

SHIONOGI Concludes a Contract for the Commercialization of Rizmoic[®] (naldemedine), an Opioid-Induced Constipation Therapeutic Agent, in Germany, the UK, and the Netherlands

OSAKA, Japan and AMSTERDAM, Netherlands, April 11, 2019 - Shionogi & Co., Ltd. (Head Office: Osaka, Japan; President & CEO: Isao Teshirogi, Ph.D.; hereafter "Shionogi") announced today that Shionogi concluded a distribution contract with Sandoz (Headquarters: Holzkirchen, Germany; CEO a.i: Francesco Balestrieri hereinafter "Sandoz") for the sale of Rizmoic[®] (naldemedine) for the treatment of opioid-induced constipation (OIC) in adult patients previously treated with a laxative in the key European markets of Germany, the UK, and the Netherlands, plus right of first refusal for certain other European markets.

Sandoz has a strong presence in the European market for opioid analgesics, as well as a complementary strategic focus on innovative therapeutic alternatives to combat opioid dependency. According to this contract, Sandoz will commercialize Rizmoic[®] in Germany, the UK, and the Netherlands, and Shionogi will be responsible for its manufacturing and development. Dr. John Keller, Chief Executive Officer of Shionogi B.V., the subsidiary of Shionogi in Europe, said "Through this contract, we are able to bring together Sandoz's commercial expertise in Europe, particularly in the field of opioid analgesics with the OIC treatment know-how of Shionogi, which has been developing naldemedine globally. We therefore expect Rizmoic[®] to contribute significantly to OIC treatment in clinical settings in European countries in the future."

On February 18, 2019, the European Commission (EC) granted the Marketing Authorization (MA) for Rizmoic[®] for the treatment of OIC in adult patients who have previously been treated with a laxative.¹ Rizmoic[®] is planned to be launched in Germany and the UK in 2019 and in the Netherlands in 2020. Rizmoic[®] was launched under the brand name Symproic[®] in Japan in June 2017, and in the United States in October 2017.^{2,3} Shionogi plans to initiate a clinical study of naldemedine in paediatric patients with OIC in EU, in accordance with an agreed paediatric investigation plan, as well as a clinical study in adult patients with post-operative ileus.

Shionogi's research and development efforts target pain/CNS as one of its priority areas in the mid-term business plan, SGS2020, in which Shionogi has positioned "Grow sustainably as a drug discovery-based pharmaceutical company contributing to a more vigorous society through improved healthcare" as its vision. Shionogi constantly strives to improve the quality of life of patients who suffer from pain or side effects of analgesics by bringing forth innovative drugs.

About Opioid-induced Constipation

Constipation is one of the most commonly reported side effects associated with opioid treatment, including among patients with chronic non-cancer pain and patients with cancer pain.⁴ OIC is a result of increased fluid absorption and reduced gastro-intestinal (GI) motility due to mu-opioid receptor binding in the GI tract. OIC is defined as a change in bowel habits that is characterized by any of the following after initiating opioid therapy: reduced bowel movement frequency, development or worsening of straining to pass bowel movements, a sense of incomplete rectal evacuation, or harder stool consistency.⁵ In patients receiving opioid therapy for chronic non-cancer pain, the prevalence of OIC ranges from approximately 40-60 percent.⁶

About Rizmoic[®]

Rizmoic[®] (naldemedine) is indicated for the treatment of opioid-induced constipation (OIC) in adult patients who have previously been treated with a laxative. Rizmoic[®] is a peripherally-acting mu-opioid receptor antagonist (PAMORA) that has been developed by Shionogi as a once-daily treatment of OIC. The efficacy and safety of naldemedine have been evaluated in randomized, double-blinded, placebo-controlled studies in adult patients with OIC who have chronic non-cancer pain or who have cancer pain⁷⁻¹¹. Rizmoic[®] is expected to be a new treatment option that can improve the quality of life significantly in patients with OIC in pain management with opioid analgesics.

About Shionogi

Shionogi & Co., Ltd. (“Shionogi”) is a Japanese 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.” The company currently markets products in several therapeutic areas including anti-infectives, pain, CNS disorders and gastroenterology. Shionogi’s research and development currently target two therapeutic areas: infectious diseases and pain/CNS disorders. For more information on Shionogi, please visit <http://www.shionogi.co.jp/en/>. Shionogi B.V. is the European subsidiary of Shionogi & Co., Ltd. based in Amsterdam, Netherlands. For more information on Shionogi B.V. please visit <http://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.

Press Release



For further information contact:

Shionogi Europe

Dr. Mark Hill, Shionogi, mark.hill@shionogi.eu

Mirjam Korn, Shionogi, mirjam.korn@shionogi.eu

Shionogi & Co., Ltd.

Corporate Communications Department

Telephone: +81-6-6209-7885

Reference

1. [Release on February 22, 2019](#)
Shionogi announces European Union Marketing Authorisation for Rizmoic[®] (naldemedine) for the treatment of opioid-induced constipation in adults previously treated with a laxative
2. [Release on June 7, 2017](#)
Opioid-Induced Constipation therapeutic agent ‘Symproic[®] (naldemedine) Tablets 0.2mg’ launched in Japan
3. [Release on October 12, 2017](#)
Shionogi Inc. and Purdue Pharma L.P. Announce U.S. Availability of Symproic[®] (naldemedine) for the Treatment of Opioid-Induced Constipation in Adults with Chronic Non-Cancer Pain
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5. Camilleri M, et al. Emerging treatments in neurogastroenterology: a multidisciplinary working group consensus statement on opioid-induced constipation. *Neurogastroenterol Motil.* 2014;26: 1386-1395.
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7. Hale M, et al. Naldemedine versus placebo for opioid-induced constipation (COMPOSE-1 and COMPOSE-2): two multicentre, phase3, double-blind, randomised, parallel-group trials. *Lancet Gastroenterol Hepatol.* 2017. Published online May 30, 2017.
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