



# Creating Innovative Drugs That Address Unmet Medical Need



In 2017, Chugai spent ¥88.9 billion on research and development. As a percentage of revenues, Chugai's R&D expenditures are 16.6%, which is relatively low compared with other Japanese pharmaceutical companies. This is a reflection of the efficiency of Chugai's R&D expenditures, made possible by the strategic alliance with Roche. Taking advantage of this, we have continued to focus on the evolution of our unique research technologies. As a result, 13 products in our development pipeline originate from our own research. Our products currently on the market are already addressing unmet medical need; including products in-licensed from Roche, 74% percent of our product sales qualify for premium pricing, an exceptionally high percentage.

## Strengths

- Cutting-edge drug discovery technologies, especially biotechnology (Technology-driven drug discovery that enables differentiation)
- Strategic alliance with the Roche Group (Sharing of infrastructure, including a rich compound library)

## Challenges

- Increasing difficulty and escalating cost of new drug development worldwide
- Potential paradigm shift in drug discovery due to disruptive technologies
- Lack of adequate standards for governments to assess the value of innovation
- Lack of attractive infrastructure in Japan for retaining top researchers

## Chugai's Commitment to Innovation and Results

Pharmaceuticals have come a long way since the discovery of penicillin in 1928. The application of organic synthesis techniques and genomic technologies, the emergence of therapeutic antibodies, molecular targeted therapies, and other innovative therapies have made a significant contribution to medical treatment. Nevertheless, there are still people suffering from disease all over the world.

The business models of pharmaceutical companies vary, but given our technologies, knowledge, alliance structure and other characteristics, it is clear that continuously creating new treatments to address unmet medical need is the reason for Chugai's existence, and that is linked to benefiting patients worldwide. Rather than allocating capital and resources to development and marketing of generic drugs or expansion of our overseas marketing network, we are committed to creating new drugs through innovation – drugs with the potential to be first-in-class or best-in-class.

This approach has produced real results. We have announced a number of proprietary antibody engineering technologies, such as our Recycling Antibody<sup>®</sup> and bispecific antibody technologies, and we continue to steadily create products from our own research in an industry where development of novel drugs is becoming more and more difficult. Five BTDs from the FDA have been granted for our products, proof that our drug discovery capabilities are global-standard.

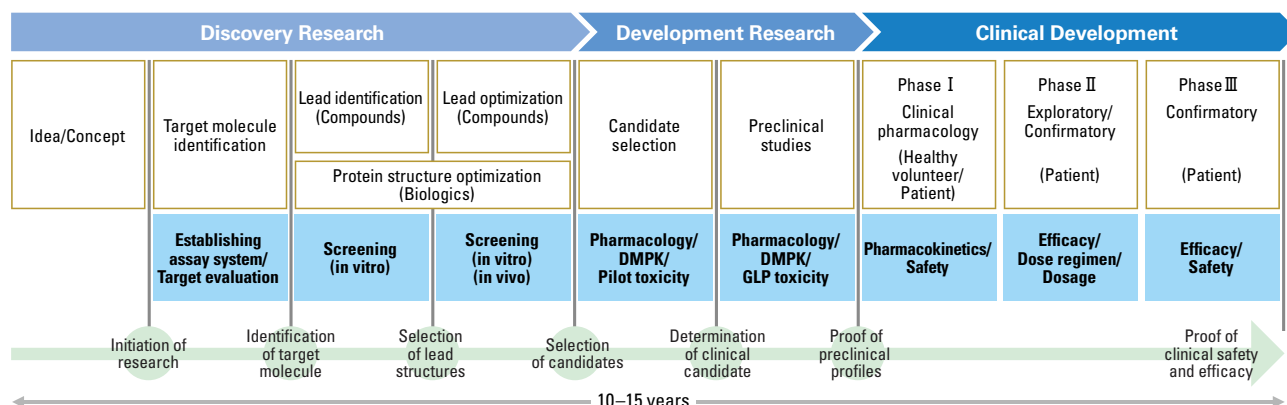
## The Business Model and Technologies That Enable Innovative Discovery and Development

One of Chugai's strategic advantages that enables it to continuously create innovative drugs is its ability to concentrate resources on innovative research. Efficient development in Japan of projects in-licensed from Roche provides a stable revenue base while we conduct global development of projects from our own research in collaboration with Roche. This enables us to concentrate personnel and funds on groundbreaking in-house projects, leading to the creation of a steady stream of innovative drugs. Another powerful advantage is our access to Roche's global research infrastructure. The ability to share Roche's global research resources and infrastructure, including a rich compound library for use in high-throughput screening,<sup>2</sup> is a significant plus for Chugai in terms of cost, efficiency and other factors, and has dramatically increased our research productivity.

The key to this business model is Chugai's antibody engineering and other drug discovery technologies. Chugai's world-leading discovery technologies enable the Roche Group to sell innovative products globally, which helps drive the Group's overall growth. It is a win-win relationship. Chugai began conducting research and development of biopharmaceuticals more than 30 years ago, and the former Nippon Roche had also established world-class technology for the discovery of chemically synthesized agents. Over the years, we have cultivated knowledge and experience through our own pioneering initiatives while also incorporating outside technologies. As a result, we have

1. Avastin, which was subject to special market-expansion repricing, is counted as a product qualifying for premium pricing because it was assumed to meet the conditions for such pricing in 2017.
2. A technology that conducts evaluations at a high speed with 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

## Process and Milestones of Drug Development



continuously evolved our technologies, and have built a technology platform that we can flexibly and appropriately apply to drug discovery.

This disciplined approach to research and technology has become integral to Chugai's identity. In the relationships we are building with our research and development partners, including Roche, Genentech and academia, we recognize each other's technological strengths and expertise, which leads to valuable discussions. At the discovery research stage, which includes basic research, open innovation is essential for acquiring new candidate compounds, and here too, our technological strengths have helped us to build a productive external network.

## Innovating to Accelerate the Creation of New Drugs

Going forward, the environment for drug discovery is expected to be dramatically transformed by advances in disruptive technologies such as artificial intelligence and the Internet of Things, even as the difficulty of creating new drugs increases. To continue addressing unmet medical need in these circumstances, we believe it is imperative to speed up the drug discovery process, and at the same time to achieve new innovations that are not simply an extension of our current technologies.

To enable continuous generation of engineered antibody projects we need to increase the speed

of drug discovery. For that reason, we established Chugai Pharmabody Research (CPR) in Singapore in 2012 to specialize in creating new therapeutic antibodies. In 2016, SKY59 and ERY974, which were discovered at CPR, entered the clinical phase of development.

In technological innovation, we are focusing on middle molecule drug discovery technologies and oncology/immunology research as part of the priority agenda of IBI 18 in order to establish a next-generation drug discovery technology platform. We are ahead of the competition in examining technical challenges and establishing the foundation for middle molecule drug discovery, which is showing promise even for previously undruggable targets, and are now setting our sights on the creation of middle molecule drugs. In oncology/immunology research, we entered into an agreement with Osaka University for comprehensive collaboration with the Immunology Frontier Research Center (IFReC) in May 2016 to further strengthen our research infrastructure. The combination of IFReC's cutting-edge immunology research and Chugai's proprietary technologies and expertise in discovery research is expected to lead to the creation and development of innovative new drugs. We are also looking to innovate the drug discovery process itself, including for next-generation personalized healthcare, by applying the highly advanced genomic analysis techniques and other capabilities of FMI, which joined the Roche Group in 2015.

### Collaboration Scheme with IFReC

1. IFReC researchers will continue academic basic research without restriction.
2. Research outcomes of independent research projects<sup>1</sup> conducted at IFReC will be regularly disclosed (reported) to Chugai twice per year.
3. Chugai will select research projects<sup>2</sup> for joint research on the basis of the reports.
4. IFReC researchers will engage in joint research with Chugai.
5. During and after the final stages of non-clinical research, Chugai may engage in translational research projects independently.

1. Excluding research projects already under contract with a third party.

2. The number of joint research projects to be engaged in will be decided through discussions between IFReC and Chugai.

## FOCUS

**Establishment of discovery technologies for middle molecule drugs is progressing. We want to deliver these next-generation medicines to patients.**

### Takeo Iida

Researcher  
Chemical Biotechnology Group  
Discovery Technology Research Dept.

Today there are numerous innovative drugs that have revolutionized medical treatment. However, they can act on only a small fraction of the targets that cause disease. One of the roles we have taken on to help patients still suffering from illness is to create middle molecule drugs.

Small molecule drugs can penetrate into cells, but are unable to block protein-protein interactions. Conversely, therapeutic antibodies are able to act strongly and specifically on targets, but their size prevents them from passing through cell membranes. Combining the advantages of both of these drug categories, middle molecule drugs are next-generation medicines that can approach previously undruggable targets because they can both enter into cells and act strongly and specifically on targets.

Chugai has been conducting basic research on middle molecules for more than a decade. We have accelerated these efforts in the last few years, and are now building a middle molecule compound library and establishing basic drug discovery technologies, including a compound

screening method. We have started applying these technologies to various discovery stage projects, which has yielded a steady stream of candidate compounds.

There have been many hurdles, but drug discovery experts in every area, including biotechnology, chemistry, pharmacology, pharmacokinetics and safety, have collaborated to build better compounds and assay methods, which has led to the advances we are seeing today. These advances are the result of the continuous efforts of team members to overcome challenges for the benefit of patients.

However, unprecedented challenges will continue to arise. Chugai is making company-wide efforts to bring this new kind of medicine to patients, and by surmounting the issues faced at every stage – not only in research but in manufacturing, clinical development and regulatory filings – we intend to be a pioneer in creating and developing middle molecule drugs.





# Quickly Bringing New Treatment Options to Patients



With its own innovative projects along with numerous compounds in-licensed from Roche, Chugai currently has 41 pipeline projects, among the most of any Japanese pharmaceutical company. Cooperation with Roche, a cross-departmental lifecycle management system, and production functions that support rapid product launches and simultaneous development of multiple projects have led to a steady succession of product launches and new indications – a total of seven from 2015 through 2017. As a result, we have been able to make innovative products available to patients in a timely and appropriate manner, and currently hold the top market share in Japan for oncology and therapeutic antibody products.

## Strengths

- One of the richest pipelines in Japan
- High product potential that addresses unmet medical need
- Strategic alliance with the Roche Group (Global development using Roche's network)

## Challenges

- Escalating measures in various countries to contain healthcare costs
- Stricter standards for development and production worldwide
- Intensifying global competition in development

## Internal Collaboration and Integrated Production System for Patients

No matter how many innovative drug candidates we discover, they will be of no use unless we can quickly develop them into commercial products amid intense global development competition and make them available to patients through regulatory approval in various countries. We also have to ensure a stable supply of those products.

Accordingly, to bring Chugai's innovative drugs to patients as quickly as possible, we have established a lifecycle management system that coordinates multiple functions, including research and clinical development, manufacturing, drug safety, regulatory affairs, and sales and marketing. Function leaders are assigned from different departments for each development project, and cross-departmental lifecycle teams work together under lifecycle leaders, who have been given authority over certain personnel matters, to expedite the progress of each project and the filing of applications for approval.

In manufacturing, we have shortened development time by building a seamless, integrated production system from CMC<sup>2</sup> development to commercial production. We continue to upgrade and enhance these technologies and systems to ensure high-quality, stable supplies of innovative drugs on a commercial scale.

## Business Process Innovation Aimed at Global Competitiveness

In the global market, where multiple pharmaceutical companies compete fiercely to develop drugs for a single molecular target, quickly proving scientific value is vital. We have therefore been working to speed up global development by following a development model with a higher probability of success and by making efforts to prove the value of in-house projects from the early stages of development. As a result, Alecensa took just seven years from concept to launch in Japan, and Hemlibra (ACE910) was out-licensed to Roche less than two years after the start of clinical development, two unprecedented achievements for Chugai. In addition, Chugai's new approach of managing multinational studies has been successful for satralizumab (SA237) and nemolizumab (CIM331), leading to the out-licensing of both compounds.

Continuing innovation in our business process, in August 2014 we amended our business agreement with Roche regarding out-licensing. Among the changes, we now offer Roche compounds for in-licensing upon achievement of early PoC.<sup>3</sup> This enables Chugai to prioritize allocation of resources to the acceleration of early clinical development and proof of medical and economic value. We are working to speed up development overall by designing global development plans and negotiating

1. Copyright © 2018 IQVIA. Source: JPM 2017. Reprinted with permission. The scope of the market is defined by Chugai.
2. Chemistry, Manufacturing and Control: A concept that integrates API process research and pharmaceutical development research with quality evaluation research
3. Proof of concept: Confirmation that the therapeutic effect conceived in the research stage is effective in humans. Early PoC means that in addition to safety, signs of efficacy or pharmacological effect have been confirmed in a limited number of cases.

with partners earlier. Moreover, we have shifted to unified management in our three key regions of Japan, the United States and Europe by integrating and reorganizing our overseas subsidiaries under the Translational Clinical Research (TCR) Division established in 2015. By promoting cooperation between research and development from an earlier stage, we are establishing a faster, more competitive global development strategy while taking on a certain level of risk.

## A New Production System Designed for Flexibility and Speed

In its production operations, Chugai is aiming for simultaneous development of multiple products for the quickest launches possible to continuously bring to market the innovative development projects generated from its research. Flexible application of equipment and staff between investigational new drug production and commercial production lines has raised the level of GMP<sup>4</sup> and promoted technology sharing, enabling a dramatic reduction in development time. Now Chugai is working on new changes to further increase flexibility, speed and productivity.

Specifically, at the Ukima Plant, we have achieved a significant increase in capacity utilization by employing plastic single-use bioreactors, and are constructing UK3, a new antibody API facility capable of high-mix, low-volume production from late-stage development to initial commercial products to prepare for development candidates that apply next-generation antibody technologies. At the Utsunomiya Plant, we have increased production flexibility by installing tray fillers that can handle filling of liquid medicines without making line changes or modifications, regardless of the syringe type.

In technology development, we are focusing on building a technology platform that leads to the early establishment of manufacturing methods. We are taking positive steps to build and patent such a platform for commercial production of innovative medicines such as next-generation antibodies and middle molecules, as we believe it will give us a distinct advantage in the future.

At the same time, regulatory authorities in Japan and other countries are raising the standards required for product quality. It is thus becoming increasingly important to continuously strengthen quality control and quality assurance, and to transfer quality management technology and expertise from development to manufacturing plants in order to obtain approvals without delay and maintain a world-class level of quality. We inaugurated the Quality Development Department in 2016, and have since integrated quality-related development and testing functions and carried out various initiatives, including centralizing management of related functions at production bases and horizontal deployment of technologies and expertise.

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



Exterior of UK3

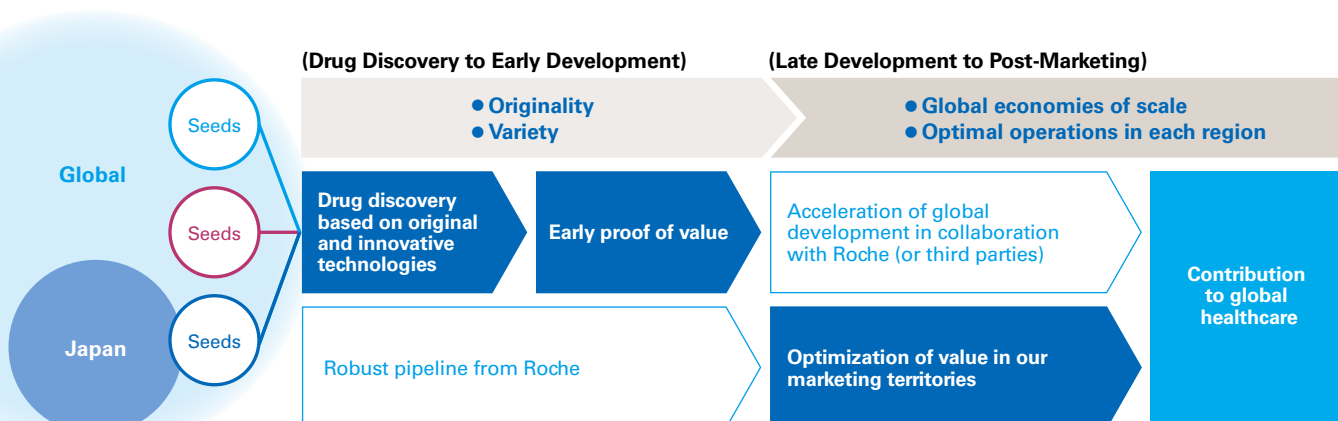


6,000 L bioreactor in UK3

### Biological API Production: Our Facility Portfolio

Plant	Target	Bioreactors	Features	Products
Utsunomiya	Commercial production (Large-scale)	10,000 L x 8 (UT1, UT2: Stainless steel tanks)	<ul style="list-style-type: none"> <li>Competitive low-cost production</li> <li>Dedicated facilities</li> </ul>	Actemra
Ukima	Commercial production/ Production of investigational APIs (Large-to-medium-scale)	6,000 L x 6 (UK3: Stainless steel tanks)	<ul style="list-style-type: none"> <li>Emphasis on flexibility</li> <li>Can handle high-mix, low-volume production</li> </ul>	Future development projects (Initial commercial production)
Ukima	Commercial production/ Production of investigational APIs (Small-scale)	2,000 L x 4 (UK1, UK2: Single-use)	<ul style="list-style-type: none"> <li>Improved capacity utilization through the application of single-use bioreactor technology</li> </ul>	Future development projects (Initial commercial production)

### Our Business Model for Generating Continuous Innovation



## FOCUS

**UK3, a new manufacturing facility at the Ukima Plant, will enable rapid launches of therapeutic antibodies and simultaneous development of multiple projects.**

**Akinori Imamura**

Group Manager  
Manufacturing Group 5  
Ukima Plant

Chugai has a rich pipeline of biopharmaceuticals as a result of the continuous creation of new drug candidates made possible through the use of its antibody engineering technologies. The key to making these new drug candidates available to patients as quickly as possible is to increase speed at every stage from development to commercial production and enable the manufacture and supply of multiple products.

The Ukima Plant has been developing therapeutic antibodies using two manufacturing facilities, UK1 and UK2, for the supply of investigational drugs for early development. With the completion of UK3, a new facility for handling late clinical development to initial commercial production, we have established an end-to-end production system from early clinical development to launch that enables rapid development of multiple projects. This integrated system is not only top level in Japan, it is world-class.

Flexibility is the key feature of UK3. By flexibly combining its six 6,000-liter bioreactor tanks with two purification lines, it will be capable of simultaneously producing two products in the amounts required. Its design is also adaptable to the different manufacturing methods specific to engineered antibodies. The flexibility of this

innovative facility will enable us to supply our proprietary engineered antibody drug candidates to patients at an unprecedented speed.

The UK3 building is also seismically isolated and contains emergency power generators, making the facility highly disaster resistant and capable of uninterrupted supply of medicines. Moreover, the production lines have a closed system design to the maximum extent possible to preserve a high level of quality and greatly reduce risk of contamination. In addition, the new facility has been designed to incorporate information technology for compiling production records and other data, enabling continuous improvement in terms of quality and cost.

Installation of equipment is complete, and performance testing has begun. Given the sophistication and complexity of this equipment, training of technicians and information sharing among members is essential. Members of the numerous departments concerned are working toward the start of trial production in the third quarter of 2018. We are committed to achieving the stable operation of this advanced production facility so that Chugai's innovative medicines can be delivered to patients as quickly as possible.





# Providing Solutions for Better Healthcare

Cases where safety information was collected in post-marketing studies

136,151

Customer inquiries

57,488<sup>1</sup>

Satisfaction ranking based on healthcare providers' assessments

3rd<sup>2</sup>

Providing solutions to healthcare providers is another way in which Chugai contributes to patients and their treatment. Our initiatives for promoting appropriate use of drugs include proposing treatment options and adverse event management strategies according to regional characteristics and patient need, providing various kinds of information, and supporting these efforts by collecting and evaluating a vast amount of safety information from around the world. We provide appropriate information based on state-of-the-art science in response to the approximately 60,000 inquiries we receive each year from healthcare providers and other customers. As a result of these initiatives, Chugai ranks 3rd in assessments from healthcare providers.

## Strengths

- High product potential that addresses unmet medical need
- Commitment to safety management
- Support for healthcare delivery
- Knowledge and experience as a pioneer in personalized healthcare (PHC)

## Challenges

- Policies to dramatically reduce drug costs in Japan (revision of drug pricing system)
- Tightening of regulations for safety, quality assurance and marketing
- Increasing specialization and sophistication of healthcare providers' information requirements

## Providing Solutions in All Disease Areas Is Our Duty

Addressing unmet medical need involves more than simply providing medicines. To ensure that those medicines are used properly, it is also essential to provide product-related medical information and comprehensive safety information to healthcare providers. As Chugai holds a leading position in a number of disease areas, including oncology and bone and joint diseases, it is responsible for addressing issues from the onset of the patient's disease to medical examination, testing and diagnosis, prescription and treatment continuation in all disease areas. Our roles include encouraging potential patients who may not be aware of their illness to be examined by a physician, promoting appropriate tests and proposing adverse event management to healthcare providers to support the continuation of treatment.

To perform those roles, we have created a database compiled from real-world data, including incidence rates, examination rates, diagnosis rates, availability of platform, sales of various pharmaceuticals and treatment continuation rates. This database enables us to visualize the flow of patients and the coordination of care among medical institutions. The solutions that we provide address problems at the points where the various elements intersect in the patient journey.

## Changing Our Framework for Providing Solutions in Japan

Under healthcare system reforms in Japan scheduled to take effect in April 2018, healthcare delivery will be overseen by prefectural governments. This is expected to lead to regional diversification of patient flow and functional division among medical institutions. Treatment of specialty diseases will no longer be centered in advanced treatment hospitals, and coordination of care between regional core hospitals and primary care physicians will be essential.

In response to these changes, in April 2017 Chugai led the industry in establishing a new cooperative cross-functional structure for its Marketing & Sales, Medical Affairs and Drug Safety divisions, which are in charge of providing solutions. We are now taking steps to provide more sophisticated and diverse solutions through cooperation and division of roles according to the responsibilities and expertise of each division.

## Providing Solutions for Each Region and Demonstrating Value Including Coordination of Different Industries

Our basic activities in providing solutions for each region are consulting, which focuses on proposing treatment options and adverse event management

1. Number of inquiries to the Medical Information Department (including telephone, e-mail and fax inquiries)

2. Based on a survey of overall assessments of companies by physicians in hospitals with 100 or more beds, as defined by Chugai

plans tailored to individual patients, and liaison, in which we act as an intermediary between local healthcare providers and between local healthcare institutions. Our recent structural reforms will accelerate the optimization of these functions based on our branch network, which we have further broken down by region. In addition, we abolished the disease-area unit structure, which had been divided into the Oncology Unit and Primary Unit, and assigned general MRs, who cover all disease areas and deal with core hospitals and other general healthcare institutions, and specialty MRs for specialty disease areas such as oncology and autoimmune diseases.

With three major products to be launched in 2018, we will bolster training for MRs on how to present and support these new products. For area-based liaison functions, the Liaison Conference, where the activities of MRs in their respective regions are announced, has been held since 2013, and has helped to raise the level of MR activities and led to sharing of knowledge.

In addition, we began new initiatives in 2017. We are partnering with large cosmetics manufacturers and major life insurance companies to promote disease awareness programs in the areas of bone and joint diseases and oncology, and are working to provide new kinds of value through collaboration with local governments, public organizations and companies in other industries.

## Delivering Product Value Backed by Science

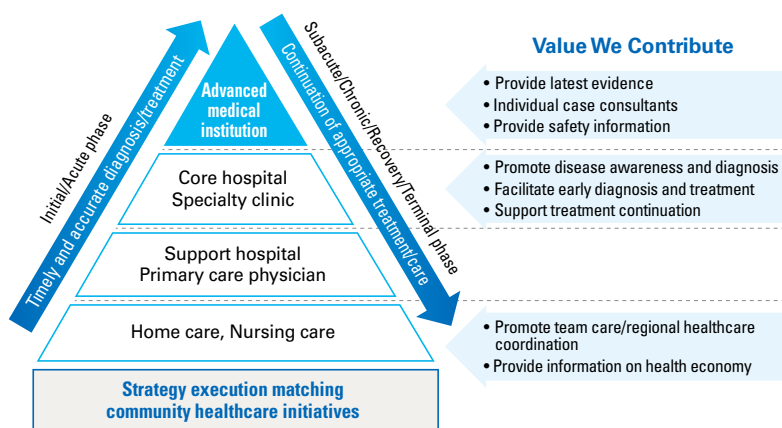
In medical affairs, we conduct and support contract-based post-marketing studies to generate, communicate and disseminate evidence on efficacy and safety in the clinical setting and non-clinical studies (basic research) to shed light on the modes of action of drugs. Conducted in cooperation with medical institutions and healthcare providers, these studies are based on complete transparency. The newly established Medical Liaison Coordination Section supports the provision of area-based solutions. In addition, the Medical Information Department, which was established in 2016 with the transfer of the function from the Marketing & Sales Division, responds to inquiries from customers by providing relevant information backed by the latest science as a consistent global voice in cooperation with Roche and Chugai's overseas subsidiaries.

## Leading the Industry in Promoting the Use of Safety Information

In drug safety, we are building a safety management system in line with global standards to support the consistent collection and analysis of safety information from the preclinical and clinical stages, with the aim of establishing expertise in safety evaluation. Our timely collection and provision of safety data has attracted interest from the medical community and the industry overall. In particular, our ability to rapidly provide information according to patient characteristics using the post-marketing surveillance database tool (PMS DB tool) and safety information database tool (SI DB tool) that we developed in 2016 has won praise from healthcare providers.<sup>3</sup> This same system, which includes post-marketing surveillance and domestic post-marketing safety data, allows us to respond in a more timely manner to needs for urgent safety information. Also, at certain core hospitals we have commenced a trial service of an app<sup>4</sup> that supports adherence to medication in conjunction with a multidisciplinary social networking service (SNS). The app helps to alleviate the anxiety of patients undergoing treatment by facilitating smooth communication between patients and their healthcare providers. In addition, we have added Safety Experts as professionals to the staff of each regional management office to support risk communication geared to local characteristics, and are strengthening safety-related consultation according to needs and building networks with local doctors and pharmacists.

3. Source: Online article by Nikkei Medical Publishing, Inc. on AGING Web "Chugai's Ideal Information Prescription: 'PMS and SAFETY Database Tools' Providing Necessary Information to Those Who Need It, When They Need It" (Japanese only) Part 1 (November 10, 2017) <http://www.nikkeibp.co.jp/aging/article/innovator/2017111001/> Part 2 (November 17, 2017) <http://www.nikkeibp.co.jp/aging/article/innovator/2017111701/>
4. A service developed by Chugai to support multidisciplinary team care in cancer treatment. The app is linked with MedicalCareSTATION, a completely private SNS developed exclusively for healthcare providers and operated by Embrace Co., Ltd., and promotes drug adherence and adverse event management.

### System to Provide Solutions in Japan



### Key Success Factors

<b>Strengthen Expertise</b>	<ul style="list-style-type: none"> <li>Concentrate MR resources on specialty and acute care hospitals</li> <li>Strengthen input of specialty MRs in oncology, RA, kidney and transplant/immunology disease areas</li> </ul>
<b>Area Optimization</b>	<ul style="list-style-type: none"> <li>Planning and execution of prefectural-based detailed strategies</li> <li>Delegation to branch offices, and maintenance of back office system</li> <li>Cooperative support system covering both oncology and primary areas, backed by allocation of general MRs</li> <li>Creation of a system to facilitate access to treatment for potential patients</li> <li>Execution of a flexible, effective area-specific distribution strategy</li> </ul>





## FOCUS

**We cooperated with people in various occupations to establish a clinic/hospital referral system to increase the treatment rate of osteoporosis.**

### Aya Kawai

Yokohama General Sect. 4  
Yokohama Branch  
(Currently assigned to  
Oncology Sect. 3, Tokyo Branch 1)

Osteoporosis increases the risk of bone fractures even in normal daily life. Fractures of the femoral neck and spine in particular can severely impact patients' quality of life, for example, by causing them to become bedridden. Because of this, osteoporosis has attracted public attention. However, unless a bone density test is done, many people are unaware that they have the disease until they suffer a bone fracture. Consequently, the treatment rate of osteoporosis in Japan is estimated at only about 20 percent.

Kanagawa Prefecture, which my team was in charge of, is Japan's second largest prefecture by population but ranked third lowest in the screening rate. The treatment rate was only average, and the number of qualified osteoporosis managers\* was low considering the number of patients requiring diagnosis or treatment. We wanted to do whatever we could to improve conditions for osteoporosis treatment in the region, so we set out to establish a diagnosis and treatment model with the cooperation of various people within and outside the Company.

Our first task was to make it easier for potential patients to get tested and receive treatment. Since the number of facilities with bone density testing

equipment is limited, we worked to establish a clinic/hospital referral system by creating a referral list and sharing information on facilities so that patients could receive advice from general practitioners about testing facilities and receive referrals to suitable treatment facilities if diagnosed. At the same time, we held workshops and meetings to share best practices with physicians in specialty areas including orthopedic surgery, gynecology and internal medicine, as well as pharmacists and laboratory and other medical technicians, and actively worked to create a structure for raising awareness. We also promoted long-term treatment and improvement in drug adherence using Chugai products and other medicines.

As a result of these initiatives, there has been a noticeable increase in the number of referrals. Our efforts have also received recognition, and the commitment of Chugai employees to addressing the issues facing patients and healthcare providers has helped to build trust. In 2017, our initiatives were commended at the Liaison Conference, an event for sharing activities within the Company. We plan to spread success stories such as this nationwide, and want to further evolve the clinic/hospital referral system.

\* Medical staff who are certified by the Japan Osteoporosis Society as specialists in osteoporosis liaison services



## Priority Issues to Enhance Corporate Value

# Environmental, Health and Safety Management throughout the Value Chain

Energy consumption per employee

**296 GJ**

-16.6% compared with 2010

Recycling ratio for industrial waste

**76.4%**

-1.8% pts YoY

Certified in 2018 as a White 500 company<sup>1</sup>

Environmental protection, which has a significant impact both in and outside the Company, and health and safety management underpin Chugai's business activities for realizing its mission to benefit the medical community and human health around the world. Accordingly, we conduct a wide range of environmental, health and safety (EHS)-related initiatives throughout the Company. We are enhancing environmental management at all business sites to ensure efficient use of energy and appropriate use of water and discharge of wastewater. In health and safety initiatives, we emphasize the physical and mental health of employees, and in recent years have been focusing in particular on activities to support cancer treatment and mental health. The extensive support provided through our personnel systems and organizational culture has received external recognition.

### Strengths

- Integrated environmental, health and safety management
- Ongoing initiatives to address environmental issues based on mid-term goals
- Timely sharing of issue resolution through cooperation with the Roche Group

### Challenges

- Enhance supplier management system
- Develop EHS auditors
- Strengthen ability to address increasingly sophisticated EHS issues

## Our Objective: More Unified and Holistic EHS Management

As a healthcare company, Chugai is engaged in many specialized scientific activities. One aspect of those activities involves handling antibodies and highly active pharmaceutical substances. Our responsibilities in environmental protection and health and safety are numerous, and we consider them an important foundation for all our business activities. Therefore, we have included "Protection of the Global Environment" in the Chugai Business Conduct Guidelines (BCG), and are carrying out proactive environmental initiatives. At the same time, we recognize the importance of the well-being

of our employees, and have been taking measures to maintain and promote their health.

As the demands of society have grown more diverse and sophisticated, integrated management of EHS is now required worldwide because of the close connection between "environmental protection" and "health and safety." Accordingly, Chugai has developed an integrated management system for EHS and implements the plan – do – check – act (PDCA) cycle at each facility.

We consider EHS management to extend throughout the value chain, from the procurement of raw materials and supply of products to the disposal of products after use by healthcare providers and

1. A certification given by Japan's Ministry of Economy, Trade and Industry and Nippon Kenko Kaigi to large companies in Japan that practice outstanding health and productivity management. For details, see the website of Japan's Ministry of Economy, Trade and Industry ([http://www.meti.go.jp/english/press/2018/0220\\_003.html](http://www.meti.go.jp/english/press/2018/0220_003.html)).

## Initiatives by Theme

Theme	Approach to Initiative
Reduction of Climate Change Risk	Reduce greenhouse gas emissions by reducing energy consumption and phasing out the use of CFCs and HCFCs. Focus not only on energy management at plants and laboratories, but also on Company-wide initiatives. Promote eco-friendly cars in MR fleet, etc.
Resource Conservation/Waste Management	Achieve zero emissions of waste by improving recycling ratio and further reducing landfill waste.
Biodiversity Protection	Prevent emissions of pollutants into the environment by observing regulatory limits for air, water quality and soil. In particular, focus on controlling emissions into water with whole effluent toxicity (WET) tests and other methods to protect the water environment.
Chemical Substance Management	Promote the establishment of a system for proper management of chemical substances to ensure safety and prevent environmental pollution.
Reduction of Environmental Risk	Ensure thorough compliance with environmental laws and regulations by conducting extensive environmental law checks through external consultants.
Implementation of Risk Assessment	Create work environments that are free from unacceptable risks.
Employee Health Management	Maintain a support system based on cooperation with the health management organization and related departments. Improve health literacy.
Support for Employees with Cancer	Provide enhanced support for continuing to work while undergoing cancer treatment. Raise cancer screening rates.
Measures to prevent and treat lifestyle diseases among employees	Recommend check-ups for high-risk individuals and provide health guidance to those diagnosed.
Measures for employees' mental health	Conduct a return-to-work program for employees on leave due to mental health issues.
Measures to address employee presenteeism (working while sick)	Plan and implement measures based on survey results.
Measures to prevent workplace injury	Conduct measures based on EHS risk assessments.

patients. Going forward, we intend to broaden our activities to cover the overall value chain in closer cooperation with customers and suppliers, partners and industry organizations.

To utilize the PDCA cycle effectively, we introduced health and safety risk assessment in 2014 to remove workplace health and safety hazards. Since 2008, we have implemented an assessment system throughout the Chugai Group to reduce the risk of occupational injuries from exposure to all substances handled, not only restricted substances.

## Implementing the PDCA Cycle with Mid-Term and Annual Environmental Goals

Chugai has set the following four mid-term environmental goals focusing on management of energy consumption and waste, with 2020 as the final year, to promote a medium-to-long-term perspective in environmental protection activities. We are implementing the PDCA cycle and conducting initiatives to meet these goals and the associated annual goals.

<b>Mid-Term Environmental Goals</b>	<ul style="list-style-type: none"> <li>Energy consumption per employee: 20 percent reduction compared with 2010</li> <li>Discontinuance of the use of chlorofluorocarbons (CFCs) and hydrochlorofluorocarbons (HCFCs)</li> <li>Zero emissions of waste<sup>2</sup>: Three facilities</li> <li>Average fuel efficiency of MR fleet: 16 km/L or higher</li> </ul>
<b>Environmental Goals for 2017</b>	<ul style="list-style-type: none"> <li>Energy consumption and greenhouse gas (GHG) emissions: Reduction of 2 percent or more compared with 2016</li> <li>Ratio of eco-friendly cars<sup>3</sup>: 60 percent or higher; average fuel efficiency of MR fleet: 16 km/L or higher</li> <li>A recycling ratio of 80 percent or higher, a final disposal ratio of 2 percent or lower, and on-site verification of 40 percent or more of waste disposal contractor facilities</li> <li>Plain paper copier (PPC) paper purchased: Less than the previous year; recycling ratio of 80 percent or higher</li> </ul>

## Progress of Initiatives in Climate Change, Waste Disposal, Recycling and Biodiversity<sup>4</sup>

To mitigate climate change risk, Chugai is working to reduce its GHG emissions through measures including reducing energy consumption, introducing eco-friendly cars, and reducing the use of CFCs and HCFCs toward eventual discontinuance. In resource conservation and waste management, we aim to increase the waste recycling ratio and further reduce landfill waste to achieve zero emissions of waste, and our initiatives are yielding results.

Water is an important raw material in pharmaceutical manufacturing, and it is also a crucial global resource. Chugai therefore monitors the volume of

water it uses and the wastewater it discharges each year, and is building awareness of the effective use of water resources. Moreover, from the standpoint of protecting biodiversity, we began conducting WET tests in 2013 to ascertain the ecological impact of wastewater discharged from our facilities. In 2017, we conducted WET tests once at all plants and research laboratories, and confirmed that there were no problems.

2. A waste recycling ratio of 99 percent or higher
3. Includes hybrids and fuel-efficient vehicles
4. We received independent verification of our 2017 GHG emissions associated with energy consumption, leakage of CFCs and HCFCs, use of aircraft for business travel, and industrial waste generated.

## Sound Organizational and Individual Health Is the Foundation for Growth

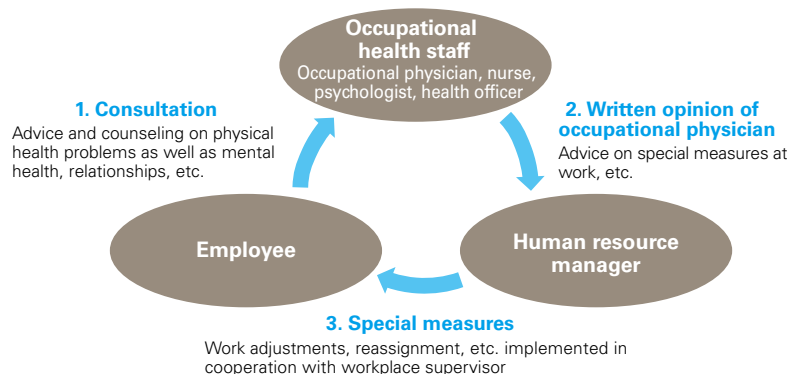
Chugai believes that sound employee physical and mental health and a satisfying and rewarding work environment where all employees can do their jobs with enthusiasm are the foundation for growth. Based on a policy of cooperating with the health insurance society and the labor union in simultaneous pursuit of both individual health and organizational health, we are proactively upgrading promotion frameworks, ensuring safety, preventing occupational injuries, promoting health maintenance, taking measures for mental health and creating vibrant, healthy work environments throughout the Company. (See "Focus" on the next page for details.)

Furthermore, we are conducting ongoing awareness programs to promote understanding of mental health issues, including training for managers on how to deal with such issues appropriately.

## 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 in order 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 for a cumulative total of 1,205 participants at 74 organizations as of December 31, 2017. Post-training surveys have shown improvement in work engagement, workplace identification and other items.

### Basic Health Management Structure





## FOCUS

## Chugai has announced its Health Declaration. Quantitative targets will take health management to the next level.

### Nobuaki Kato

Environment, Health and Safety Group,  
Corporate Social Responsibility Department

Chugai has issued a “Health Declaration” to accelerate the “health and productivity management” that it has focused on up to now, and announced health management policies and priority agenda targets. Employee health management applies not just to employees who are having problems or are on leave due to illness or injury, but to all employees who need special consideration for their health status, including people with anomalies observed in health checkups, people working long hours, expectant and nursing mothers, and employees with disabilities. Occupational physicians, nurses, psychologists, health officers and other occupational health staff have provided the necessary support in cooperation with human resources staff and workplace managers and supervisors. These measures have produced results to a certain extent, and we plan to continue them while also focusing on prevention, including health and disease education.

One area where Chugai has been in the forefront is enhancement of support systems for mental health and cancer treatment.

To facilitate a smooth return to work for employees on leave due to mental health issues, we conduct an ongoing program tailored to each individual. We have found that this program improves the relapse-free job retention rate one year after the return to work. In addition, as a leader in the field of oncology, Chugai has enhanced its support for employees who are working while undergoing cancer treatment so that they can do both. We continue to maintain and improve the consultation system for carrying out measures in accordance with treatment conditions as well as the support system for working during outpatient treatment.

A new initiative is to use employees’ self-evaluation of their performance to quantify and analyze measures for employee health and the work environment. As a result, we will be able to set targets for each measure, which will enable more effective actions.



## Priority Issues to Enhance Corporate Value

# Developing Talent That Generates Innovation

Number of employees  
(Consolidated)

**7,372**  
+127 YoY

Percentage of  
employees using the  
telecommuting system<sup>1</sup>  
(Non-consolidated)

**Male 13.0%**  
(+4.2% pts YoY)  
**Female 29.7%**  
(+6.2% pts YoY)

Percentage of  
female managers<sup>2</sup>  
(Non-consolidated)

**12.5%**  
+1.2% pts YoY

Chugai has more than 7,000 employees. We believe that they can perform to their full potential by sharing and embodying Chugai's mission. Our human resource management is focused on developing employees who will generate innovation in line with our management strategies. In particular, among the various goals of our diversity and inclusion (D&I) initiatives, we aim to increase the percentage of female managers and the percentage of employees using the telecommuting system. We see the yearly increase in these percentages as a sign of progress in fostering an inclusive organizational culture.

### Strengths

- An organizational culture that emphasizes adherence to the Chugai Business Conduct Guidelines (Chugai BCG)
- A PDCA cycle aimed at raising the level of human resource capabilities
- Implementation of an integrated system for productivity improvement, work-life synergy and D&I
- Infrastructure for personnel exchanges with the Roche Group

### Challenges

- Increase awareness of Chugai among new graduates
- Strengthen our ability to recruit global talent
- Enhance our organizational ability to respond flexibly to changes in the external environment
- Establish workplaces that enable diverse employees to perform at their best

## The Type of People We Seek as a Top Pharmaceutical Company

At Chugai, we place high importance on human resource management based on our conviction that people are an invaluable asset in realizing a company's growth and development. As the foundation for that growth, all employees must embody Chugai's Mission Statement,<sup>3</sup> and we must develop human resources who will generate the innovation needed to achieve our fundamental goal of becoming a top pharmaceutical company.

## Reforming Our Human Resource Strategy to Accelerate Innovation

Since 2012, we have created the various measures and systems that form our human resource strategy for becoming a top pharmaceutical company, including introducing talent management, promoting diversity and revising our personnel systems.

At the same time, in promoting the priority agenda objectives of IBI 18 – “Acquisition and implementation of competitiveness at a top global level” and “Selection and concentration strategy for acceleration of growth” – innovation is more important than ever, and the quality and speed of strategy execution must be at a top global level. Therefore, in IBI 18 we have set priorities for raising organizational capabilities in human resource management. We clearly define the type of human resources we seek in order to achieve the goals of IBI 18, and are taking various measures to secure those resources.

- 1) “Talent management” for developing and securing employees who will play a leading role in achieving our top pharmaceutical company vision and advancing our management strategies
- 2) “Competency-based development through personnel systems” to raise organizational and individual capabilities
- 3) “Establishment and enhancement of the foundations of human resource management,” including fostering an organizational culture through the promotion of D&I

We formerly used a survey to implement the PDCA cycle for improving the capabilities of our employees. In 2018, we introduced an updated

1. Percentage of eligible employees
2. Number of female managers as a percentage of the total number of managers in the Company
3. The Chugai Group upholds its Mission Statement – consisting of its mission, its core values and its envisioned future – in order to be a business that meets a diverse array of stakeholder expectations as it realizes its corporate responsibility to society. It is on the basis of this Mission Statement and its business philosophy, “Innovation all for the patients,” that the Chugai Group conducts its business operations.

### Challenges for Achieving IBI 18 (Organizational and Human Resource Capabilities)

#### IBI 18 Priorities

Acquisition and implementation of competitiveness at a top global level

Selection and concentration strategy for acceleration of growth

#### Improve Organizational Capabilities

Responsiveness to change

Intelligence and analytical capabilities

Strategy formulation capabilities

Global business execution capabilities

#### Improve Human Resource Capabilities

Human resources that innovate and displays leadership

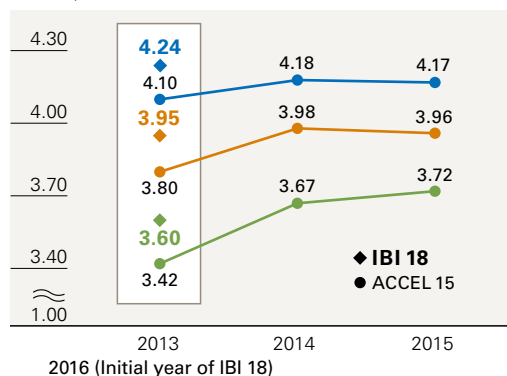
Human resources that initiate planning and implements strategy

Human resources that lead global business

survey. Although indicators such as the degree of penetration of strategies, which is directly linked to growth, have been rising steadily, the new survey is intended to raise our human resource capabilities based on factors such as comparison with major global pharmaceutical companies because we aim to compete at a top global level.

#### Degree of Promotion of Strategies (All-employee survey results)

(On a 5-point scale)



2016 (Initial year of IBI 18)

Evaluation Item

- I understand why it is necessary to achieve the targets of ACCEL 15/IBI 18 (Understanding)
- I am doing what I must to carry out ACCEL 15/IBI 18 (Action)
- My workplace has started to change for the better due to activities for ACCEL 15/IBI 18 (Realization)

Note: This survey was not conducted in 2017.

#### Talent Management for Becoming a Top Pharmaceutical Company:

### Structuring Human Resource Development Plans with the Strong Commitment of Management

Since 2012, Chugai has built a talent management system for developing individuals based on visualization of human resources and their capabilities. Each department held discussions on medium-to-long-term human resource development policies and formulated development plans. At the same time, we have created a talent pool of future management candidates. In addition, we clarified our succession plan by selecting successor candidates for a total of 94 general manager and department manager positions in Japan. The Company-wide plan for grooming successor candidates, including medium-to-long-term career paths for each candidate, is being formulated through discussions by executive management and department managers.

In IBI 18, we have expanded talent management to a global scale, creating a new system that will enable Chugai to systematically and continuously recruit, develop and promote people who can perform internationally. For key positions in strategy execution, in addition to internal candidates, we also consider hiring from outside the Company, whether in Japan or overseas, and candidate selection is under the direct supervision of the president.

On the other hand, we still face challenges when it comes to general hiring across the Company. Due to the tendency toward uniform recruiting activities, particularly when hiring recent university graduates in Japan, differences in hiring outcomes have arisen between departments. However, since the type of employees we are looking for has become clearer through talent management, we plan to redesign our recruiting strategy to focus our efforts on hiring a large number of people who can generate innovation.

#### Competency-Based Development Through Personnel Systems:

### Changing to Global-Level Standards and Foundations

In competency-based development, which is a prerequisite for implementing talent management, we have clarified the mindset and behavior that Chugai requires and have standardized the competencies on which employees are evaluated.

In IBI 18, we have redefined these competencies as the standards needed at the global level. A key question is how we will develop our human resources based on these competencies. Accordingly, we are conducting workshops and training for the managers of individual organizations to encourage dialogue between supervisors and their staff based on these competencies.

In 2017, we revamped our backbone system for human resource management to reflect the evolution of the talent management system described above. The new system, called "CAPTAIN" (Chugai All Persons Talent Information system), is a multilingual, cloud-based global personnel system. The use of a common personnel database throughout the Chugai Group will enable unified talent management and real-time monitoring and analysis of organizational conditions by managers, leading to faster, more effective enhancement of our human resource capabilities.

#### Establishment and Enhancement of the Foundations of Human Resource Management:

### Integrated Management of D&I, Work-Life Synergy and Productivity Improvement

Chugai has positioned D&I as a priority issue for the establishment and enhancement of the foundations of human resource management. We believe that D&I, which leads to the creation of a diverse workforce that works together with enthusiasm, is essential in order for employees to generate new value – in other words, diversity is necessary for generating innovation. As such, in 2010 we launched a working team led by the president, and in 2012 we established a dedicated organization that has since been conducting initiatives to promote diversity. To promote gender diversity, we are actively providing opportunities for women to succeed. We set a target for 2018 of a 13 percent female manager



ratio, and have focused on career planning and development measures for women. To promote the success of older employees and foreign employees in Japan, we are building awareness of their potential through training and other programs and creating environments including workplace systems to help them play active roles. Under IBI 18, we are making special efforts to practice inclusion, which focuses on individual differences, and are taking steps to use diversity to vitalize our organization and contribute to our business success.

We also provide work arrangements and support systems so that all employees can have individual work styles and lifestyles that accommodate a variety of life events including but not limited to childbirth, child care and nursing care. With respect to “work style reform,” which is currently a focal issue in Japan, studies and discussions between labor and management are under way toward not only raising productivity, but even changing our business itself.

These D&I and work-life synergy initiatives are integrally linked with productivity improvement in IBI 18, and are aimed at raising our corporate value.

By promoting D&I and work-life synergy, we will create workplace environments where all employees can maximize their potential, which will increase the productivity of the entire organization and enable us to increase corporate value over the medium to long term. Along with these interconnected initiatives, we are conducting rational testing and analysis of the relationship of each productivity measure to D&I and work-life synergy.

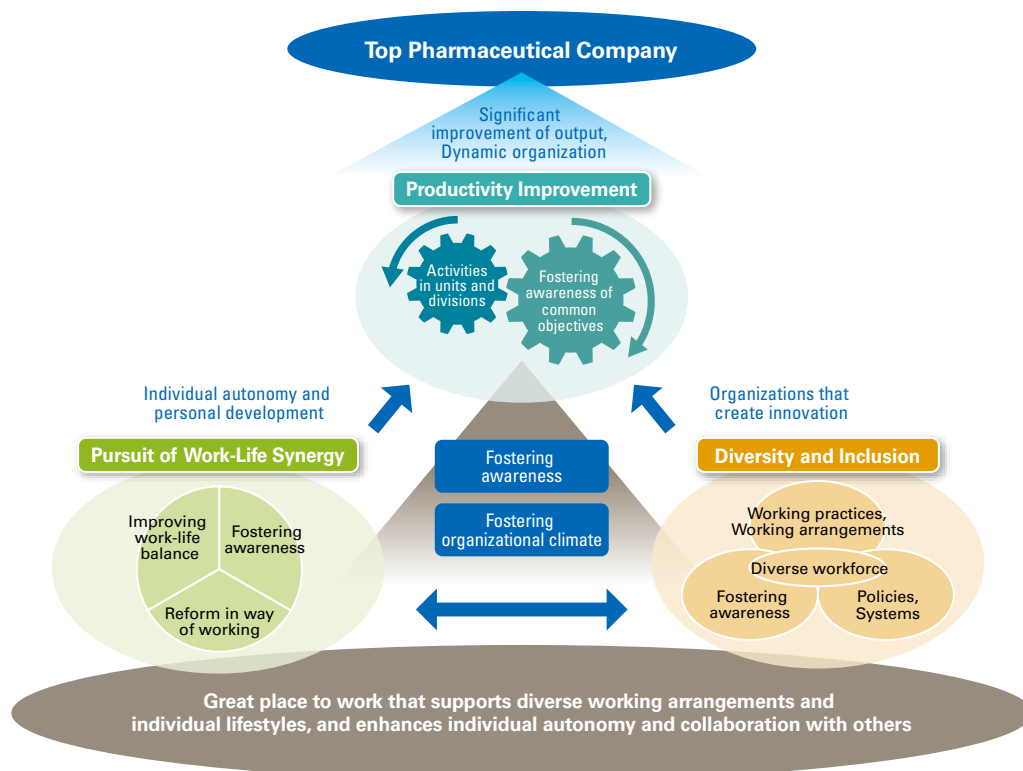
## Sharing of Core Values Is an Ongoing Effort

For Chugai, it is essential that all employees embody its Mission Statement. Therefore, promoting understanding and penetration of the Chugai BCG and human rights issues is an ongoing priority. Training is conducted for all employees every year. Emphasis is on corporate ethics in the first half and respect for human rights in the second half. In 2017, workplace training was conducted under the topics “The Global Compliance Framework” and “Prevention of Maternity Harassment” in the first half, and “Anti-Bribery Measures” and “LGBT: Consideration of Individual Differences” in the second half.



For four years in a row, Chugai has been selected as a Nadeshiko Brand for its exceptional record in promoting the success of women.

## Productivity Improvement, Work-Life Synergy and Diversity and Inclusion



## FOCUS

**Through the evolution of talent management, we will advance a human resource strategy aligned with Chugai's management strategies.**

**Koma Oki**

Group Manager  
Global HR Group  
Human Resources Management  
Department

IBI 18 is a strategic plan designed to raise Chugai's competitiveness to a global level, and requires greater quality and speed in each of its functions. We are also entering fields and specialty areas that cannot be handled with conventional approaches, so we need to identify people who have the necessary capabilities. Ensuring diversity to build a foundation for generating innovation is also becoming more important.

Accordingly, Chugai further upgraded its talent management system in 2017, restructuring it on a global basis. The new system places emphasis on assessing human resources in terms of individual qualities such as ability, experience, aptitude and career orientation. Specifically, we are building a globally shared personnel database, defining global competencies, clarifying key positions for execution of strategies, and identifying candidates for them.

The global competencies we have defined are in the form of seven standards to provide a simpler, more universal framework than we had previously. These clearer evaluation measures will enable employees to identify the gaps between the standards and their own performance, and apply that knowledge to improving their capabilities. At the same time,

managers can engage in dialogue with those employees about their improvement actions and career plans, and promote human resource development. These efforts have already begun.

The foundation for evolution is now in place, but the key to assessing human resources and unlocking their full potential is to provide opportunities and environments that make the most of people's talents, allowing each individual to flourish. To realize this objective, we will promote communication on human resources and employee development, and foster an organizational culture in which they are given priority.

**Global Competencies**

Decision-making Standards	Customer Focused
	Global Perspective
	Integrity
Behavioral Standards	Strategic Thinking
	Collaboration
	Commitment
	Team & People Development