PRESSRELEASE

SHIONOGI

Shionogi announces positive results from Phase 2 human challenge trial of Respiratory Syncytial Virus (RSV) 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") today announced 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 Izuhara), has achieved its primary endpoint in a Phase 2 human challenge trial (HCT) conducted by hVIVO.

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 and confirming the antiviral effect of S-337395 in healthy volunteers. In the highest dose group of the trial, there was an 88.94% reduction in viral load (P<0.0001) and a statistically significant improvement in clinical symptom scores was also demonstrated. Additionally, S-337395 was generally 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 for RSV infection that inhibits the activity of the viral L protein, which is essential for virus replication.[1, 2] S-337395 received Fast Track designation from the U.S. Food and Drug Administration (FDA) in October 2024.[3]

RSV is a common respiratory virus that infects the nose, throat, and lungs, and can also cause severe illness such as bronchiolitis or pneumonia in children younger than 1 year of age and respiratory infections in people aged 60 years and older[4,5,6]. Effective antiviral treatment options for RSV remain limited, and there continues to be a significant unmet medical need in this area.[5]

In response to the ongoing global threat of acute respiratory viral infections, Shionogi is engaged in the research and development of multiple therapeutic treatments and is working to expand its portfolio for the benefit of patients who need these treatments. To accelerate these efforts, Shionogi will continue to advance the development of S-337395.

About S-337395
S-337395 is a novel investigational oral treatment for RSV infection discovered through joint research with UBE Corporation (Head office: Minato-ku, Tokyo; President and Representative Director: Masato Izuhara). 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 virus infection of cells extracellularly, S-337395 works by preventing the proliferation of new viruses 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 progressing with the joint development of this drug.

About the Phase 2 Human Challenge Trial (HCT)
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 reduction in 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
Respiratory syncytial virus (RSV) infection is responsible for an estimated 33 million acute lower respiratory tract infections (LRTIs) and over 3 million hospitalisations in children below 5 years old worldwide each year[5]. In addition, older adults and immunosuppressed patients are also at high risk of severe disease[5]. In adults aged 60 years and older, the seasonal global incidence of RSV infection is 16.11 cases per 1000 people.[6] RSV can also severely impact the elderly, with an estimated 27.44% developing pneumonia and 24.48% requiring hospitalization[6].

About Shionogi in Infectious Disease
Since 1953, Shionogi has been a leader in the R&D of treatments for infectious diseases. Our R&D story extends beyond antibiotics to include novel medications for HIV and influenza. Today, our global pipeline includes investigational agents to address global health challenges including antimicrobial resistance, COVID-19, influenza, rare fungal diseases and respiratory syncytial virus.

About UBE Corporation
UBE Corporation 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/

About hVIVO
hVIVO plc (ticker: HVO) is a fast-growing specialist contract research organisation (CRO) and the world leader in testing infectious and respiratory disease vaccines and therapeutics using human challenge clinical trials. The Group provides end-to-end early clinical development services to its large, established and growing repeat client base, which includes four of the top 10 largest global biopharma companies.

The Group's fast-growing services business includes a unique portfolio of 11 human challenge models, with a number of new models under development, to test a broad range of infectious and respiratory disease products. The Group has world class challenge agent manufacturing capabilities, specialist drug development and clinical consultancy services via its Venn Life Sciences brand, and a lab offering via its hLAB brand, which includes virology, immunology biomarker and molecular testing. The Group also offers additional clinical field trial services such as patient recruitment and clinical trial site services.

hVIVO runs challenge trials in London - its new state-of-the-art facilities in Canary Wharf opened in 2024 and is the world's largest commercial human challenge trial unit, with highly specialised on-site virology and immunology laboratories, and an outpatient unit. To recruit volunteers / patients for its studies, the Group leverages its unique clinical trial recruitment capability via its FluCamp volunteer screening facilities in London and Manchester.

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 28, 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. Nguyen-Van-Tam JS, et al. Burden of respiratory syncytial virus infection in older and high-risk adults: a systematic review and meta-analysis of the evidence from developed countries. Eur Respir Rev. 2022 Nov 15;31(166).

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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