Press Release

Shionogi Files for Approval of S-217622, a Therapeutic Drug for COVID-19, in Japan

OSAKA, Japan, February, 25, 2022 - Shionogi & Co., Ltd. (Head Office: Osaka, Japan; President and CEO: Isao Teshirogi, Ph.D.; hereafter "Shionogi") today announced that Shionogi has completed the analysis of primary endpoints[a), b)] in the Phase 2b part of a Phase 2/3 clinical trial of S-217622, an orally administered antiviral drug for COVID-19, and has filed for manufacture and sales approval, requesting review under the conditional early approval system in Japan.

[a)] Change from baseline on Day 4 (after the 3rd dose) in SARS-CoV-2 viral titer
[b)] Time-weighted average change in the total score of 12 COVID-19 symptoms from the initiation of administration (Day 1) up to 120 hours (Day 6)

This Phase 2b part of the Phase 2/3 clinical trial is a randomized, placebo-controlled, double-blind study in
428 SARS-CoV-2 infected subjects with mild/moderate symptoms (419 in Japan and 9 in South Korea). This study was conducted mainly in infected patients after the Omicron variant wave of the epidemic, and its main purpose is to confirm the antiviral effect and clinical symptom improvement of S-217622 (2 dose groups) when orally administered once daily for 5 days. The main results are outlined below.

- Antiviral effect
  - At both doses, the S-217622 arms showed a significant difference on day 4 (after the 3rd dose), in comparison to the placebo arm, with respect to each of the following:
    - Rapid reduction in viral titer (achieved primary endpoint)
    - The proportion of subjects with positive viral titer, which was below 10% in the S-217622 treated arms, and decreased to a greater degree than seen in the Phase 2a part, [1] in comparison with the placebo arm

- Clinical symptom improvement
  - No significant difference in the time-weighted average change in the total score of 12 COVID-19 symptoms from initiation of administration up to 120 hours while they changed in the direction of improvement (primary endpoint not achieved)
  - Of the 12 symptoms, a significant improvement effect in the total score of respiratory symptoms (stuffy or runny nose, sore throat, cough, shortness of breath), highly characteristic symptoms in the population enrolled in this study, was observed at both doses

- Safety
  - TEAE and treatment-related TEAE were consistent with those observed in the Phase 2a part, and no new adverse events of concern were observed at the time of this analysis

Shionogi will promptly submit further analyses of the data from this study to the Pharmaceuticals and Medical Devices Agency (PMDA) so that we can provide this therapeutic drug in Japan as early as possible. In parallel, Shionogi will accelerate the ongoing Phase 3 part of the study in patients with mild/moderate symptoms (target subject number: 1,260) and Phase 2b/3 part of the study in patients with asymptomatic/only mild symptoms (target subject number: 300 to 600) and will submit those data sequentially to the PMDA, as they are obtained.

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 building awareness, epidemiologic monitoring, 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 new products and services to address this pandemic, and will keep all stakeholders informed regarding the progress of our efforts.

About S-217622

S-217622, a therapeutic drug for COVID-19, is a 3CL protease inhibitor created through joint research between Hokkaido University and Shionogi. SARS-CoV-2 has an enzyme called 3CL protease, which is essential for the replication of the virus. S-217622 suppresses the replication of SARS-CoV-2 by selectively inhibiting 3CL protease. Shionogi has already been submitting the non-clinical, manufacturing/CMC data, and clinical trial data obtained so far to the PMDA. Currently the Phase 3 part of a Phase 2/3 clinical trial in patients with mild/moderate symptoms and the Phase 2b/3 part in patients with asymptomatic/only mild symptoms are in progress.

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

1. Press release on February 7, 2022
   Shionogi Presents Phase 2/3 Clinical Trial Results of the COVID-19 Therapeutic Drug S-217622

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