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For Global Distribution

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An Announcement Concerning the Nation Strategy Special Zone Business Certification

- We aim to further strengthen the manufacturing and development of nucleic acid drug substance –

We have been certified as a designated project of the National Strategy Special Zone: "drug substance development project by setting up Nucleic Acid Medicine API (※ 1) Development Center". Currently under construction.

Nucleic acid medicine (※ 2) is for a wide range of applications for human genes, as it can respond to various diseases with nucleic acid sequence, and because it is a chemically synthesized product, it is difficult to deteriorate and can be stored for a long time. It is attracting attention as a next-generation biopharmaceutical field following antibody drugs, and R & D is underway worldwide.

Under such circumstances, we will proceed with the development toward practical application of nucleic acid production and advanced functions, introducing the largest nucleic acid investigational drug manufacturing facility in Japan, and will introduce the first domestic pharmaceutical manufacturing Accept business license did. Furthermore, in order to proceed with application for manufacturing approval of the developed product, we set up Nucleic Acid Pharmaceutical CMC * 3 Research Center in Heisei 20 years, and have studied analysis technology development and physicochemical evaluation.

In this project, in order to respond to the growing demand for nucleic acid drug substance, we will further develop nucleic acid production technology by solid phase synthesis method which we have developed so far, and further develop the technology developed by Ajinomoto Co., Ltd. By applying manufacturing technology based on the phase synthesis method (AJIPHASE®) 4) to nucleic acids, it is possible to supply nucleic acid drug substances in units of t (tons) from the development stage required by pharmaceutical companies and R & D agencies I will. In order to develop this manufacturing technology, we newly established the "Nucleic Acid Pharmaceutical API Development Center" in compliance with GMP (* 5, promote the practical use of drug substance manufacturing, flexibly respond to various pipelines in the early stages of development of nucleic acid drugs. We aim to provide a system that consistently supports from the entrance of development to commercial production.

Based on this project, we will establish a new research and development center for new nucleic acid drug manufacturing technology and establish new manufacturing technology, Japan will establish state-of-the-art nucleic acid drug manufacturing technology base technology, advance rapid advancement of nucleic acid drugs in the future In addition to becoming a region, we believe that it can contribute to strengthening international competitiveness in advanced medical fields by leading companies in the world as development and manufacturing consignment companies (* 6).

References

1. Business outline Primary drug development project by establishing Nucleic Acid Pharmaceutical API Development Center
2. Project implementation place Osaka Prefecture Ibaraki-shi Saruto Asagi 7 - chome No. 29

3. Project implementation period: February 1, 2018 - March 31, 2022

Nucleic Acids Pharma API Development

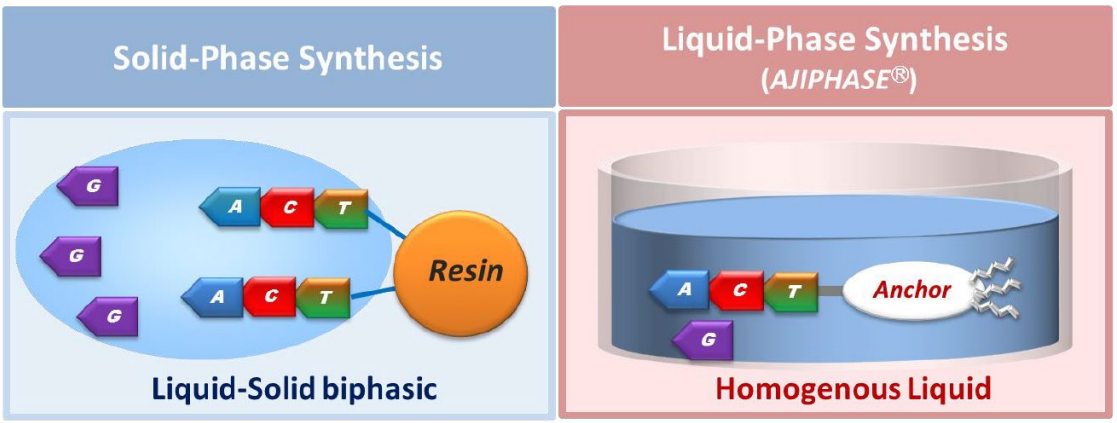
- Explanation of terms -

※ 1 API: Abbreviation for active pharmaceutical ingredient that exerts its medicinal effect in medicine, drug substance drug.

※ 2 Nucleic acid drugs: Oligonucleic acid in which a nucleic acid or a modified nucleic acid is linearly bound is used as a drug main body and protein expression is mediated
It directly acts on living organisms, and refers to medicines produced by chemical synthesis. As the main type. Is a small interfering RNA (siRNA) or antisense, which inhibits the function of messenger RNA. Clo RNA inhibitors and supplements, CpG oligos acting on immune regulation, aptamers with similar functions to antibodies. There are decoys that inhibit transcription factors. Nucleic acid pharmaceuticals can be made reproducibly by chemical synthesis. It is possible to target targets for which low molecule drugs and antibody drugs cannot act, the mechanism of action is clear and specific. Due to its features such as high heterosexuality, development is rapidly advanced as the next generation pharmaceutical.

※ 3 CMC: Chemistry, manufacturing and control. Various forms of basis for research and development of pharmaceutical manufacturing It involves physical property data and analytical techniques that are the basis of quality control.

※ 4 AJIPHASE®: This means the CDMO business of nucleic acids and peptides using "liquid phase synthesis method" successfully developed by Ajinomoto. Liquid phase synthesis method is superior to mass synthesis in comparison with general solid phase synthesis method.



The left figure is a schematic diagram of the solid phase synthesis method and the right figure is the schematic view of the liquid phase synthesis method. Normally, in the production of oligonucleic acids, the "solid phase synthesis method" is used in which nucleic acid chains are sequentially bound and extended to a solid phase surface such as a polymeric carrier (Resin in the figure). On the other hand, in the "liquid phase synthesis method", instead of a polymer carrier in the solid phase synthesis method, use a protecting group (Anchor in the figure) which is soluble in an organic solvent. By using Anchor, even when the oligonucleic acid chain extends, it exists as a homogeneous solution, not only is it excellent in high efficiency of synthesis but also enables isolation / purification using Anchor's properties, enables high product It is a technology that can bring about purification. "Liquid phase synthesis method" is suitable for large-scale synthesis without the need for a special solid phase synthesizer necessary for "solid phase synthesis method". On the other hand, the "solid phase synthesis method" is suitable for synthesizing small quantities of various kinds at short delivery times.

※ 5 GMP: Good Manufacturing Practice (standard of manufacturing control and quality control of pharmaceuticals etc.). In recent years, global harmonization centered on Japan, the United States and Europe has been attempted as a requirement for manufacturing pharmaceutical products (legal requirements in Japan).

* 6 Development and manufacturing consignment company (CDMO = Contract Development & Manufacturing Organization) It refers to companies and organizations that develop from the pharmaceutical companies, academia drug discovery agencies, etc., the manufacture of pharmaceuticals and manufacturing contracts to preclinical, trial and commercial stages as their main business.