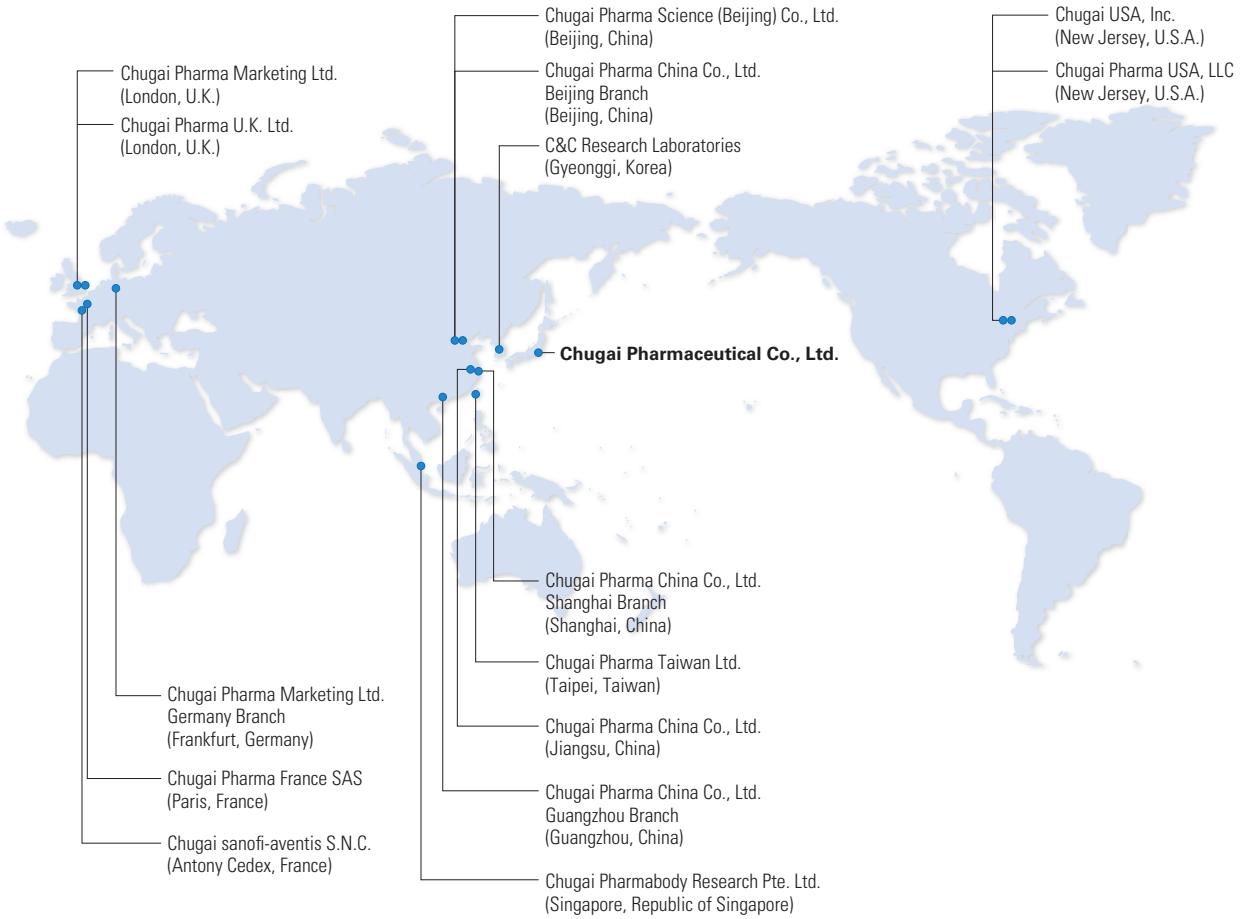
Chugai Pharmabody Research Pte. Ltd.
3 Biopolis Drive, #04-11 to 17 Synapse,
Singapore 138623
Tel +65-(0)6933-4888

C&C Research Laboratories

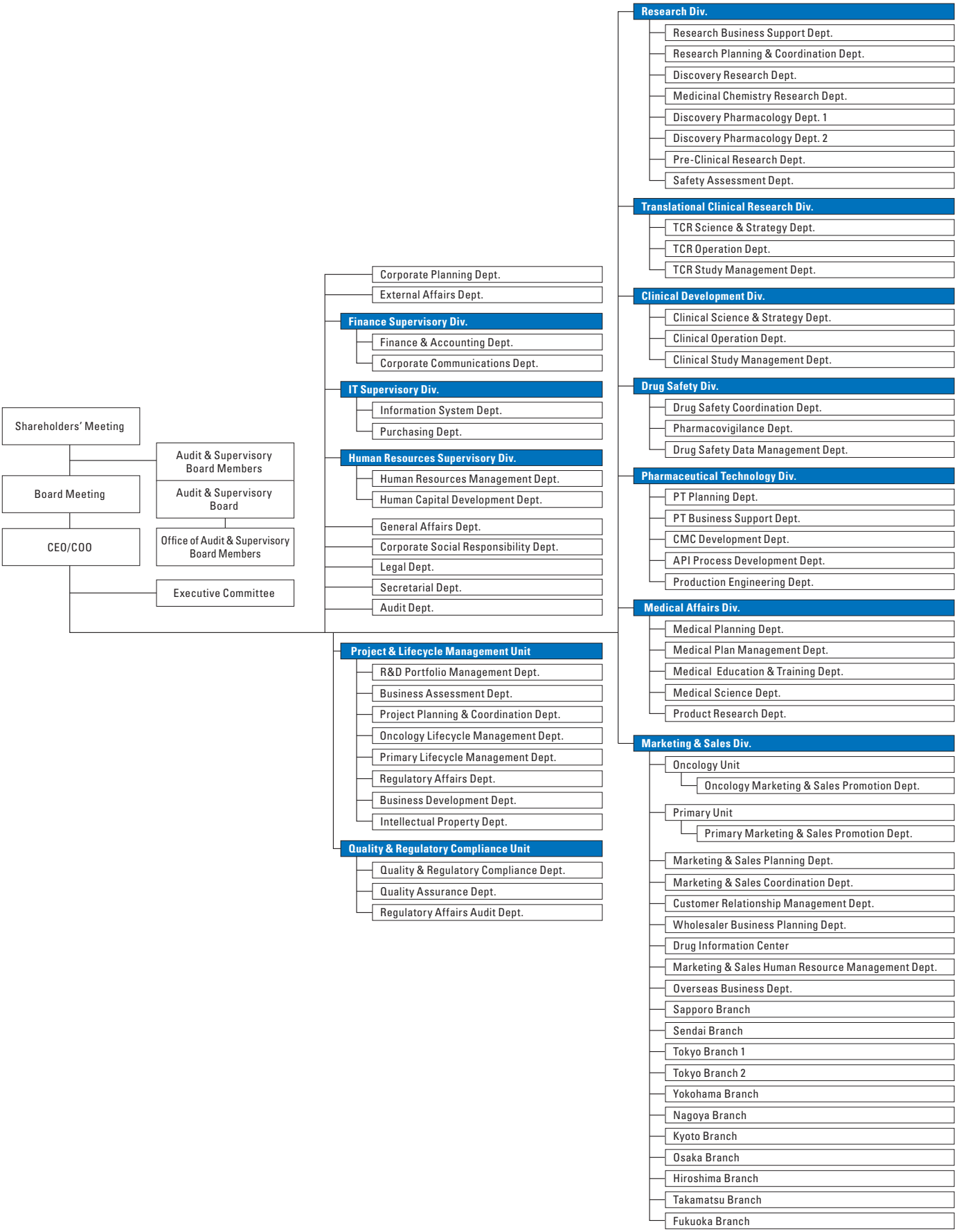
Discovery Research Center
DRC Natural Sciences Campus,
Sungkyunkwan University,
Cheoncheon-dong, Jangan-gu,
Suwon-si, Gyeonggi-do 440-746 Korea
Tel +82-(0)31-8014-6603

Clinical Research Center
903 E&C Venture Dream Tower 3Cha,
197-33 Guro-Dong, Guro-Gu,
Seoul 152-719 Korea
Tel +82-(0)2-858-6226

Chugai's Global Network



Organization (As of April 1, 2015)



Shareholder Information (As of December 31, 2014)

Major Shareholders*

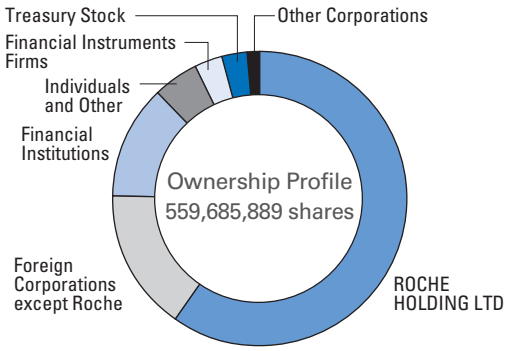
Name	Number of Shares Held (Thousands)	Percentage of Voting Rights (%)
ROCHE HOLDING LTD	335,223	61.48
The Master Trust Bank of Japan, Ltd. (Trust Account)	18,176	3.33
Japan Trustee Services Bank, Ltd. (Trust Account)	15,254	2.79
Nomura Securities Co., Ltd.	7,541	1.38
Goldman Sachs and Company Regular Account	6,289	1.15
Tokio Marine & Nichido Fire Insurance Co., Ltd.	3,787	0.69
BNP Paribas Securities (Japan) Limited	3,610	0.66
Trust & Custody Services Bank, Ltd. (Trust Collateral Account)	3,589	0.65
Chugai Pharmaceutical Employee Shareholders' Association	3,338	0.61
BNP PARIBAS SEC SERVICES LUXEMBOURG/JASDEC/ ABERDEEN GLOBAL CLIENT ASSETS	3,228	0.59

* 14,258,437 shares of treasury stock held by the Company are not included in the above breakdown of major shareholders.

Stock Price Information

	Stock Price	
	Low	High
From January 1, 2014 to December 31, 2014		
First Quarter	¥2,107	¥2,643
Second Quarter	2,405	2,899
Third Quarter	2,797	4,015
Fourth Quarter	2,897	3,500

Classification of Shareholders



ROCHE HOLDING LTD
Shares: 335,223,645 59.89% (Shareholder: 1)

Foreign Corporations except Roche
Shares: 87,080,735 15.55% (Shareholders: 544)

Financial Institutions
Shares: 69,423,557 12.40% (Shareholders: 80)

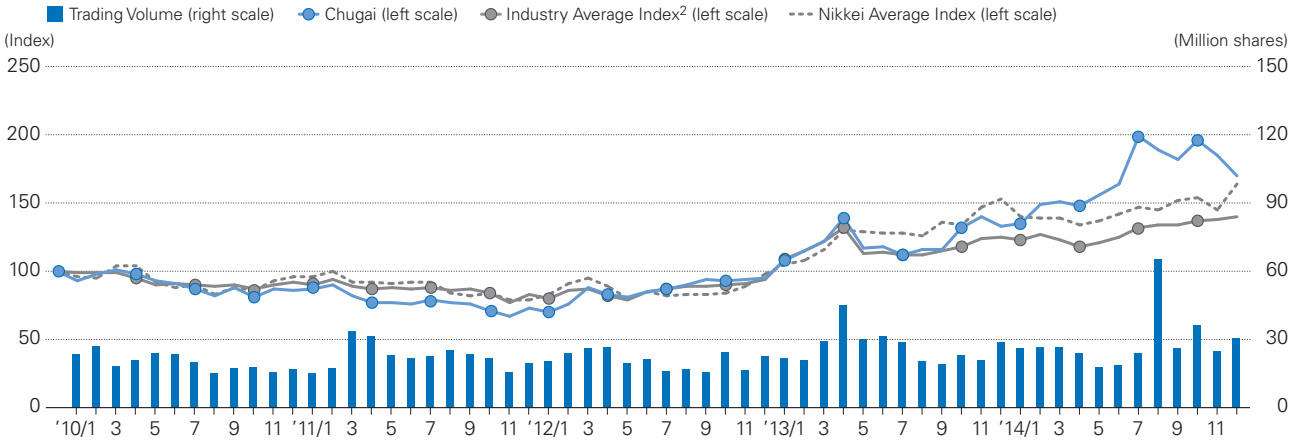
Individuals and Other
Shares: 27,503,413 4.91% (Shareholders: 29,144)

Financial Instruments Firms
Shares: 18,497,083 3.30% (Shareholders: 59)

Treasury Stock
Shares: 14,258,437 2.54% (Shareholder: 1)

Other Corporations
Shares: 7,699,019 1.37% (Shareholders: 210)

Share Performance[1] and Trading Volume

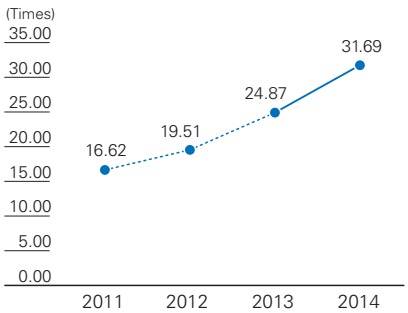


1. Closing price on January 4, 2010 = 100
2. Calculated from the share price of the following eight companies: Takeda, Daiichi-Sankyo, Astellas, Shionogi, Eisai, Mitsubishi-Tanabe, Dainippon-Sumitomo, and Chugai

Share Price Indicators

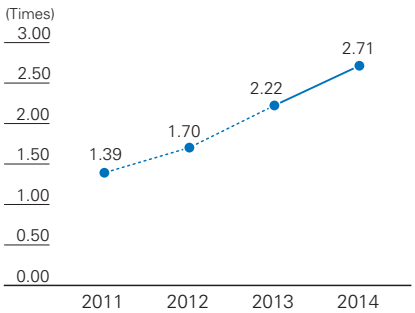
Price/Earnings Ratio

Year-end share price ÷ Basic net income per share



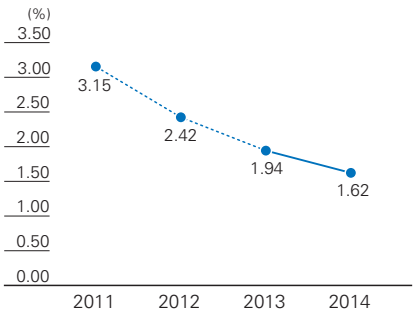
Price/Book Ratio

Year-end share price ÷ Equity per share attributable to Chugai shareholders



Dividend Yield

Dividends per share ÷ Year-end share price



Corporate Data (As of December 31, 2014)

Company Name
Chugai Pharmaceutical Co., Ltd.

Year of Foundation
1925

Year of Establishment
1943

Address
1-1, Nihonbashi-Muromachi 2-chome, Chuo-ku,
Tokyo 103-8324 Japan

Stated Capital
¥72,967 million

Number of Employees
7,023 (Consolidated)

Number of Shares Issued of Common Stock
559,685,889

Number of Shareholders
30,039

Stock Listing
Tokyo Stock Exchange, First Section

Fiscal Year-End
December 31

General Meeting of Shareholders
March

Transfer Agent
Mitsubishi UFJ Trust and Banking Corporation

Public Notices
Public notices are made electronically on the Chugai website (http://www.chugai-pharm.co.jp/ir/) in Japanese. In case electronic communications are unavailable, public notices will be made in the newspaper *Nihon Keizai Shimbun*.

IR website
http://www.chugai-pharm.co.jp/english/ir

CSR website
http://www.chugai-pharm.co.jp/english/csr/

Note: Renewal scheduled for June 30, 2015

For further information, please contact:

Corporate Communications Dept.
Tel: +81-(0)3-3273-3313
Fax: +81-(0)3-3281-6607
E-mail: ir@chugai-pharm.co.jp

Our Corporate Branding Activities

Chugai has renewed its corporate branding and is conducting activities to share its envisioned future and distinctive features and approaches with its stakeholders inside and outside the Company. Our brand website can be viewed using the QR code on the right.

INNOVATION BEYOND IMAGINATION

Innovation all for the patients

CHUGAI PHARMACEUTICAL CO., LTD.

Roche Group

CHUGAI PHARMACEUTICAL CO., LTD.

A member of the Roche group

1-1, Nihonbashi-Muromachi 2-chome, Chuo-ku
Tokyo 103-8324, Japan