Press Release

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Shionogi Presents the Interim Report (Top-line Results) of a Phase 2/3 Additional Dose Clinical Trial for the COVID-19 Vaccine, S-268019

OSAKA, Japan, March, 4, 2022 - Shionogi & Co., Ltd. (Head Office: Osaka, Japan; President and CEO: Isao Teshirogi, Ph.D.; hereafter "Shionogi") announces the interim report of a Phase 2/3 additional dose clinical trial of S-268019, a preventive vaccine for COVID-19. This clinical trial was conducted at Tokyo Shinagawa Hospital (principal investigator: Masaharu Shinkai, M.D., Ph.D.) and the interim report is being submitted as a paper[*1].

*1 The title is “Immunogenicity and Safety of Booster Dose of S-268019-b of Tozinameran in Japanese Participants: An Interim Report of Phase 2/3, Randomized, Observer-Blinded, Noninferiority Study”.

The primary endpoint of the Phase 2/3 additional clinical trial is the geometric mean antibody titer (GMT) of neutralizing antibody titer and seroresponse rate[*2] of SARS-CoV-2 neutralizing antibody titer on the 29th day (28 days after inoculation). The non-inferiority of immunogenicity compared to COMIRNATY intramuscular injection (hereafter “COMIRNATY”) when S-268019 or COMIRNATY was vaccinated for the 3rd time in 206 adults, 6 months or more after receiving two inoculations of COMIRNATY, as well as safety were evaluated. The interim report, which was pre-determined by the protocol, includes the results from all subjects up to 29th day (28 days after inoculation). The interim report results are presented in outline below.

*2 Percentage of subjects whose SARS-CoV-2 neutralizing antibody titer was 4 times or more that of the baseline.

Regarding the GMT of the neutralizing antibody titer and the seroresponse rate of the SARS-CoV-2 neutralizing antibody titer on the 29th day (28 days after inoculation), the non-inferiority of the S-268019 group to the COMIRNATY group was confirmed, and this trial achieved the primary endpoint. Regarding safety, there were no serious treatment-related adverse events, deaths, or adverse events of special interest in both groups. The incidence of treatment-related adverse events (TRAEs) was 96.1% (99/103 cases) in S-268019 group and 98.1% (101/103 cases) in COMIRNATY group. The most frequent TRAEs were fever, headache, fatigue, myalgia and injection site pain. Most of the solicited systemic TRAEs[*3] and the solicited local TRAEs[*4] were grade 1-2 in both group. Compared with COMIRNATY, S-268019 led to a lower incidence of solicited TRAEs.

*3 TRAEs that occurred up to 7 days after inoculation of the investigational drug: fever, nausea/vomiting, diarrhea, headache, fatigue, myalgia, arthralgia, chills

*4 TRAEs that occurred up to 7 days after inoculation of the investigational drug: pain, erythema/redness, swelling at the injection site

Shionogi has been conducting five pivotal clinical trials, including this trial. From February 2022, we initiated prior consultations with the Pharmaceuticals and Medical Devices Agency (PMDA) in preparation for approval application in Japan. We will continue to consult closely with the Ministry of Health, Labor and Welfare, PMDA and other organizations based on the results from these pivotal clinical trials.

Shionogi is committed to “Protect people worldwide from the threat of infectious diseases” as our key focus. We are working towards total care for infectious diseases, through building awareness, epidemiological surveillance, prevention, diagnosis, and addressing exacerbations, as well as 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.

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.

【About a Japanese Phase 1/2 clinical trial[1]】

The Phase 1/2 clinical trial is double-blind and placebo-controlled study to evaluate safety, tolerability and immunogenicity of two doses of the vaccine. 60 adults are enrolled in the trial. For more information about this clinical trial, please refer to jRCT No.:2031210269. Subject registration for this trial has been completed. In the evaluation up to 28 days of two doses of the vaccine, confirmed tolerability and safety, neutralizing antibody titer equal to or higher than that of convalescent serum.

【About a Japanese Phase 2/3 clinical trial[2]】

The Phase 2/3 clinical trial is an open-label study to evaluate safety, tolerability and immunogenicity of s-268019 in 3,100 adults and elderly people. For more information about this clinical trial, please refer to jRCT No.:2031210383. Subject registration for this trial has been completed.

【About a Japanese Phase 2/3 additional dose clinical trial[3]】

This clinical trial is a randomized, active controlled, double-blind trial. In this trial, the efficacy and safety of an additional dose of COMIRNATY or S-268019 in 200 adults, 6 months or more after receiving a primary series of COMIRNATY, will be compared. For more information about this clinical trial, please refer to jRCT No.:2031210470. Subject registration for this trial has been completed.

【About a Japanese Phase 3 additional dose clinical trial】

This clinical trial is an open-label trial. In this trial, the safety and immunogenicity of an additional dose of S-268019 in 150 adults aged 20 to 64 years who received 2 inoculation of Spikevax intramuscular injection (hereafter “Spikevax”) and elderly people aged 65 years or older who received 2 inoculation of a primary series of COMIRNATY or Spikevax (in each case, those who have passed 6 months or more and 8 months or less after the second vaccination). For more information about this clinical trial, please refer to jRCT No.:2031210613. Subject registration for this trial has been completed.

【About Phase 3 active control neutralizing antibody comparative clinical trial[4]】

This clinical trial is a double-blind randomized active controlled trial to evaluate a neutralizing antibody

titer after the primary series of Vaxzevria or S-268019 in 1,000 adults and the elderly people.For more information about this clinical trial, please refer to jRCT No.: 2051210151.

【About Global Phase 3 placebo-controlled onset prevention clinical trial[5]】

This clinical trial is a randomized, placebo-controlled, double-blind trial to evaluate the onset prevention effect for COVID-19 after primary series of S-268019 compared with placebo. Approximately 50,000 adults and the elderly people will be enrolled and randomly assigned 2:1 to S-268019 and placebo. This clinical trial adopted crossover assignment, then all participant can get an opportunity to access active control. Currently, we are proceeding with subject registration in Vietnam, the first country in which this trial have been approved. For more information about this clinical trial, please refer to NCT05212948.

In any clinical trial, subjects can decline to participate in the trial at any time during the trial period if they want.

Phase 1/2 Clinical Trial was supported by Japan Agency for Medical Research and Development (AMED).

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

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

References

1. Press release on December 7, 2021
   Shionogi Presents Japanese Phase 1/2 Clinical Trial Results of COVID-19 Recombinant Protein-based Vaccine at Conference
2. Press release on October 21, 2021
   Notice Regarding the Progress of Phase 2/3 Clinical Trial for New Formulation of COVID-19 Recombinant Protein-based Vaccine
3. Press release on December 3, 2021
   Notice Regarding an Initiation of a Additional Dose Clinical Trial for COVID-19 Recombinant-based Vaccine
4. Press release on January 17, 2022
   Notice Regarding the Initiation of an Active Control Neutralizing Antibody Comparative Clinical Trial for COVID-19 Recombinant Protein-based Vaccine, S-268019 in Japan
5. Press release on December 27, 2021
   Notice Regarding the Initiation of a Global Phase 3 Clinical Trial for COVID-19 Recombinant Protein-based Vaccine, S-268019