BioDelivery Sciences Acquires U.S. Commercial Rights to Symproic®

April 10, 2019

Long-term revenue potential of over $75 million for NME with IP protection through 2031

Leverages existing commercial capabilities to provide a novel treatment option for OIC

Total 2019 Company Net Sales expected to be $92-$100 million with Symproic Net Sales of $7-$9 million

Long-term potential of BELBUCA® and Symproic® combined Net Sales expected to be $325-$400 million

RALEIGH, N.C., April 10, 2019 (GLOBE NEWSWIRE) -- BioDelivery Sciences International, Inc. (NASDAQ: BDSI), a rapidly growing commercial-stage specialty pharmaceutical company dedicated to patients living with chronic pain, today announced that it has entered into an exclusive licensing agreement with Shionogi, Inc., to commercialize Symproic® (naldemedine) tablets 0.2 mg in the United States and Puerto Rico effective immediately. Symproic is indicated for the treatment of opioid-induced constipation (OIC) in adults 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 is a comprehensively studied OIC product with seven global Phase III clinical trials and received the highest category of endorsement from the American Gastroenterological Association in patients with laxative-refractory OIC.

It is estimated that approximately 40% - 60% of adults with chronic non-cancer pain on non-buprenorphine based opioid therapy will experience OIC, making it one of the most commonly reported side effects in this patient population and can significantly interfere with the appropriate management of chronic pain. Symproic has the potential to become a leading therapy option for OIC given its proven clinical profile and differentiation.

"We are very excited to add Symproic to our commercial portfolio of highly differentiated products for patients suffering from chronic pain and its associated conditions," stated Herm Cukier, CEO of BDSI. "The product fits very synergistically both strategically and operationally with BELBUCA® (buprenorphine buccal film) CIII, enabling us to leverage our existing commercial organization and capabilities. We are confident Symproic has the potential to become a leading treatment option for OIC and expect to see an accretive contribution to cash flow in the first half of 2020."

Under the terms of the agreement, BDSI will pay Shionogi, Inc., an initial payment of $20 million and an additional $10 million in six months. In addition, Shionogi is eligible to receive tiered royalty payments based on Net Sales of Symproic.

With the addition of Symproic, the company expects the long-term net sales potential of its product portfolio to be in the range of $325 - $400 million. Additionally, the company has reaffirmed its expectation to become operating cash flow positive by the end of 2019.

ABOUT SYMPROIC

Symproic® (naldemedine) tablets 0.2 mg 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.

IMPORTANT SAFETY INFORMATION ABOUT SYMPROIC®

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.

References:

1. Sehgal N, Colson J, Smith HS. Chronic pain treatment with opioid analgesics: benefits versus harms of long-term therapy. Expert Rev Neurother. 2013;13:1201-1220.
2. Camilleri M, Drossman DA, Becker G, Webster LR, Davies AN, Mawe GM. Emerging treatments in neurogastroenterology: a multidisciplinary working group consensus statement on opioid-induced constipation. Neurogastroenterol Motil. 2014;26: 1386-1395.
3. Kalso E, Edwards JE, Moore RA, McQuay HJ. Opioids in chronic noncancer pain: systematic review of efficacy and safety. Pain. 2004;112:372–80.
4. Cook SF, Lanza L, Zhou X, et al. Gastrointestinal side effects in chronic opioid users: results from a population based survey.Aliment Pharmacol Ther. 2008;27(12):1224-1232.
5. Brown RT, Zuelsdorff M, Fleming M. Adverse effects and cognitive function among primary care patients taking opioids for chronic nonmalignant pain. J Opioid Manag. 2006;2(3):137–146.
6. Tuteja AK, Biskupiak J, Stoddard GJ, Lipman AG. Opioid induced bowel disorders and narcotic bowel syndrome in patients with chronic non-cancer pain. Neurogastroenterol Motil. 2010;22(4):424-430.

IMPORTANT SAFETY INFORMATION ABOUT BELBUCA®

BELBUCA® (buprenorphine buccal film), CIII is indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

Limitations of Use

Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with long-acting opioid formulations, reserve BELBUCA® for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.

BELBUCA® is not indicated as an as-needed (prn) analgesic.

WARNING: ADDICTION, ABUSE, AND MISUSE; RISK EVALUATION AND MITIGATION STRATEGY (REMS); LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL EXPOSURE; NEONATAL OPIOID WITHDRAWAL SYNDROME; and RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES AND OTHER CNS DEPRESSANTS

Addiction, Abuse, and Misuse

BELBUCA® exposes patients and other users to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Assess patient's risk prior to prescribing BELBUCA ®, and monitor patients regularly for these behaviors and conditions.

Risk Evaluation and Mitigation Strategy (REMS)

To ensure that the benefits of opioid analgesics outweigh the risks of addiction, abuse, and misuse, the FDA has required a REMS for these products. Under the requirements of the REMS, drug companies with approved opioid analgesic products must make REMS-compliant education programs available to healthcare providers. Healthcare providers are strongly encouraged to

- **complete a REMS-compliant education program,**
- **counsel patients and/or their caregivers, with every prescription, on safe use, serious risks, storage, and disposal of these products,**
- **emphasize to patients and their caregivers the importance of reading the Medication Guide every time it is provided by their pharmacist, and**
- **consider other tools to improve patient, household, and community safety.**

Life-Threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression may occur with use of BELBUCA®. Monitor for respiratory depression, especially during initiation of BELBUCA® or following a dose increase.

Accidental Exposure

Accidental exposure to even one dose of BELBUCA®, especially by children, can result in a fatal overdose of buprenorphine.

Neonatal Opioid Withdrawal Syndrome

Prolonged use of BELBUCA® during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.

Risks from Concomitant Use with Benzodiazepines or Other CNS Depressants

Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing for use in patients for whom alternative treatment options are inadequate; limit dosages and durations to the minimum required; and follow patients for signs and symptoms of respiratory depression and sedation.

BELBUCA® is contraindicated in patients with significant respiratory depression; acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment; known or suspected gastrointestinal obstruction, including paralytic ileus; and hypersensitivity (e.g., anaphylaxis) to buprenorphine.

BELBUCA® contains buprenorphine, a Schedule III controlled substance. As an opioid, BELBUCA® exposes users to the risks of addiction, abuse, and misuse. Although the risk of addiction in any individual is unknown, it can occur in patients appropriately prescribed BELBUCA® and in those who obtain the drug illicitly. Addiction can occur at recommended doses and if the drug is misused or abused.

Potential serious adverse events caused by opioids include addiction, abuse, and misuse; life-threatening respiratory depression; neonatal opioid withdrawal syndrome; risks due to interactions with benzodiazepines or other central nervous system depressants; risk of life-threatening respiratory depression in patients with chronic pulmonary disease or in elderly, cachectic, or debilitated patients; adrenal insufficiency; QTc prolongation; severe hypotension; risks of use in patients with increased intracranial pressure, brain tumors, head injury, or impaired consciousness; hepatotoxicity; risk of overdose in patients with moderate or severe hepatic impairment; anaphylactic/allergic reactions; risk of use in patients with gastrointestinal conditions; increased risk of seizures in patients with seizure disorders; risks of use in cancer patients with oral mucositis; risks of driving and operating machinery.

The most common adverse reactions (≥5%) reported by patients treated with BELBUCA® in the clinical trials were nausea, constipation, headache, vomiting, fatigue, dizziness, somnolence, diarrhea, dry mouth, and upper respiratory tract infection.

For full Prescribing Information, including Boxed Warning, visit www.belbuca.com.

To report SUSPECTED ADVERSE REACTIONS, contact BioDelivery Sciences International, Inc. at 1-800-469-0261 or FDA at 1-800-FDA-1088 or www.fda.gov/safety/medwatch.

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 it serves. 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 it serves. The company currently markets products in several therapeutic areas including anti-infectives, pain, cardiovascular diseases and gastroenterology. Its pipeline is focused on infectious disease, pain, CNS and oncology. For more information 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/).

CAUTIONARY NOTE ON FORWARD-LOOKING STATEMENTS

This press release, the presentation described herein, and any statements of employees, representatives, and partners of BioDelivery Sciences International, Inc. ("BDSI") related thereto contain, or may contain, among other things, certain "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements involve significant risks and uncertainties. Such statements may include, without limitation, statements with respect to the BDSI's plans, objectives, projections, expectations and intentions and other statements identified by words such as "projects," "may," "will," "could," "would," "should," "believes," "expects," "anticipates," "estimates," "intends," "plans," "potential" or similar expressions. These statements are based upon the current beliefs and expectations of the BDSI's management and are subject to significant risks and uncertainties, including those detailed in the BDSI's filings with the Securities and Exchange Commission.

Actual results (including, without limitation, the anticipated benefits to the Company related to the preferred access to additional commercial lives as described herein) may differ significantly from those set forth or implied in the forward-looking statements. These forward-looking statements involve certain risks and uncertainties that are subject to change based on various factors (many of which are beyond the BDSI's control). BDSI undertakes no obligation to publicly update any forward-looking statements, whether as a result of new information, future presentations or otherwise, except as required by applicable law.

© 2019 BioDelivery Sciences International, Inc. All rights reserved.

Contacts
Mary Coleman
Vice President, Investor Relations
BioDelivery Sciences International, Inc.
919-582-9050
mcoleman@bdsi.com

Source: BioDelivery Sciences International, Inc.