# Press Release

## Congress Presentation on Clinical Study of S-600918, a Drug Candidate for the Treatment of Refractory/Unexplained Chronic Cough

**- Favorable Results of Phase II Study Presented at the European Respiratory Society International Congress (ERS 2019) -**

**OSAKA, Japan, October 2, 2019 -** Shionogi & Co., Ltd. (Head Office: Chuo-ku, Osaka; President & CEO: Isao Teshirogi, Ph.D., hereafter “Shionogi” or “the Company”) presented favorable results of the Phase II Study of S-600918, a drug candidate discovered by the company for the treatment of refractory/unexplained chronic cough, at the European Respiratory Society International Congress (ERS 2019) held between September 28 and October 2, 2019 in Madrid, Spain. The summary is as follows.

S-600918 is a novel chemical compound expected to alleviate refractory/unexplained chronic cough by selectively blocking $P2X_3$ receptors that are relevant to cough reflex. A multicenter, randomized, double-blind, placebo-controlled, crossover study was conducted on 31 patients with refractory/unexplained chronic cough lasting for 6 months or longer. The efficacy and safety of S-600918 was evaluated with once-daily administration for two weeks.

The primary endpoint was the rate of change in hourly cough frequency during the daytime from the baseline to two weeks after administration of the study agent. S-600918 showed the change in the rate to be -54.1%, while the placebo was -33.0%. The rate of change of the drug candidate adjusted by placebo from the baseline accounted for -31.6% (p=0.0546). As one of the secondary endpoints, the rate of change adjusted by placebo in hourly cough frequency 24 hours after S-600918 administration from the baseline stood at -30.9%, which demonstrated a statistically significant decrease (p=0.0386). Regarding the change in scores from the baseline of the Leicester Cough Questionnaire (LCQ) that assesses quality of life (QOL) specific to cough, S-600918 showed significant improvement compared with the placebo administration (p=0.0415).

The incidence of adverse events when S-600918 was administered was 35.5%, compared to 29.0% with the placebo, which showed no significant difference. The incidence of taste disturbance, an adverse event seen with similar drugs, was 6.5% after administration of S-600918. All of the adverse events considered to have been related to the investigational agent were mild, and returned to normal without therapeutic management: High levels of safety and tolerability were confirmed.
Preparation for the multiregional phase II b study is underway based on the current favorable results.

Shionogi will strive to achieve its mission to "supply the best possible medicine to protect the health and wellbeing of the patients we serve" and thereby to improve the quality of life for patients all over the world as a drug-discovery-based pharmaceutical company.

**[About refractory/unexplained chronic cough]**

Although coughing is a defense mechanism to force out phlegm and foreign objects from the airway, it may impair QOL if it continues in an excessive manner. Chronic cough, in especial, is defined as a cough that persists longer than eight weeks.[1-3] Its prevalence in Japan is reported to be between 2% and 10%, and about 10% in Europe and the U.S.[4, 5] Among the multiple types of chronic cough, there are cases where symptoms of coughing remain even after treating the suspected causative disease (such as cough variant asthma, atopic asthma, gastroesophageal reflux disease, upper airway cough syndrome, non-asthmatic eosinophilic bronchitis and sinusitis), and where causative diseases cannot be identified even with detailed examinations. These are defined as refractory/unexplained chronic cough. Reports have suggested that patients with refractory cough account for 20% to 40% in Europe and the U.S., which is not substantially different from the percentage in Japan.[4, 6] At present, no drugs have been approved for the treatment of refractory/unexplained chronic cough. The basic concept for the treatment of cough is to identify causative diseases as much as possible and treat them in a specific manner depending on the causes. Nevertheless, a safe and effective medication has been desired against persistent refractory/unexplained chronic cough.

**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, 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.*

**For further information contact:**

Shionogi & Co., Ltd.
Corporate Communications Department
Telephone: +81-6-6209-7885

**References**


1. The Japanese Respiratory Society Preparatory Committee of Clinical Practice Guidelines for Cough and Expectoration 2019. Clinical Practice Guidelines for Cough and Expectoration 2019.
2. Gibson P, Wang G, McGarvey L, Vertigan AE, Altman KW, Birring SS, CHEST Expert Cough Panel. Treatment of Unexplained Chronic Cough: CHEST Guideline and Expert Panel Report. Chest 2016; 149(1): 27-44.
3. Morice AH, Fontana GA, Sovijarvi AR, et al. The diagnosis and management of chronic cough. Eur Respir J 2004; 24(3): 481-92.
4. Matsumoto H. Epidemiology and Classification of Prolonged/Chronic Cough, the Japanese Journal of Chest Diseases, 2015; 74(11): 1179-88.
5. Gibson PG, Vertigan AE. Management of chronic refractory cough. BMJ 2015; 351: h5590.
6. Pacheco A, Cobeta I, Wagner C. Refractory Chronic Cough: New Perspectives in Diagnosis and Treatment. Arch Bronconeumol 2013; 49(4):151-7.