Shionogi Announces Licensing of Symproic® (naldemedine) to BioDelivery Sciences International Inc.

OSAKA, Japan & FLORHAM PARK, N.J., April 11, 2019 - Shionogi Inc. (hereafter "Shionogi") announced today that BioDelivery Sciences International, Inc. (NASDAQ: BDSI), a rapidly growing commercial-stage specialty pharmaceutical company dedicated to patients living with chronic pain, has licensed full rights to commercialize Symproic® (naldemedine) tablets 0.2 mg in the United States. The transfer of rights is effective immediately.

Symproic is an oral tablet which functions as a peripherally acting mu-opioid receptor antagonist medication indicated in the U.S. for the treatment of opioid-induced constipation (OIC) in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation.

“The decision to license Symproic is part of our ongoing strategy to sharpen our commercial focus in specialty therapeutic areas,” said Dr. Isao Teshirogi, President and CEO of Shionogi & Co., Ltd. “Given BioDelivery Sciences International’s strong commercial capabilities, we feel they are the best partner to maximize the value of Symproic as a treatment option for adult patients suffering from chronic non-cancer pain and struggling with opioid-induced constipation.

Under the terms of the transaction, Shionogi Inc. will receive an upfront cash payment of $20 million, an additional $10 million in six months, as well as quarterly royalty payments.

Shionogi regained full rights to Symproic in June 2018. The exclusive rights are now granted to BioDelivery Sciences International Inc.

About Opioid-Induced Constipation (OIC)
Constipation is one of the most commonly reported side effects associated with opioid treatment, including among patients with chronic non-cancer pain.[1] OIC is a result of increased fluid absorption and reduced 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.[2] In patients receiving opioid therapy for chronic non-cancer pain, the prevalence of OIC ranges from approximately 40-50 percent.[3-6]

About Symproic
Symproic® (naldemedine) is indicated for the treatment of OIC in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation. Symproic® was made available to patients in the U.S. in October 2017.

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

IMPORTANT SAFETY INFORMATION
CONTRAINDICATIONS

Patients with known or suspected gastrointestinal (GI) obstruction and patients at increased risk of recurrent obstruction, due to the potential for GI perforation.

Patients with a history of a hypersensitivity reaction to Symproic. Reactions have included bronchospasm and rash.

WARNINGS AND PRECAUTIONS

Cases of GI perforation have been reported with use of another peripherally acting opioid antagonist in patients with conditions that may be associated with localized or diffuse reduction of structural integrity in the wall of the GI tract. Monitor for the development of severe, persistent, or worsening abdominal pain; discontinue if this symptom develops.

Symptoms consistent with opioid withdrawal, including hyperhidrosis, chills, increased lacrimation, hot flush/flushing, pyrexia, sneezing, feeling cold, abdominal pain, diarrhea, nausea, and vomiting have occurred in patients treated with Symproic.

Patients having disruptions to the blood-brain barrier may be at increased risk for opioid withdrawal or reduced analgesia. Take into account the overall risk-benefit profile when using Symproic in such patients. Monitor for symptoms of opioid withdrawal in such patients.

DRUG INTERACTIONS

Avoid use with strong CYP3A inducers (e.g., rifampin) because they may reduce the efficacy of Symproic.

Use with moderate (e.g., fluconazole) and strong (e.g., itraconazole) CYP3A inhibitors and P-glycoprotein inhibitors (e.g., cyclosporine) may increase Symproic concentrations. Monitor for potential adverse reactions.

Avoid use of Symproic with another opioid antagonist due to potential for additive effect and increased risk of opioid withdrawal.

USE IN SPECIFIC POPULATIONS

Symproic crosses the placenta and may precipitate opioid withdrawal in a fetus due to the immature fetal blood-brain barrier. Symproic should be used during pregnancy only if the potential benefit justifies the potential risk. Because of the potential for serious adverse reactions, including opioid withdrawal in breastfed infants, a decision should be made to discontinue breastfeeding or discontinue the drug, taking into account the importance of the drug to the mother.

Avoid use in patients with severe hepatic impairment. No dose adjustment of Symproic is required in patients with mild or moderate hepatic impairment.

ADVERSE REACTIONS

The most common adverse reactions with Symproic as compared to placebo in clinical trials were: abdominal pain (8% vs 2%), diarrhea (7% vs 2%), nausea (4% vs 2%), and gastroenteritis (2% vs 1%).

In pooled Studies 1 and 2, the incidence of adverse reactions of opioid withdrawal was 1% (8/542) for Symproic and 1% (3/546) for placebo. In Study 3 (52-week data), the incidence was 3% (20/621) for Symproic and 1% (9/619) for placebo.

To report suspected Adverse Reactions, contact Shionogi at 1-800-849-9707 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see accompanying Full Prescribing Information including Medication Guide for Symproic or visit www.symproic.com/pi.

About BioDelivery Sciences International Inc.
BioDelivery Sciences International, Inc. (NASDAQ: BDSI) is a rapidly growing commercial-stage specialty pharmaceutical company dedicated to patients living with chronic pain. BDSI is utilizing its novel and proprietary BioErodible MucoAdhesive (BEMA®) technology and other drug delivery technologies to develop and commercialize, either on its own or in partnership with third parties, new applications of proven therapies aimed at addressing important unmet medical needs. BDSI's marketed products and those in development address serious and debilitating conditions such as chronic pain, breakthrough cancer pain, and opioid dependence. For more information, please visit us at www.bdsi.com or follow us on Facebook.com/BioDeliverySI or Twitter BDSI @BioDeliverySI.

About Shionogi
Shionogi & Co., Ltd. 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." Shionogi Inc., the US.. 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 anti-infectives, pain, cardiovascular diseases and gastroenterology. Our pipeline is focused on infectious disease, pain, CNS and oncology. For more details on Shionogi Inc., visit www.shionogi.com (https://www.shionogi.com/). For more information on Shionogi & Co., Ltd., visit www.shionogi.co.jp.en (http://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.

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