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Otsuka Chemical Co., Ltd.
Yokogawa Electric Corporation

Otsuka Chemical and Yokogawa Electric to Launch SynCrest Inc., a Joint Venture Targeting the CRDMO Business for Middle-molecular Drugs

Otsuka Chemical Co., Ltd. and Yokogawa Electric Corporation announce the establishment of SynCrest Inc., a joint venture that will engage in research[*1], development, and manufacturing in the promising field of middle-molecular pharmaceuticals as a Contract Research, Development and Manufacturing Organization (CRDMO). Set to commence sales operations in May 2023, this new joint venture (investment ratio: Otsuka Chemical 51%, Yokogawa Electric 49%) will provide services to meet various challenges and needs across the pharmaceutical industry's drug development value chain, from research through to commercial production.

From left, Hiroyoshi Tosa, President and Representative Director of Otsuka Chemical, and Hitoshi Nara, President and CEO of Yokogawa Electric, at the signing ceremony

Background

Regarding drug modality[*2], middle-molecular drugs such as peptide and nucleotide therapeutics have been the focus of considerable research in recent years because they combine the advantages of low-molecular drugs and bio-antibody drugs, namely, high efficacy and low side effects. With respect to synthesis technology, the flow synthesis method[*3] has attracted attention because it enables continuous production and has the ability to adjust production volumes over time, in contrast to conventional batch reaction[*4] methods. Also, because it is a closed system, it can handle hazardous reactions and other kinds of chemical reactions that are difficult to perform in conventional batch reaction tanks. This provides the flexibility to produce a wide variety of chemical compounds in varying amounts.

With its real-time assurance of precision, robustness, and quality, the flow synthesis method enables the high quality, low cost, and on-demand production of middle-molecular drugs that have highly potent activity and low side effects. As such, it will help to revitalize Japan's pharmaceutical and drug development industries.

Strengths of the Two Companies

Otsuka Chemical positions the manufacturing of active pharmaceutical ingredients (APIs) and intermediates for drugs as one of its core businesses, and is especially strong in specific antibiotics. In recent years, the company has focused on middle-molecular drugs and built up experience in production using the solid-phase and conventional liquid-phase methods. In addition, the company has been developing a flow synthesis method for the production of special raw materials that are essential for middle-molecular APIs. By combining the flow synthesis method with the GMP[*5] management know-how, advanced quality control, halogenation, and original catalyst technologies that it has cultivated through the manufacture of antibiotics and other low-molecular drugs, Otsuka Chemical has been able to achieve a higher level of purity and synthesize special raw materials that cannot be produced using conventional methods.

Yokogawa provides measurement and control solutions to the oil & gas, chemical, pulp & paper, steel, pharmaceutical, and other industries. The company has a wealth of experience in delivering technologies and products for the control of production processes and management of production operations in process plants. In recent years, it has been focusing on the development of in-line sensing technology that enables non-destructive and non-contact real-time monitoring, and is applying this technology in the life science, fine chemical, and pharmaceutical fields.

Objectives of the Joint Venture

Under the shared objective of entering the CRDMO business in the pharmaceutical field, particularly for middle-molecular drugs, Otsuka Chemical and Yokogawa began working in 2020 on the joint development of a flow synthesis method mainly targeting the production of middle-molecular APIs, intermediates, and raw materials. By combining Otsuka Chemical's cutting-edge flow synthesis technology, middle-molecular drug manufacturing technology, and GMP management know-how with Yokogawa's production process management powered by advanced measurement and control technologies, the companies have developed an industry-leading solution that integrates the continuous flow synthesis method with in-line measurement[*6], making it possible to carry out non-destructive measurements in real-time with a high level of precision.

The newly established joint venture will help researchers and producers of middle-molecular drugs be more productive by providing integrated services ranging from basic drug research through to process development and commercial manufacturing. In addition, the joint venture will respond to challenges and needs related to quality, delivery, and cost in the manufacturing value chain for middle-molecular drugs and other pharmaceuticals that can be chemically synthesized by providing the desired quantity of products at the right time and with optimal quality.

Overview of the Joint Venture

Company name: SynCrest Inc.
Sites:
- Headquarters, R&D: Shonan Health Innovation Park, Fujisawa, Kanagawa, Japan
- Naruto Plant: Naruto, Tokushima, Japan (in Otsuka Chemical's Naruto Factory)

Capital: JPY 98 million
Shareholders: Otsuka Chemical 51%, Yokogawa Electric 49%
Planned start of operations: Mid-March 2023 (subject to clearance by the related regulatory authorities)

Production Facilities

At the end of December 2022, construction of the Naruto Plant, a multi-purpose facility for the manufacturing of middle-molecular APIs, intermediates, and raw materials, was completed. Located at Otsuka Chemical's Naruto Factory, this is the first multi-purpose, multi-product plant in Japan that utilizes the continuous flow synthesis method while also being in compliance with GMP for drugs with highly potent activities (OEB Category 4[*7]). It also has a non-GMP area, enabling a diverse and flexible production system and environment. Moreover, it is equipped with solid phase synthesis equipment, analyzers, and other state-of-the-art equipment, enabling high-purity on-demand production of not only middle-molecular drugs but also middle-molecular and other APIs, intermediates, and raw materials.

SynCrest's Naruto Plant

Deliverables and Services

SynCrest will deliver a one-stop service, including library synthesis for drug discovery, process development, manufacturing of experimental medicine for clinical studies, CMC[*8] support, document preparation for new product releases, and on-demand commercial production.

In particular, by greatly reducing the number of manufacturing processes and ratio of impurities for special amidites, the new joint venture can reduce costs and dramatically improve purity. A new manufacturing method for special amino acid intermediates has also been developed that enables the synthesis of more than 100 types of non-natural amino acids with high quality and short delivery times. With its in-house development and manufacturing capabilities for special raw materials used in the development of middle- and low-molecular pharmaceuticals, SynCrest aims to be a total solution provider that comprehensively covers the diversified needs of the middle-molecular pharmaceutical field.

Tsuyoshi Abe, a senior vice president and head of the Marketing Headquarters at Yokogawa Electric, stated, "We are very excited to enter this business with Otsuka Chemical. There are various challenges in the development and manufacturing of middle-molecular drugs. Based on our three core competencies of measurement, control, and information, we will combine our expertise in operational technology (OT) and engineering technology (ET) with the experience, advanced technologies, and manufacturing capabilities of Otsuka Chemical to create shared value and become an industry leader."

Yoichi Nishioka, director in charge of the chemicals business at Otsuka Chemical, said, “Our company has been considering the CRDMO business for middle-molecular drugs as our next core business. We have developed flow synthesis technology, which forms the basis for this business, as a key technology that can solve various problems in the development and manufacturing of middle-molecular drugs. By integrating Yokogawa's measurement and control technology, we have been able to achieve an even higher level of innovation. Together we will aim to become a flagship company for middle-molecular drug CRDMO, and endeavor to provide value that satisfies our customers throughout the entire process.”

*1 The Research function at SynCrest will initially focus on library development and library synthesis.
*2 Types of basic pharmaceutical technology, such as low-molecular-weight drugs, antibody drugs, nucleic acid drugs, and cell therapy
*3 A method in which a thin tube is used as the reaction vessel, raw materials are continuously introduced from one end of the tube, mixed and reacted, and the product is continuously obtained from the other end. The flow synthesis method is said to have higher energy productivity and produce less waste than the batch reaction method.
*4 A method in which all raw materials are put into a reaction vessel and the final product is extracted after all the reactions of the substances have been completed.
*5 Standards for manufacturing and quality control for the production of safe and effective pharmaceuticals and foods. Each country has its own rules and guidelines.
*6 A flow synthesis method that enables process continuity by rigorously controlling multiple processes in production, from reaction to purification/extraction, with in-line measurement.
*7 Operational Exposure Band. This is the permissible exposure amount control category for active pharmaceutical ingredients.
*8 The management of information regarding the chemistry, manufacturing, and quality control of active pharmaceutical ingredients and drug formulations that is required for drug approval application documents.

About Otsuka Chemical
Established in 1950, Otsuka Chemical contributes to the lives of people around the world by utilizing the power of materials. Centered on hydrazine, inorganic materials, compound materials, and pharmaceutical intermediates, Otsuka Chemical provides products globally in the fields of automobiles, electrical and electronic products, housing, and medicine through its production and marketing bases around the world.
For more information, visit https://www.otsukac.co.jp/en/

About Yokogawa
Yokogawa provides advanced solutions in the areas of measurement, control, and information to customers across a broad range of industries, including energy, chemicals, materials, pharmaceuticals, and food. Yokogawa addresses customer issues regarding the optimization of production, assets, and the supply chain with the effective application of digital technologies, enabling the transition to autonomous operations.
Founded in Tokyo in 1915, Yokogawa continues to work toward a sustainable society through its 17,000+ employees in a global network of 122 companies spanning 61 countries.
For more information, visit www.yokogawa.com