

March 29th, 2021

Notice concerning Completion of GMP Manufacturing for Oligonucleotide API

Nippon Shokubai (Headquarters: Osaka, Japan, President: Yujiro Goto, hereinafter "Nippon Shokubai") has signed a joint commercialization contract with TAK-Circulator Corporation (Headquarters: Tokyo, Japan, President: Yasuhiro Nishi, hereinafter "TAK-Circulator") to work on the project to develop the oligonucleotide drug "TAKC-02 (development code)" (Gapmer-type antisense oligonucleotide*¹) for the treatment of Steroid-resistant Severe Asthma*². TAKC-02 is a drug developed by TAK-Circulator based on the results of joint research with the University of Tokyo.

This is a notification that Nippon Shokubai completed the GMP*³ manufacture and release of TAKC-02 API for the Phase I clinical study following manufacture at the GMP-compliant manufacturing facility of API*⁴ constructed in 2019.

According to the joint commercialization contract, TAK-Circulator is responsible for conducting the nonclinical and clinical studies of TAKC-02, as well as the licensing of the drug; meanwhile, Nippon Shokubai is responsible for the manufacture of API for clinical studies and the provision of support for clinical development. On this occasion, Nippon Shokubai manufactured the API under GMP for the Phase I clinical study and released the API on March 15, 2021. TAK-Circulator will be conducting the Phase I clinical study using the investigational product manufactured from the API. The release of the API was the first shipment of middle-molecule API manufactured under GMP by Nippon Shokubai.

TAKC-02 is an antisense oligonucleotide drug that targets the Mex3B gene expression, which is involved in the production of cytokines that mediate Steroid-resistant Severe Asthma. The inhaled administration of the drug is expected to suppress the expression of Mex3B, which leads to the suppression of inflammatory cytokine production and improvement of severe refractory asthma. Approval of TAKC-02 for Steroid-resistant Severe Asthma, a condition that shows poor response to existing drugs, will lead to medical needs being met. Nippon Shokubai will continue to contribute to the development of TAKC-02 as an API supplier and a partner of TAK-Circulator in the joint commercialization project of TAKC-02.

The facility of API manufacturing at Nippon Shokubai includes multiple manufacturing lines for the manufacture of middle-molecular APIs, such as oligonucleotides APIs. The facility is capable of the consigned manufacture not only for TAKC-02 but also for other nucleic acid medicines suitable

for a variety of customers' needs. The full-scale consigned manufacture business for middle-molecular APIs will commence this April based on the manufacturing results obtained for the API above. Nippon Shokubai will continue to contribute to the continual development of society by promoting the supply of various oligonucleotide medicines to support the lives and health of people.

- *1 Oligonucleotide medicine that suppresses the expression of the target gene by binding to the specific sequence site of the target mRNA and induces its degradation through endogenous nuclease activity. Gapmer-type antisense oligonucleotides are high-performance antisense nucleic acids with bridged nucleic acids integrated into both terminals of antisense nucleic acid molecules that consist of natural DNA sequence.
- *2 Severe asthma is difficult to treat because of the resistance to steroid treatments.
- *3 Good Manufacturing Practice; refers to the standard of manufacturing control and quality control for pharmaceuticals and quasi-drugs.
- *4 Completed in January 2019, there are manufacturing facilities, such as equipment for the synthesis of oligonucleotides and peptides API, Large scale purification chromatograph, and freeze dryer, as well as analytical instruments for quality control.



Pic.: Facility for manufacturing middle-molecule drug APIs

About NIPPON SHOKUBAI Co., Ltd.: Since 1941, Nippon Shokubai has grown up its business with unique catalyst technology. Nippon Shokubai has supplied, for example, ethylene oxide, acrylic acid, automobile catalysts, process catalysts and so on. Among all, our global market share of superabsorbent polymers is the largest in the world now. Nippon Shokubai is a global chemical company operating under its corporate mission "TechnoAmenity – Providing affluence and comfort to people and society, with our unique technology."

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