# Press Release

SHIONOGI

## Shionogi Presents Japanese Phase 2/3 Clinical Trial Results of COVID-19 Recombinant Protein-based Vaccine at Conference

**OSAKA, Japan, Apri 22, 2022 -** Shionogi & Co., Ltd. (Head Office: Osaka, Japan; President and CEO: Isao Teshirogi, Ph.D.; hereafter "Shionogi") announced that Shionogi presented results from the Japanese Phase 2/3 clinical trial of S-268019, a recombinant protein-based vaccine for COVID-19, caused by the novel coronavirus (SARS-CoV-2), at the 96th Meeting of The Japanese Association for Infectious Diseases.

This clinical trial was designed to evaluate the safety, tolerability and immunogenicity of S-268019 in Japanese adults (including naïve*1 subjects, vaccinated subjects*2, and subjects with history of infection*3) and elderly individuals. This is an open label trial including more than 3,000 patients. The evaluation period is 28 days after the second inoculation (Day 57), and the observation period is one year after the second inoculation.

* 1 Subjects with no history of SARS-CoV-2 infection and SARS-CoV-2 vaccination
* 2 Subjects with a history of SARS-CoV-2 vaccination with or without a history of SARS-CoV-2 infection
* 3 Subjects with a history of SARS-CoV-2 infection and no history of SARS-CoV-2 vaccination

The results can be summarized as follows:

【Safety】

- At the time of the interim analysis (Day 57 assessment completed for all subjects), solicited treatment-related adverse events (TRAEs)※1 after inoculation were observed in many subjects, but no serious safety concerns were found, and tolerability was confirmed.
  - There was no significant difference in the incidence of solicited TRAEs among 2,957 naïve adult, 76 vaccinated adults, and 68 with a history of infection.
  - 118 naïve elderly subjects were enrolled with a rate of solicited TRAEs lower than in other naïve adults.

※1 TRAEs that occurred up to 7 days after inoculation of the investigational drug: solicited systemic TRAEs (fever, nausea/vomiting, diarrhea, headache, malaise, muscle pain), solicited local TRAEs (pain , erythema/redness, inoculation pain, swelling at the injection site))

【Immunogenicity】

- Immunogenicity after S-268019 vaccination was confirmed in adults (304 naïve, 76 vaccinated, 68 with history of infection) and 115 naïve elderly.
  - In naïve adults, the geometric mean antibody titer (GMT) of SARS-CoV-2 neutralizing antibodies 14 days after the second inoculation of S-268019 was confirmed to be significantly higher than the GMT in recovered patient serum.
  - In naïve elderly, an increase in GMT of SARS-CoV-2 neutralizing antibody titer was confirmed 14 days after the second inoculation of S-268019.
  - In vaccinated subjects and those with a history of infection, an increase in GMT of SARS-CoV-2 neutralizing antibody titer was confirmed after the first inoculation of S-268019.
  - The seroresponse rate of SARS-CoV-2 neutralizing antibody titer※2 28 days after the second inoculation was: naïve adults: 95.9%, vaccinated adults: 100%, subjects with a history of infection: 97.0%, naïve elderly: 85.5%

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

Shionogi has been conducting five pivotal clinical trials of S-268019, including this trial. Starting in February 2022, we have engaged in prior consultations with the Pharmaceuticals and Medical Devices Agency (PMDA) in preparation for the 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.*

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**【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

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**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