FOR IMMEDIATE RELEASE

SHIONOGI

NALDEMEDINE MEETS PRIMARY ENDPOINT IN PHASE 3 STUDY FOR THE TREATMENT OF OPIOID-INDUCED CONSTIPATION

OSAKA, JAPAN and FLORHAM PARK, NJ (August 3, 2015) – Shionogi today announced that once-daily naldemedine met its primary and secondary endpoints in a phase III study (COMPOSE II) for the treatment of opioid-induced constipation (OIC) in adult patients with chronic non-cancer pain. Naldemedine is an investigational, oral, peripherally acting mu-opioid receptor antagonist (PAMORA). This is the third Phase III trial in which naldemedine met its primary and key secondary endpoints.

Study results showed that a 0.2 mg tablet of naldemedine given once daily significantly improved the frequency of spontaneous bowel movement (SBM) compared with placebo over 12 weeks. Naldemedine was generally well-tolerated with the most commonly reported side effects being gastrointestinal disorders.

"We are very encouraged by the results of this study, as it brings us another step closer to our goal of delivering a new therapeutic solution to the millions of patients whose daily lives can be severely impacted by OIC," said Juan Camilo Arjona Ferreira, MD, Senior Vice President Clinical Development. "OIC is different from other forms of constipation as it is the most common side effect of chronic opioid therapy. OIC can hamper everyday activities, reduce work productivity and negatively affect a person's well-being."

About COMPOSE

The COMPOSE program is a global comprehensive development program comprised of seven clinical studies being conducted in patients with OIC with cancer or chronic non-cancer pain.

COMPOSE II is a 12-week, multicenter, randomized, double-blind, placebo-controlled, parallel-group study. The study was designed to evaluate the efficacy and safety of naldemedine therapy, versus placebo, in 553 patients receiving chronic opioid therapy for at least three months, and who experience OIC accompanied by chronic non-cancer pain.

Shionogi previously announced that naldemedine met its primary and secondary endpoints in COMPOSE I and COMPOSE IV. COMPOSE I evaluated the efficacy and safety of naldemedine therapy, versus placebo, in patients receiving chronic opioid therapy, who experience OIC accompanied by chronic non-cancer pain. COMPOSE IV was conducted in Japan and evaluated the

efficacy and safety of naldemedine therapy, versus placebo, in patients receiving chronic opioid therapy for cancer pain and who experience OIC.

About Opioid Induced Constipation (OIC)

Opioid-induced constipation (OIC) is characterized by any of the following: reduced bowel movement frequency, development or worsening of straining to pass bowel movements, a sense of incomplete rectal evacuation, or harder stool consistency.[1] It is estimated that 40-50 percent of chronic opioid patients, about 11 million Americans, experience OIC, with fewer than half reporting satisfactory results with laxatives.[2] Managing OIC and its clinical consequences places a significant burden on the healthcare system and the patient.

About Shionogi

Shionogi & Co., Ltd., is a Japanese pharmaceutical company with a 137-year history discovering and developing innovative therapies. Shionogi Inc., the U.S. based subsidiary of Shionogi & Co., Ltd., continues this focus on the development and commercialization of high quality medicines that protect the health and well-being of the patients we serve. The company currently markets products in several therapeutic areas including women's health, anti-infectives, pain and cardiovascular diseases. Our pipeline is focused on infectious disease, pain, CNS, and oncology. For more details, visit www.shionogi.com. For more information on Shionogi & Co., Ltd., visit www.shionogi.co.jp/en

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.

[1] Camilleri. M, Drossman D.A., Becker G.,Webster L.R., Davies A.N., Mawe G.M. Emerging treatments in neurogastroenterology: a multidisciplinary working group consensus statement on opioid-induced constipation. *Neurogastroenterology Motil.* 2014. 26, 1386-1395

[2] Pappagallo M. Incidence, Prevalence, and Management of Opioid Bowel Dysfunction. *The American Journal of Surgery.* 182 (Suppl to November 2001) 11s-18s

Media Contact:
Lisa Ellen
Mobile: 973-803-6317
Office: 973-307-3423
lisa.ellen@shionogi.com

# # #