Research and Development at Chugai

Chugai's mission in research and development is to continue pursuing the creation and development of innovative drugs for patients facing diseases and medical challenges for which effective treatments remain unavailable. To deliver drugs that are truly needed, we place patients at the center of every decision we make in research and development.

At Chugai, we have continuously created first-in-class*1 and best-in-class*2 drugs by developing drug discovery technologies and matching them with disease targets best suited to those technologies. We call this approach "technology-driven drug discovery." As a foundation for this approach, Chugai has established a broad range of drug discovery modalities capable of addressing diverse targets and mechanisms of action. We possess world-class capabilities in two major modalities: antibodies (large-molecule), exemplified by Actemra, Japan's first domestically created antibody drug; and small molecules, represented by Alecensa, the first therapy approved globally for tumor-agnostic treatment of ALK-positive solid tumors, as well as FOUNDAYO*3, the world's first small-molecule GLP-1 receptor agonist. In recent years, Chugai has led the industry through its proprietary antibody engineering technologies, which have significantly expanded the potential of antibody drugs. One example is ART-Ig, our bispecific antibody production technology that was used in the creation of emicizumab.

*1 Drugs with a high degree of novelty and utility that have the potential to fundamentally change existing treatment paradigms.
*2 Drugs that demonstrate clear advantages over existing therapies within the same category, such as those targeting the same molecule.
*3 Under regulatory review in Japan and Europe; commercially launched in the United States.

◆Bispecific Antibody Production Technology (ART-Ig)

Conventional antibodies bind to a single antigen. In contrast, bispecific antibodies can bind to two different antigens through two distinct antigen-binding sites. The development of ART-Ig enabled the commercial-scale production of bispecific antibodies, opening up new approaches to drug discovery by enhancing therapeutic efficacy and creating entirely new mechanisms of action.

Research on emicizumab began in earnest in 2002 at Chugai's former Fuji Gotemba Research Laboratories. The project originated from an unconventional idea conceived by our researchers: using an antibody to substitute for the function of coagulation Factor VIII. Building upon Chugai's antibody research platform and a research collaboration with Nara Medical University, the team pursued extensive studies and countless rounds of trial and error. Through years of dedication and refinement, emicizumab was ultimately created.

◆Drug Discovery Technologies

Following ART-Ig, Chugai has developed a range of proprietary antibody engineering technologies that address limitations of conventional antibody drugs, including SMART-Ig

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(recycling and sweeping antibody technologies) and Switch-Ig (switch antibody technology).

Today, in addition to antibody and small-molecule drugs, Chugai is focusing on establishing technologies for Snipe-tide, the macrocyclic peptides. Through the development of drugs capable of reaching intracellular targets while also offering the potential for oral administration, we aim to address unmet medical needs that have been difficult to tackle using conventional technologies.

Reference: Research and Development at Chugai
https://www.chugai-pharm.co.jp/english/innovation/rd/

◆Organizational Culture

At Chugai, delivering new value to patients is the starting point of all research and development activities. Creating and developing innovative drugs requires an organizational culture that fosters free thinking and original ideas.

Chugai was among the first companies in Japan to pursue biopharmaceutical research and development in the 1980s. Since then, we have pioneered proprietary technologies, including antibody engineering technologies and macrocyclic peptide technologies. Behind these achievements lies a pioneering spirit that embraces challenges in unexplored fields and a venture-minded culture that seeks to create new value without being constrained by conventional thinking. We respect the creativity of individual researchers and foster a bottom-up R&D culture that encourages ideas and challenges that may differ from accepted norms.

These unique cultural values and mindsets, cultivated over many years, have been formalized as our R&D Principles, which serve as the guiding philosophy for research and development at Chugai. Guided by these principles, our researchers strive to create drugs that are truly needed by patients and healthcare professionals by advancing proprietary technologies, pursuing the highest quality, and challenging conventional thinking.

✧ **Technology-Driven Drug Discovery**

Rather than starting with a disease area, we begin by advancing proprietary technologies and then identify medical challenges that can be addressed by matching those technologies with disease targets and mechanisms of action. Our goal is to make previously undruggable targets and mechanisms druggable, and we have developed unique capabilities across antibody, small-molecule, and Snipe-tide (the macrocyclic peptide) modalities to achieve this.

✧ **Highest-Quality Development Candidates**

We pursue the highest-quality drugs achievable with today's technologies. We place strong emphasis on creating development candidates with exceptional overall quality, never compromising on efficacy, safety, pharmacokinetics, or other critical attributes.

✧ **Selection of Target Diseases Based on Biology and Drug Characteristics**
We select disease areas in which our technologies and drug candidates can create the greatest value. Rather than limiting ourselves to specific therapeutic areas, we focus on identifying where we can deliver the greatest benefit to patients.

✧ **Clinical Development Focused on Maximizing Patient Benefit**
Our patient-centered approach extends beyond research into clinical development. From the earliest stages of development, we explore the potential application of new drugs across multiple diseases to deliver value to as many patients as possible, as quickly as possible.

Reference: Chugai R&D Principles
https://www.chugai-pharm.co.jp/english/innovation/rd/principles/

◆Research Sites
Chugai conducts its research and development activities primarily at Chugai Life Science Park Yokohama in Kanagawa Prefecture, Japan. This integrated research center began operations in April 2023 to enhance collaboration across research and development functions and accelerate pharmaceutical innovation by consolidating the capabilities of Chugai's former Kamakura Research Laboratories and Fuji Gotemba Research Laboratories. By bringing together research, development, and translational research functions, the site serves as a hub for the creation of innovative drugs.

Reference: Chugai Life Science Park Yokohama
https://www.chugai-pharm.co.jp/english/innovation/rd/structure.html#sec01