SHIONOGI & CO., LTD.

Shionogi Announces Positive Top-Line Results for S-033188 Phase 3 Study (CAPSTONE-1) in Otherwise Healthy Influenza Patients

Osaka, Japan, July 24, 2017 - Shionogi & Co., Ltd. (hereafter "Shionogi") has announced that S-033188, a novel cap-dependent endonuclease inhibitor targeting influenza, demonstrated superiority to placebo in a global Phase 3 study in otherwise healthy patients. Time to alleviation of symptoms (TTAS) was significantly reduced with S-033188 compared to placebo ($p<0.0001$), as were other important secondary endpoints such as viral titer.

The S-033188 CAPSTONE-1 study enrolled 1,436 influenza A or B patients, aged 12-64 years old, in a double-blind randomized study versus placebo or oseltamivir. Safety and efficacy were assessed for one-time single doses of 40 mg or 80 mg of S-033188 (depending on body weight) compared to placebo or 75 mg oseltamivir phosphate dosed twice-daily for 5 days.

Top-line results for the CAPSTONE-1 study include the following:

- S-033188 demonstrated a statistically significant reduction in TTAS compared to placebo, and thus achieved the primary study objective ($p<0.0001$). Reduction in TTAS for S-033188 and oseltamivir were similar.
- S-033188 demonstrated statistically significant differences in reduction of virus titer on the first and second days following dosing, and in duration of viral shedding, compared to either placebo or oseltamivir.
- S-033188 was well tolerated. For patients treated with S-033188, the incidence of treatment-related adverse events was comparable to those treated with placebo. S-033188 demonstrated a statistically significant decrease in incidence of treatment-related adverse events compared to oseltamivir. Of note, the incidence of nausea was less frequent for patients treated with S-033188 compared to patients treated with oseltamivir.

“We are very excited about S-033188, a novel cap-dependent endonuclease inhibitor” said Dr. Tsutae Den Nagata, Chief Medical Officer, “this result confirms the robust efficacy and safety profile we have seen previously, and further, demonstrates very rapid viral load reduction and reduced duration of virus shedding compared with oseltamivir.”

Based on the results from CAPSTONE-1, Shionogi plans to submit a New Drug Application (NDA) to the PMDA in Japan later this year. Shionogi is currently conducting another global Phase 3 study (CAPSTONE-2) in individuals at high risk for influenza-associated complications; patient enrollment in the study is ongoing.

About CAPSTONE-1 study

The CAPSTONE-1 study was a randomized, double-blind, multicenter, parallel-group, placebo- and active-controlled study that enrolled 1,436 patients diagnosed with influenza. Patients aged 20 to 64 years were randomly assigned in a ratio of 2:1:2 to receive a single dose of 40 or 80 mg of S-033188, according to body weight, placebo, or 75 mg BID of oseltamivir for 5 days. Patients in the 12 to 19 year age stratum were randomly assigned in a ratio of 2:1 to receive either a single dose of S-033188 or placebo. Patients who weighed <80 kg at screening received 40 mg of S-033188 and patients who weighed ≥80 kg at screening received 80 mg of S-033188.

About S-033188

S-033188 is a cap-dependent endonuclease inhibitor with a novel mechanism of action being studied for the treatment of influenza using a one-time dosing regimen. Development and commercialization are in collaboration with F. Hoffmann-La Roche Ltd.

About Influenza

Epidemic and pandemic influenza remain a major public health concern, and novel influenza drugs that will offer significant improvement over current therapy are urgently needed. Worldwide, annual influenza epidemics are estimated to result in 3 to 5 million cases of severe illness, and about 250,000 to 500,000 deaths[1]. In general, those at highest risk of influenza-associated complications include children under 2 years of age, adults over 65 years of age, pregnant women, and people of any age with certain medical conditions, including chronic heart, lung, metabolic diseases (such as diabetes) and weakened immune systems.

About Shionogi

Shionogi & Co., Ltd. is a major research-driven pharmaceutical company 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." Shionogi's research and development currently target two therapeutic areas: infectious diseases, and pain/CNS disorders. For over 50 years, Shionogi has developed and commercialized innovative oral and parenteral anti-infectives. In addition, Shionogi is engaged in new research areas, such as obesity/geriatric metabolic disease and oncology/immunology. Contributing to the health and quality of life of patients around the world through development in these therapeutic areas is Shionogi's primary goal. For more details, please visit www.shionogi.co.jp/en/. For more information on Shionogi Inc., the U.S. –based subsidiary of Shionogi & Co., Ltd., headquartered in Florham Park, NJ, USA, please visit www.shionogi.com. For more information on Shionogi Ltd., the UK-based subsidiary of Shionogi & Co. Ltd., headquartered in London, England, 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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References

1. http://www.who.int/mediacentre/factsheets/fs211/en/ WHO website, Influenza (Seasonal), Fact sheet N°211, March 2014