Creating Innovative Drugs That Address Unmet Medical Need

R&D expenditures (Core basis)
¥88.9 billion
+¥6.3 billion YoY

In-house products in development pipeline
13
No change YoY

Percentage of product sales qualifying for premium pricing
74%[1]
+1.0 pt YoY

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® 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.

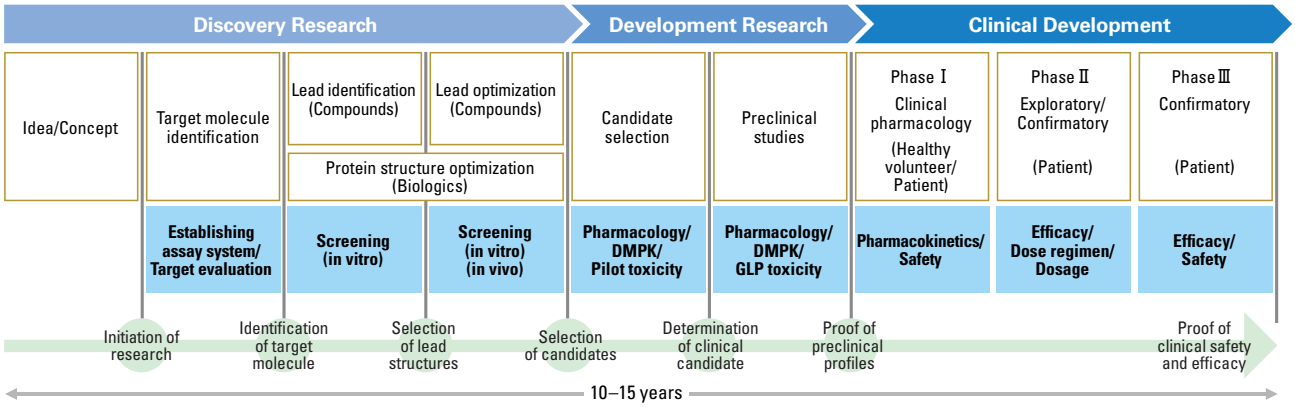
The Business Model and Technologies That Enable Innovative Discovery and Development

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,[2] 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[1] conducted at IFReC will be regularly disclosed (reported) to Chugai twice per year.
3. Chugai will select research projects[2] 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.