NALDEMEDINE PHASE 3 STUDY SHOWS SIGNIFICANT IMPROVEMENT FOR PATIENTS WITH OPIOID-INDUCED CONSTIPATION

Osaka, Japan and Florham Park, NJ (February 19, 2016) – Shionogi today announced pivotal phase III study (COMPOSE I) results showing that once-daily treatment with naldemedine significantly improved opioid-induced constipation (OIC) compared to placebo in patients with chronic non-cancer pain. The data, which are being presented today (poster # 192) at the American Academy of Pain Medicine (AAPM) 2016 Annual Meeting in Palm Springs, CA, also showed that naldemedine was generally well tolerated, with a low incidence rate of gastrointestinal (GI) related side effects.

Naldemedine is an investigational, oral, peripherally acting mu-opioid receptor antagonist (PAMORA) being studied for the treatment of OIC. The study found that for the primary endpoint* 47.6 percent of patients taking an oral, once-daily 0.2 mg tablet of naldemedine experienced an increase in the frequency of spontaneous bowel movements (SBMs) from baseline for at least nine out of 12 weeks (including three out of the last four weeks) compared with 34.6 percent of patients on placebo over 12 weeks. Additionally, naldemedine significantly improved all key secondary endpoints, which included a significant increase in complete SBMs (CSBMs) per week, as well as SBMs without straining per week, from baseline to the last two weeks of the study period, as compared to placebo. Abdominal pain and diarrhea were the only treatment related adverse events that were reported in five percent or more of patients, with abdominal pain reported in 6.3 percent of patients on naldemedine vs. 1.8 percent on placebo, and diarrhea reported in 6.6 percent of patients on naldemedine vs. 2.9 percent on placebo.

“The millions of patients on chronic opioid therapy often suffer from constipation, which can be extremely debilitating and may lead to non-adherence and improper use of pain medications,” said Juan Camilo Arjona Ferreira, MD, Senior Vice President Clinical Development. “We are very encouraged by the naldemedine study results, both in terms of its effect in treating OIC and its safety profile. We look forward to potentially delivering a new therapeutic solution to patients suffering from OIC.”

* The primary endpoint was the responder rate, which is defined as nine positive response weeks or more out of the 12- week treatment period and three positive response weeks out of the last four weeks of the 12-week treatment period. A positive response week is defined as ≥ three SBMs per week and an increase from baseline of ≥ one SBM per week for that week.

About COMPOSE

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

COMPOSE I was 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 547 patients on opioid therapy for at least three months and on a stable dose of opioids for at least four weeks, and who experience chronic non-cancer pain accompanied by OIC.

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

In the studies, a bowel movement occurring within 24 hours after rescue laxative therapy was not considered an SBM.

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] Approximately 11 million Americans experience OIC[2], representing about 40-50 percent of all chronic opioid patients. Fewer than half of OIC sufferers report satisfactory results with laxatives.[3] 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] 2012 IMS Data

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

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