Press Release

SHIONOGI

Notice Regarding the Progress of Phase 1/2 Clinical Trial for New Formulation of COVID-19 Recombinant Protein-based Vaccine

OSAKA, Japan, August 24, 2021 – Shionogi & Co., Ltd. (Head Office: Osaka, Japan; President and CEO: Isao Teshirogi, Ph.D.; hereafter "Shionogi") today announced that the initial administration to all subjects in a Japanese Phase 1/2 clinical trial with a new formulation of a prophylactic vaccine candidate for COVID-19 (code No. S-268019), caused by the novel coronavirus (SARS-CoV-2) infection, was completed on August 19, 2021. All adverse reactions that occurred up to 3 days after the initial administration were mild or moderate, and no safety concerns have been identified.

Shionogi has been pursuing the discovery and development of a recombinant protein vaccine for COVID-19, using a unique technology, "BEVS [1]", established by UMN Pharma Inc., a subsidiary of Shionogi. A Phase 1/2 clinical trial has been ongoing since December 2020, using antigen protein expressed and purified by BEVS and an adjuvant [2] selected with an emphasis on Th1/Th2 balance [3]. Based on the results of various studies and knowledge obtained since then, as disclosed in the previous conference call (1st Quarter of Fiscal 2021 Financial Results), we started a new phase 1/2 clinical trial in Japan at the end of July 2021, using a new formulation with a modified adjuvant to achieve a higher neutralizing antibody titer, while maintaining the Th1/Th2 balance.

1 Baculovirus Expression Vector System. UMN Pharma's technology enables purification of antigen protein without contamination with baculovirus and insect cell-derived components including pathogenic viruses.

2 Substance that strengthens vaccine efficacy by immune activation

3 A balance of two helper T cells that regulate the immune responses. For details, refer to "About Th1/Th2 Balance"

The Phase 1/2 clinical trial initiated in July (jRCT No.: 2031210269) is a randomized, double-blind and placebo-controlled study with a vaccine consisting of the same antigen protein as the previous trial and the newly selected adjuvant in combination. Sixty Japanese adults are enrolled in the trial. The safety, tolerability, and immunogenicity of two doses of the vaccine, administered 3 weeks apart, will be assessed, and then the optimal dose will be investigated, including testing lower amounts of antigen protein. Trial participants will be followed up for a year after vaccination. After selecting the dose, we will promptly move to the next phase trial in about 3,000 Japanese subjects, further investigating the safety and efficacy. We are proceeding with preparations for initiating the pivotal trials by the end of the year. We will continue to consult closely with the Ministry of Health, Labor and Welfare, Pharmaceuticals and Medical Devices Agency (PMDA) and other organizations regarding the design and implementation of these large-scale trials and regarding application for approval.

Shionogi is committed to "Protect people worldwide from the threat of infectious diseases" as our key focus. We are not only pursuing the research and development of therapeutics, but are also working towards total care for infectious diseases, through awareness building, epidemiological surveillance, prevention, diagnosis, and addressing exacerbations, as well as the treating the infection itself. As SARS-CoV-2 continues to have a major impact on people's lives and to represent a global threat, we will seek to contribute to re-establishing the safety and security of society by developing, delivering, and producing, in Japan, a vaccine for COVID-19. Shionogi will work closely with collaborators,

including manufacturing sites, clinical trial sites, and related ministries and agencies, as well as the PMDA, to accelerate our efforts. Furthermore, we continue to be committed to bring forward new oral therapeutics, which are being progressed with the highest priority along with vaccines, to support early containment of the pandemic, and will keep all stakeholders informed regarding the progress of our efforts.

About Recombinant Protein-based Vaccine

The recombinant protein vaccine contains a purified target antigen protein, produced using genetic information from the virus. Compared to other technologies, such as mRNA vaccines, which rely on the subject's body to produce the target antigen protein, the recombinant protein vaccine needs a certain development period for antigen expression and purification before initiating dosing trials. However, recombinant protein vaccine technology is well established and reliable, and already approved and marketed vaccines, such as an influenza prophylactic vaccine, utilize BEVS.

About Th1/Th2 Balance

Immune responses are controlled by two types of helper T cells, Th1 and Th2. It is known that Th1 cells mainly activate cell-mediated immunity, whereas Th2 cells mainly activate humoral immunity involved in antibody production. Once the balance of Th1/Th2 immunity is disrupted due to genetic factors, transplant surgery, vaccination, and other external factors, various immune disease can be caused. From previous studies on Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS), it has been considered that the Th1/ Th2 balance is important to reduce the risk of immune-related vaccine induced disease enhancement (VDE) and antibody-dependent enhancement (ADE).

Forward-Looking Statements

This announcement contains forward-looking statements. These statements are based on expectations in light of the information currently available, assumptions that are subject to risks and uncertainties which could cause actual results to differ materially from these statements. Risks and uncertainties include general domestic and international economic conditions such as general industry and market conditions, and changes of interest rate and currency exchange rate. These risks and uncertainties particularly apply with respect to product-related forward-looking statements. Product risks and uncertainties include, but are not limited to, completion and discontinuation of clinical trials; obtaining regulatory approvals; claims and concerns about product safety and efficacy; technological advances; adverse outcome of important litigation; domestic and foreign healthcare reforms and changes of laws and regulations. Also for existing products, there are manufacturing and marketing risks, which include, but are not limited to, inability to build production capacity to meet demand, lack of availability of raw materials and entry of competitive products. The company disclaims any intention or obligation to update or revise any forward-looking statements whether as a result of new information, future events or otherwise.

For Further Information, Contact:
SHIONOGI Website Inquiry Form：https://www.shionogi.com/global/en/contact.html

References
Our efforts against COVID-19 are updated on our website as needed. A considerable amount of valuable information on COVID-19 from other websites is also summarized on this page, so please use it for reference: SHIONOGI website