Press Release

New Data for Shionogi's COVID-19 Once-Daily Oral Antiviral S-217622 Show Rapid Virus Clearance

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OSAKA, Japan, April 24, 2022 – Shionogi & Co., Ltd. (hereafter "Shionogi") today announced new results from two late-breaking presentations of S-217622 at the 32nd European Congress of Clinical Microbiology & Infectious Diseases (ECCMID) in Lisbon, 23 – 26 April. S-217622 is an investigational 3CL protease inhibitor that was studied for once-daily oral administration in mainly vaccinated patients (~85%), with no risk factors for severe complications, within five days of COVID-19 symptom onset.

At the meeting, Shionogi presented new late-breaking Phase 2b results from the Phase 2/3 clinical trial of S-217622, completed in Asia (presenter: Norio Ohmagari, Disease Control and Prevention Center, National Center for Global Health), which followed previously reported topline results from the Phase 2b study. These new data showed:

Antiviral effect:

- S-217622 demonstrated rapid clearance of the infectious SARS-CoV-2 virus.
- On day four of treatment (following the third dose), the proportion of patients with positive viral titer decreased by approximately 90% versus placebo.
- S-217622 shortened infectious virus shedding by 1-2 days versus placebo.
- S-217622 showed a significant reduction in viral RNA on days 2, 4, 6 and 9 versus placebo (difference versus placebo in the Least Squares mean change from baseline in viral RNA; under -1.0 $\log_x$ copies/mL on day four at each dose).

Clinical symptom improvement:

- There was no significant difference in total score of 12 COVID-19 symptoms between treatment arms, however, S-217622 showed improvement in composite score of five "respiratory and feverish" symptoms (post-hoc analysis).

Safety:

- Both the Phase 1 and 2a/b parts of the Phase 2/3 clinical trials showed that S-217622 was well-tolerated, with few discontinuations due to drug, and no reports of serious adverse events or death. Treatment-emergent adverse events in these trials were generally mild to moderate, and resolved without treatment.

The Phase 2b study was conducted with 428 patients in Japan and South Korea. Its main purpose was to confirm the antiviral effect and clinical symptom improvement of S-217622 when orally administered once daily for five days, versus placebo.

A second late-breaking presentation by Shionogi reported results from both the Phase 1 clinical trial and the Phase 2a part of the Phase 2/3 clinical trial of S-217622 completed in Japan (presenter: Hiroshi Yotsuyanagi, The Institute of Medical Science, The University of Tokyo),

which demonstrated it was generally well-tolerated, and rapidly cleared SARS-CoV-2. The full abstracts and oral presentations are available on the ECCMID website.

"These results demonstrate that S-217622 rapidly eliminates SARS-CoV-2 in patients versus placebo, marking its potential, if approved, as an effective treatment option for COVID-19. As infections continue to rise in areas worldwide, it is important we have access to a range of easily administered treatment options to ease the pressures on our healthcare systems," said Isao Teshirogi, Ph.D., President and CEO at Shionogi & Co., Ltd. "We look forward to continued study of this antiviral in Phase 3 trials."

A separate global Phase 3 study of S-217622 is underway aiming to recruit participants globally to support regulatory filings this year.

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About S-217622
S-217622, an investigational therapeutic drug for COVID-19, is an 3CL protease inhibitor created through joint research between Hokkaido University and Shionogi. SARS-CoV-2 utilizes an enzyme called 3CL protease that is essential for the replication of the virus. S-217622 suppresses the replication of SARS-CoV-2 by selectively inhibiting 3CL protease.

In the Phase 2 trial (Phase 2a and 2b parts), completed in Japan and Korea, patients treated with S-217622 showed a significant and rapid decrease in viral titer and/or viral RNA on day 4 (after the 3rd dose) compared to the placebo, and no serious safety concerns were reported. The Phase 3 part of the Phase 2/3 clinical trial is in progress. Additionally, in the preliminary *in vitro* study, S-217622 exhibited similar antiviral activity against the Omicron subvariant BA.2 and other existing variants. Recognizing the urgent global need for more therapies to address COVID-19, Shionogi has already begun working with worldwide health authorities including those located in Japan, where it filed for manufacture and sales approval on February 25, 2022, as well as in the United States.

Shionogi's commitment to fight COVID-19
With continued social disruption caused by the worldwide spread of the novel coronavirus (SARS-CoV-2), Shionogi continues intensive efforts to deliver pharmaceutical products to patients in need in a reliable and stable manner. As a pharmaceutical company with a major focus on infectious diseases, Shionogi is also working with public institutions, academia, and partner companies to address COVID-19, by pursuing the discovery of novel therapeutics and the development of vaccine and diagnostic products. We will continue to strive to fulfil our social responsibility and to contribute to re-establishing the safety and security of society by bringing forward new tools and technologies for the diagnosis and treatment of COVID-19 to support ending this pandemic. Shionogi will work closely with government, industry, and academia to accelerate our efforts and will keep all stakeholders informed regarding the progress of our efforts.

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About Shionogi
Shionogi & Co., Ltd. is a leading global research-driven pharmaceutical company based in Japan, dedicated to bringing benefits to patients based on its corporate philosophy of "supplying the best possible medicine to protect the health and wellbeing of the patients we serve." The company has discovered and developed novel medicines for HIV, influenza and antimicrobial resistance, and currently markets products in several therapeutic areas including anti-infectives with the first siderophore cephalosporin, cefiderocol. Other therapeutic areas and the focus of the company's pipeline include CNS/psychoneurological diseases, oncology and pain. For more information on Shionogi & Co., Ltd., visit https://www.shionogi.com/global/en/. Shionogi Inc. is the U.S. subsidiary of Shionogi & Co., Ltd. based in N.J. For more information on Shionogi Inc., please visit https://www.shionogi.com. Shionogi B.V. is the European headquarters of Shionogi & Co., Ltd. For more information on Shionogi B.V., please visit www.shionogi.eu.

Forward Looking Statement
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, unavailability 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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