Shionogi Announces FDA New Drug Application (NDA) and EMA Marketing Authorization Application (MAA) Acceptances for Lusutrombopag (S-888711)

In the United States, Lusutrombopag Granted Priority Review by the FDA

OSAKA, Japan and FLORHAM PARK, N.J., February 26, 2018 - Shionogi & Co., Ltd. (hereafter "Shionogi") announced today that the New Drug Application (NDA) for lusutrombopag (S-888711), an investigational, once-daily, orally administered, small molecule thrombopoietin (TPO) receptor agonist, has been accepted for filing and has been granted Priority Review by the U.S. Food & Drug Administration (FDA). In the United States, Shionogi is seeking FDA approval of lusutrombopag for the treatment of thrombocytopenia in patients with chronic liver disease who are at increased risk for bleeding associated with invasive procedures.

The submission is based on two Phase 3 clinical trials, L-PLUS1 and L-PLUS2, in which lusutrombopag met the pre-specified primary and all key secondary endpoints with statistically significant results. The Prescription Drug User Fee Act (PDUFA) date for an FDA decision is August 26, 2018.

“I am very pleased the FDA has granted Priority Review for lusutrombopag’s New Drug Application. This step emphasizes an urgent need exists for more advanced medicines for the treatment of thrombocytopenia in patients living with chronic liver disease (CLD) who have to undergo invasive procedures,” said John Keller, President and Chief Executive Officer, Shionogi Inc. “We at Shionogi look forward to the upcoming FDA review, and the near future in which patients and physicians have additional, advanced therapeutic options beyond platelet transfusions which are the current standard of care.”

The FDA Priority Review status accelerates the review time from a standard 10-month review to a goal of six (6) months from the date of acceptance of filing. A Priority Review designation will direct overall attention and resources to the evaluation of applications that, if approved, would be significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions when compared to standard applications.

The European Medicines Agency has validated for review Shionogi’s standard Marketing Authorization Application (MAA) for lusutrombopag. In Europe, the MAA submission is based on the same two Phase 3 clinical trials as the FDA filing.

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 CLD in patients undergoing an elective invasive procedure.

About Thrombocytopenia in Chronic Liver Disease

Thrombocytopenia is a common complication of CLD, which may be caused by multiple factors including decreased production of TPO. Thrombocytopenia is frequently observed in patients with CLD, with studies suggesting that it occurs in up to 78% of patients with cirrhosis.[1] CLD-associated thrombocytopenia is defined as a platelet count of less than 150,000/μL and is the most common hematologic complication of CLD.[2,3,4] 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.[5] The annual health care cost of a patient with CLD with thrombocytopenia is more than three times that of a patient with CLD without thrombocytopenia.[5] 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 diagnostic procedures and patient care, such as liver biopsy and medically indicated or elective procedures for cirrhotic patients, resulting in delayed or cancelled curative treatment.[6]

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. *Peck-Radosavljevic M. Liver Int. 2017; 37(6):778-793.*
2. *Giannini EG. Aliment Pharmacol Ther. 2006; 23(8):1055-1065.*
3. *Koruk M, et al. Hepatogastroenterology. 2002; 49(48):1645-1648.*
4. *Aref S, et al. Hematology. 2004; 9(5/6):351-356.*
5. *Poordad F, et al. J Med Econ. 2012; 15:112-124.*
6. *Hayashi H, et al. World J Gastroenterol. 2014; 20: 2595-2605.*