Shionogi Announces U.S. Availability of Mulpleta® (Lusutrombopag) for the Treatment of Thrombocytopenia in Adults with Chronic Liver Disease Scheduled to Undergo a Procedure

OSAKA, Japan and FLORHAM PARK, N.J., August 30, 2018 - Shionogi & Co., Ltd. (hereafter "Shionogi") announced today that Mulpleta® (lusutrombopag), a once-daily, orally administered, small molecule thrombopoietin (TPO) receptor agonist for the treatment of thrombocytopenia in adult patients with chronic liver disease (CLD) who are scheduled to undergo a procedure, is now available throughout the United States.

"We are very excited about the launch of Mulpleta in the United States, recently approved as a new, safe and effective treatment," said Takayuki Yoshioka, President and Chief Executive Officer, Shionogi Inc. "As adult patients with CLD often undergo procedures that could put them at increased risk for bleeding, this treatment will offer physicians and patients an option other than platelet transfusions. Additionally, we have developed *Mulpleta Assist,* a support center for physicians and patients, to help make Mulpleta easier to access and ensure that patients receive Mulpleta before their procedure."

Mulpleta Assist is a full-service patient access and support program that offers healthcare providers and patients a dedicated resource to help manage medication logistics, coordinate managed care reimbursement, match financial assistance, as well as provide overall patient support. Shionogi is committed to helping patients access and afford Mulpleta and have the support necessary to achieve the full benefit of this therapy. To learn more about Mulpleta or *Mulpleta Assist*, please visit www.Mulpleta.com.

The United States Food and Drug Administration (FDA) approved Mulpleta on July 31, 2018. The FDA approval was based on consistent safety and efficacy data from two Phase 3 clinical trials, L-PLUS 1 and L-PLUS 2, in which Mulpleta met primary and secondary endpoints with statistically significant results.

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 Mulpleta

Mulpleta (lusutrombopag) is a once-daily, orally administered, small molecule TPO receptor agonist for the treatment of thrombocytopenia in adult patients with CLD who are scheduled to undergo a procedure. Mulpleta is an orally bioavailable, small molecule TPO receptor agonist that interacts with the transmembrane domain of human TPO receptors expressed on megakaryocytes to induce the proliferation and differentiation of megakaryocytic progenitor cells from hematopoietic stem cells and megakaryocyte maturation.

Mulpleta 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. The European Medicines Agency has validated for review Shionogi's standard Marketing Authorization Application for lusutrombopag and approval is expected in 1H 2019.

Please see Important Safety Information, including Warnings & Precautions and Adverse Reactions below.

INDICATION

Mulpleta® (lusutrombopag) is indicated for the treatment of thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Mulpleta is a thrombopoietin (TPO) receptor agonist, and TPO receptor agonists have been associated with thrombotic and thromboembolic complications in patients with chronic liver disease. Portal vein thrombosis has been reported in patients with chronic liver disease treated with TPO receptor agonists.
Consider the potential increased thrombotic risk when administering Mulpleta to patients with known risk factors for thromboembolism. Monitor platelet counts and for thromboembolic events and institute treatment promptly.

Mulpleta should not be administered to patients with chronic liver disease in an attempt to normalize platelet counts.

ADVERSE REACTIONS

The most common adverse reaction (≥ 3%) with Mulpleta was headache.

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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