PRESSRELEASE

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Shionogi Announces Positive Results from Phase 2 Trial of Respiratory Syncytial Virus Oral Antiviral Candidate S-337395

- Statistically Significant Reduction in Viral Load Confirmed in Clinical Trial
- Primary Endpoint Achieved
- In the highest dose group, there was an 88.94% reduction in viral load (P<0.0001)

OSAKA, Japan, Jan 30, 2025 – Shionogi & Co., Ltd. (Head Office: Osaka, Japan; Chief Executive Officer: Isao Teshirogi, Ph.D.; hereafter "Shionogi") is pleased to announce that its novel investigational respiratory syncytial virus (RSV) oral antiviral candidate S-337395, which is being jointly developed with UBE Corporation (Head office: Minato-ku, Tokyo; President and Representative Director: Masato Izumihara; hereafter "UBE"),has achieved its primary endpoint in a Phase 2 clinical trial.

This trial was a randomized, placebo-controlled, double-blind human challenge study conducted in healthy adults who were actively inoculated with RSV. The antiviral efficacy and safety of S-337395 were evaluated when administered orally once daily for five days. The S-337395 treatment group showed a statistically significant reduction in viral load compared to the placebo group, achieving the primary endpoint. In the highest dose group of S-337395, there was an 88.94% reduction in viral load (P<0.0001), and also a statistically significant improvement in clinical symptom scores. Additionally, S-337395 was generally safe and well tolerated, there were no serious or severe adverse events, and no dose-dependent increase in incidence or severity of adverse events. No participants discontinued due to adverse events.

S-337395 is an investigational oral antiviral candidate for RSV infection that inhibits the activity of the L protein, which is essential for virus replication.[1,2] Furthermore, this drug has received Fast Track designation from the U.S. Food and Drug Administration (FDA).[3]

RSV is a common respiratory virus that infects the nose, throat, and lungs, and can also cause severe illness such as bronchiolitis and pneumonia in children younger than 1 year of age.[4] In recent years, there has been a growing awareness that RSV also causes high rates of hospitalization and mortality amongst individuals aged 60 and older. It is estimated that there are over 3 million patients with RSV infection annually in the U.S. [5,6] Effective antiviral treatment options for RSV remain limited, and there continues to be a significant unmet medical need in this area.[7] We are accelerating the development of S-337395 to provide it to patients suffering from RSV infections as soon as possible.

Shionogi is committed to the principle "Protecting people worldwide from the threat of infectious diseases" as our key focus, and is working on the realization of total care for infectious diseases. In response to acute respiratory infections driving epidemics (such as influenza and COVID-19, RSV), we are working to build a new business model with an expanded portfolio of treatments achieving stable revenue.

【About S-337395】

S-337395 is a novel investigational oral treatment for RSV infection discovered through joint research with UBE. It is a low-molecular-weight compound with a novel mechanism that inhibits the RNA-dependent RNA polymerase activity of the L protein possessed by the RSV , thereby inhibiting the transcription and replication of the viral genome. Unlike F protein inhibitors, which exert their effect by preventing new viral infection of cells extracellularly, S-337395 works by preventing viral proliferation within infected cells, thus potentially offering higher efficacy and a more rapid reduction in viral load. Currently, under the joint development agreement[2] with UBE, Shionogi is advancing the global clinical development, while UBE is responsible for the development and manufacturing of the active pharmaceutical ingredient. By leveraging each company's strengths, we are advancing the joint development of this drug.

【About the Phase 2 Human Challenge Trial】

A human challenge trial is a clinical study in which healthy subjects are intentionally infected with a pathogen, such as a virus, to investigate the onset of disease and the progression of symptoms, including the viral load, after administration of a treatment or placebo. This trial was a randomized, placebo-controlled, double-blind human challenge study conducted to verify the efficacy and safety of S-337395. It involved 114 healthy adults who were actively inoculated with RSV. Participants were administered S-337395 or placebo for five days. The primary endpoint was the area under the curve (AUC) of the viral load over time.

【About RSV infection】

RSV is present worldwide without any geographical or climatic bias. It is characterized by having the greatest impact on vulnerable infants in all regions and by recurring annually, especially in urban areas. Each year in the U.S., RSV leads to approximately: 2.1 million outpatient (non-hospitalization) visits among children younger than 5 years old, 58,000–80,000 hospitalizations among children younger than 5 years old[5] and approximately 0.63 million-2.3 million outpatient (non-hospitalization) visits among adults 60 years and older, 70,555–168,130 hospitalizations among adults 60 years and older, and 3,813-15,739 deaths among adults 60 years and older[6].

【About UBE Corporation】

UBE encompasses a group of specialty chemicals businesses, of which the pharmaceuticals business comprises the core of its life sciences portfolio, progressing beyond its track record of discoveries in small molecule therapeutics into high added-value products such as ADCs (antibody-drug conjugates). Alongside is a CDMO (contract development and manufacturing organization) business, which is strengthening its existing small molecule production capacity while also acquiring capabilities in novel modalities such as oligonucleotide therapeutics. UBE's life science businesses will continue to offer solutions that enhance and protect human life and health https://www.ube.com/ube/en/

[References]

1. Press release on December 10, 2018
2. Press release on February 28, 2022
3. Press release on October 24, 2024.
4. U.S. Centers for Disease Control and Prevention. Respiratory Syncytial Virus Infection (RSV). Accessed January 23, 2025. Available at https://www.cdc.gov/rsv/causes/index.html.
5. Drysdale SB, Broadbent L. Respiratory syncytial virus (RSV): over 60 years of research but still so many unanswered questions.
   Ther Adv Infect Dis. 2023;10:20499361231159991. doi:10.1177/20499361231159991.
6. U.S. Centers for Disease Control and Prevention. Surveillance of RSV. Accessed January 23, 2025. Available at https://www.cdc.gov/rsv/php/surveillance/index.html.
7. Miloje Savic et al. Respiratory syncytial virus disease burden in adults aged 60 years and older in high-income countries: A systematic literature review and meta-analysis. *Influenza Other Respir Viruses*. 2022 Nov 11;17(1):e13031. doi: 10.1111/irv.13031

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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