Confirmatory Results of the Second Phase 3 Lusutrombopag (S-888711) Study (L-PLUS 2) Presented at the 2017 Liver Meeting® of the American Association for the Study of Liver Diseases (AASLD)

OSAKA, Japan and FLORHAM PARK, N.J., October 20, 2017 - Shionogi & Co., Ltd. (hereafter "Shionogi") announced it will present positive efficacy and safety results from a global Phase 3 study (L-PLUS 2) of lusutrombopag (S-888711), an investigational, once-daily, orally administered, small molecule thrombopoietin (TPO) receptor agonist, at the 2017 American Association for the Study of Liver Diseases (AASLD) Liver Meeting to be held October 20-24 in Washington, D.C.

L-PLUS 2 was a multi-national, double-blind, placebo-controlled study conducted in 22 countries to evaluate lusutrombopag for the treatment of thrombocytopenia in patients with chronic liver disease undergoing planned, non-emergent invasive procedures. L-PLUS 2 was the second of two Phase 3 studies of lusutrombopag demonstrating confirmatory data to support the previously reported L-PLUS 1 trial. A total of 215 patients were randomized 1:1 to receive 3 mg of lusutrombopag (n=108), or placebo (n=107), up to seven days. Therapy was initiated on Day 1 and invasive procedures were performed between Day 9 and Day 14. A pre-procedure platelet transfusion was mandated by the study protocol if a patient's platelet count prior to the invasive procedure had not reached 50,000/μL.

Key findings from the L-PLUS 2 study will be presented in a late-breaking oral session on Monday, October 23 and include the following:

- Lusutrombopag met the Phase 3 study's primary endpoint, which was defined as the proportion of patients who required no platelet transfusion prior to the procedure and no rescue therapy for bleeding through seven days following the procedure (64.8 percent of lusutrombopag patients versus 29.0 percent of placebo patients).
- 64.8 percent of patients taking lusutrombopag achieved a platelet count of at least 50,000/μL and had an increase in platelet count of at least 20,000/μL from baseline, compared to 13.1 percent of patients taking placebo.
- Among patients taking lusutrombopag who required no platelet transfusion (n=74), platelet count of at least 50,000/μL was maintained for a median of 19 days.
- 47.7 percent of lusutrombopag patients versus 48.6 percent of placebo patients experienced adverse events after initiation of study treatment
- Adverse events related to thrombosis were reported in 1.9 percent of patients in each treatment group. These events included portal vein thrombosis (PVT) which is known as a potential risk in patients with severe chronic liver disease. The L-PLUS 2 study protocol stipulated proactive assessment of thrombosis in the portal vein system by diagnostic imaging devices at the screening and after the

invasive procedures (regardless of absence or presence of symptoms of thrombosis). As a result, three PVT events were observed: one patient (0.9 percent) taking lusutrombopag versus two patients (1.9 percent) taking placebo. All PVT events were incomplete occlusion therefore considered not clinically significant and resolved with therapy.

- Adverse events related to bleeding occurred in 2.8 percent of patients in the lusutrombopag group versus 5.6 percent of patients in the placebo group, respectively. No patients taking lusutrombopag and two patients (1.9 percent) taking placebo required rescue therapy for bleeding.
- Lusutrombopag was generally well tolerated, with adverse events deemed treatment-related by the investigator in 5.6 percent of patients taking lusutrombopag versus 12.1 percent of patients taking placebo.

"There is a clear, unmet need for additional treatment options for our chronic liver disease patients with significant thrombocytopenia, as platelet transfusion is currently their only choice." said Dr. Nezam Afdhal, Director of Hepatology at Beth Israel Deaconess Medical Center and Professor of Medicine at Harvard Medical School. "The safety and efficacy of lusutrombopag may give clinicians an additional option for the treatment of thrombocytopenia in liver disease patients undergoing invasive procedures."

Lusutrombopag has been granted Fast Track designation by the Food and Drug Administration (FDA) for the treatment of thrombocytopenia in patients with chronic liver disease who are at increased risk for bleeding associated with elective invasive procedures. Shionogi has initiated rolling submission of a New Drug Application to the FDA. Shionogi plans to present L-PLUS 2 study data at the 25th United European Gastroenterology Week in Spain later this month, and at the American Society of Hematology meeting in December.

About Lusutrombopag, an investigational drug

Lusutrombopag (S-888711) is an orally administered, small molecule agonist of the human thrombopoietin receptor. Lusutrombopag was approved by the Ministry of Health, Labor and Welfare in Japan in September 2015 for the improvement of thrombocytopenia associated with chronic liver disease in patients undergoing an elective invasive procedure.

About Thrombocytopenia

Thrombocytopenia is a common complication of chronic liver disease (CLD), which may be caused by multiple factors including decreased production of thrombopoietin. CLD-associated thrombocytopenia is defined as a platelet count of less than 150,000/μL and is the most common hematologic complication of CLD.[1,2,3] Patients with CLD and thrombocytopenia are at increased risk for bleeding, requiring recurrent platelet transfusions, increased ambulatory visits and inpatient hospital stays compared with patients with CLD without thrombocytopenia.[4] The annual health care cost of a patient with CLD with hepatitis C virus with thrombocytopenia is more than three times that of a patient with the virus without thrombocytopenia.[4] In addition to the potential of thrombocytopenia**,** especially severe thrombocytopenia (platelet count less than

50,000/μL), to aggravate surgical or traumatic bleeding, it may also significantly complicate routine patient care, such as liver biopsy and medically indicated or elective procedures for cirrhotic patients, resulting in delayed or cancelled medical management.[5]

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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