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"Crovalimab could potentially become the first global drug originating from Singapore"

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There has been explosive growth in the mid-size molecules and therapeutic antibody market as many cancers, autoimmune diseases, metabolic diseases, and infectious diseases have been successfully treated.



Japanese headquartered Chugai Pharmaceutical has already developed world-class technologies for antibody engineering and mid-size molecule drug discovery which can reach some intracellular targets that were previously difficult to access, and have high binding activity, and good oral absorption. Chugai Pharma has been operating in Singapore since 2012 as a subsidiary, Chugai Pharmabody Research (CPR) developing innovative pharmaceutical products in collaboration with Singapore's biopharma R&D ecosystem. In an interaction with BioSpectrum Asia, **Dr Hisafumi Yamada, Executive Vice President (R&D) at Chugai Pharmaceutical**, echoes CPR's enduring association with the regional biopharma industry on the occasion of completing a decade of presence in Singapore.

How significant is the development of mid-size molecule drugs relative to small molecule and antibody modalities to address unmet medical needs?

With mid-size molecule technology, we aim to discover new pharmaceutical drugs that act against intracellular tough targets which are unreachable with small molecules or therapeutic antibodies.

Though they are the most common modalities among pharmaceutical drugs, antibodies can target only extracellular molecules (approximately 20 per cent of all proteins), and small molecules target only molecules with pockets (approx. 20 per cent of all proteins).

It is said that there may be approximately 2,000 proteins involved with disease. However, new drugs launched within the last 10 years target only about 50 of these proteins. Many are still considered “undruggable,” as they are difficult to reach by either small molecules or antibodies. We must find a way to reach these tough targets so that we can create innovative new drugs for patients with diseases where there are limited treatment options and high unmet medical needs.

I’m excited that our mid-size molecule platform has great potential to address this challenge, as they permeate the cell membrane where antibody pharmaceuticals do not and specifically bind to target proteins even where they do not have pockets suited to a small-molecule drug for binding. We also aim to confer oral bioavailability to mid-size molecule drugs, whereas antibodies can only be administered by injection. We believe this will add extra value for the patients.

Could you explain CPR's capabilities in cutting-edge antibody engineering technologies towards pioneering new drug discoveries?

CPR was first established in Singapore as a suitable research hub to maximise the value of Chugai’s proprietary antibody engineering technology. We have 10 research units that cover the early drug discovery process from target assessment to clinical candidate selection. Each unit has different roles in antibody research and development, and they collaborate as one to accelerate the drug discovery process.

Utilising Chugai’s antibody engineering technologies, which include Recycling Antibody technology (SMART-Ig), bispecific antibody manufacturing technology (ART-Ig), and Switch antibody technology (Switch-Ig), CPR focuses on innovative drug development that can deliver better clinical outcomes for patients. These novel antibody technologies enable Chugai to expand druggable target molecules and invent unique therapeutic actions to meet unsatisfied clinical needs. Chugai’s cutting-edge technologies have allowed us to achieve a competitive advantage in the highly intensive field of drug discovery.

Since its establishment in 2012, CPR has contributed eight projects to Chugai’s drug development portfolio. These include CPR’s successful application of recycling antibody technology to create an anti-C5 antibody called crovalimab (SKY59), which is currently in phase 3 clinical trial for paroxysmal nocturnal hemoglobinuria (PNH).

How do you describe the strategic implementation of proprietary antibody and cyclic peptide technology for treating multiple diseases, including oncological, inflammatory, fibrotic, and genetic disease? In what ways did the Singapore Economic Development Board (EDB) play a significant role?

Chugai’s drug discovery is technology-driven, which is unique and different from other big pharmaceutical companies. Chugai focuses on the identification of target molecules that best fit our novel antibody technology or cyclic peptide technology, regardless of the therapeutic area. The identification of novel target molecules by disease biology can be complex, and many novel target molecules can be classified as tough targets. Drug discovery activities for tough targets require advanced technology. Chugai’s novel proprietary antibody engineering and cyclic peptide technology can expand target space by making tough targets approachable in multiple therapeutic areas.

When CPR started operations in 2012, EDB provided the Research and Innovation Scheme for Companies (RISC) and advice on acquiring human resources and talented scientists. Since then, CPR has continuously received timely support from EDB and has expanded its operations steadily.

Describe Chugai's efforts towards developing drugs against COVID-19, dengue fever, and other diseases.

Chugai believes that collaboration with external partners is the key to innovation. With science and technology evolving at an unprecedented rate, it has become increasingly difficult for a company working alone to generate innovation. Therefore, collaboration with academia and companies that possess new modalities or technologies will be essential to achieve our goal of world-class drug discovery.

Through CPR, Chugai has begun multiple joint research projects with A*STAR and research institutes in Singapore. Our aim is to combine novel findings and the expertise of academia in Singapore with our drug discovery technologies, such as antibody engineering technologies, to discover new innovative drugs.

These efforts include antibody projects to fight COVID-19 and dengue fever, but they have not proceeded to clinical development yet. Nevertheless, I look forward to new drug candidates emerging from our collaborations in Singapore.

How do you define Chugai contribution to Singapore's R&D efforts and regional collaborations? Could you brief the investment made so far in the region? What are the other drugs in CPR's pipeline?

CPR has been contributing to Singapore's science community through collaboration, participation in training events, and remaining connected with CPR's Alumni network.

CPR has multiple partnerships within Singapore's scientific community, including startups, which I believe energises Singapore's scientific ecosystem.

Chugai has invested S$437 million into Singapore via CPR's operations over the past decade, and an additional S$282 million has been earmarked for the next five years. CPR has already played an important role in discovering multiple investigational antibodies, for which we've already started clinical studies. I am confident there are more to come.

Singapore's first global drug is being developed in collaboration with Chugai, complimenting the country's sustainable growth in the biomedical ecosystem? What is your perspective on this?

CPR played a leading role in the creation of the investigational antibody crovalimab for paroxysmal nocturnal hemoglobinuria, a potentially life-threatening blood disease. It is currently undergoing a global phase 3 clinical trial, the final phase in clinical development. The first new drug application for crovalimab was submitted in Q3 2022 in China ahead of the rest of the world, based on positive results from an in-country dedicated single-arm clinical trial. The application is currently under priority review.

We are very excited about crovalimab – if the results of the clinical trial turn out to be positive, it could potentially become the first global drug originating from Singapore. If that happens, crovalimab will become a good example of the value of Singapore.

Hithaishi C Bhaskar

hithaishi.cb@mmactiv.com