BioDelivery Sciences Announces Granting of Market Authorization Transfer by Health Canada for BELBUCA® and Associated Milestone Payment Transfer of NDS to Purdue Pharma (Canada) triggers milestone payment to BDSI

September 12, 2017

RALEIGH, N.C., Sept. 12, 2017 /PRNewswire/ -- BioDelivery Sciences International, Inc. (NASDAQ: BDSI) announced today that Health Canada has granted market authorization to formally transfer the Drug Identification Number (DIN) ownership of BELBUCA® (buprenorphine) buccal film in Canada to BDSI's commercial partner, Purdue Pharma (Canada). As previously announced, this approval triggers a milestone payment to BDSI.

Dr. Mark A. Sirgo, Vice Chairman, President and Chief Executive Officer of BDSI commented, "We congratulate our partners at Purdue Pharma (Canada) on this important milestone, and we look forward to the launch in Canada."

BELBUCA incorporates BDSI's BioErodible MucoAdhesive (BEMA®) drug delivery technology and is the first and only long-acting opioid that uses novel buccal film technology to deliver buprenorphine for appropriate patients living with chronic pain. BELBUCA was approved in Canada in June 2017 for the management of pain severe enough to require daily, continuous, long-term treatment and that is opioid-responsive and for which alternative options are inadequate.

Purdue Pharma (Canada) and BDSI announced on July 12, 2017 that the companies had signed an exclusive agreement for the licensing, distribution, marketing and sale of BELBUCA in Canada.

About BELBUCA® (buprenorphine) buccal film (CIII)

INDICATION in Canada

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

The following information is included in the US Product Label:

INDICATION in the United States

BELBUCA® (buprenorphine) buccal film 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.

IMPORTANT SAFETY INFORMATION about BELBUCA®

WARNING: ADDICTION, ABUSE, AND MISUSE; LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL EXPOSURE; AND 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 these behaviors and conditions.

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. Misuse or abuse of BELBUCA® by chewing, swallowing, snorting, or injecting buprenorphine extracted from the buccal film will result in the uncontrolled delivery of buprenorphine and pose a significant risk of overdose and death.

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.

CONTRAINDICATIONS

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, hypersensitivity (e.g., anaphylaxis) to buprenorphine

WARNINGS AND PRECAUTIONS

Addiction, Abuse, and Misuse

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.

Assess each patient's risk for opioid addiction, abuse, or misuse prior to prescribing BELBUCA®, and monitor all patients receiving BELBUCA® for the development of these behaviors and conditions. Risks are increased in patients with a personal or family history of substance abuse (including drug or alcohol abuse or addiction) or mental illness (e.g., major depression). The potential for these risks should not, however, prevent the proper management of pain in any given patient. Patients at increased risk may be prescribed opioids such as BELBUCA®, but use in such patients necessitates intensive counseling about the risks and proper use of BELBUCA®, along with intensive monitoring for signs of addiction, abuse, or misuse.

Abuse or misuse of BELBUCA® by swallowing may cause choking, overdose, and death.

Opioids are sought by drug abusers and people with addiction disorders and are subject to criminal diversion. Consider these risks when prescribing or dispensing BELBUCA®. Strategies to reduce the risk include prescribing the drug in the smallest appropriate quantity and advising the patient on the proper disposal of unused drug.

Life-Threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression has been reported with the use of opioids, even when used as recommended. Respiratory depression, if not immediately recognized and treated, may lead to respiratory arrest and death.

While serious, life-threatening or fatal respiratory depression can occur at any time during the use of BELBUCA®, the risk is greatest during initiation of therapy or following a dosage increase. Monitor patients closely for respiratory depression when initiating therapy with BELBUCA® and following dosage increases.

To reduce the risk of respiratory depression, proper dosing and titration of BELBUCA® are essential. Overestimating the dose of BELBUCA® when converting patients from another opioid product may result in fatal overdose with the first dose.

Accidental exposure to BELBUCA®, especially in children, can result in respiratory depression and death due to an overdose of buprenorphine.

Neonatal Opioid Withdrawal Syndrome

Prolonged use of BELBUCA® during pregnancy can result in withdrawal in the neonate. Neonatal opioid withdrawal syndrome, unlike opioid withdrawal syndrome in adults, may be life-threatening if not recognized and treated and requires management according to protocols developed by neonatology experts. Observe newborns for signs of neonatal opioid withdrawal syndrome and manage accordingly. Advise pregnant women using opioids for a prolonged period of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.

Risks due to Interactions with Benzodiazepines or Other Central Nervous System Depressants

Profound sedation, respiratory depression, coma, and death may result from the concomitant use of BELBUCA® with benzodiazepines or other CNS depressants (e.g., non-benzodiazepine sedatives/hypnotics, anxiolytics, tranquilizers, muscle relaxants, general anesthetics, antipsychotics, other opioids, alcohol). Because of these risks, reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate.

If the decision is made to prescribe a benzodiazepine or other CNS depressant concomitantly with an opioid analgesic, prescribe the lowest effective dosages and minimum durations of concomitant use. Follow patients closely for signs and symptoms of respiratory depression and sedation.

Risk of Life-Threatening Respiratory Depression in Patients with Chronic Pulmonary Disease or in Elderly, Cachectic, or Debilitated Patients

The use of BELBUCA® in patients with acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment is contraindicated.

Patients with Chronic Pulmonary Disease: BELBUCA®-treated patients with significant chronic obstructive pulmonary disease or cor pulmonale, and those with substantially decreased respiratory reserve, hypoxia, hypercapnia, or pre-existing respiratory depression are at increased risk of decreased respiratory drive, including apnea, even at recommended dosages of BELBUCA®.

Life-threatening respiratory depression is more likely to occur in in elderly, cachectic, or debilitated patients as they may have altered pharmacokinetics or altered clearance compared with younger, healthier patients

Monitor such patients closely, particularly when initiating and titrating BELBUCA® and when BELBUCA® is given concomitantly with other drugs that depress respiration.

Adrenal Insufficiency

Cases of adrenal insufficiency have been reported with opioid use, more often following greater than one month of use. Presentation of adrenal insufficiency may include non-specific symptoms and signs including nausea, vomiting, anorexia, fatigue, weakness, dizziness, and low blood pressure. If adrenal insufficiency is suspected, confirm the diagnosis with diagnostic testing as soon as possible. If adrenal insufficiency is diagnosed, treat with physiologic replacement doses of corticosteroids. Wean the patient off of the opioid to allow adrenal function to recover and continue corticosteroid treatment until adrenal function recovers. Other opioids may be tried as some cases reported use of a different opioid without recurrence of adrenal insufficiency. The information available does not identify any particular opioids as being more likely to be associated with adrenal insufficiency.

QTc Prolongation

BELBUCA® has been observed to prolong the QTc interval in some subjects participating in clinical trials. Consider these observations in clinical decisions when prescribing BELBUCA® ™ to patients with hypokalemia, hypomagnesemia, or clinically unstable cardiac disease, including unstable atrial fibrillation, symptomatic bradycardia, unstable congestive heart failure, or active myocardial ischemia. Periodic electrocardiographic (ECG) monitoring is recommended in these patients. Avoid the use of BELBUCA® in patients with a history of Long QT Syndrome (or an immediate family member with this condition) or those taking Class IA antiarrhythmic medications (e.g., quinidine, procainamide, disopyramide) or Class III antiarrhythmic medications (e.g., sotalol, amiodarone, dofetilide), or other medications that prolong the QT interval.

Severe Hypotension

BELBUCA® may cause severe hypotension, including orthostatic hypotension and syncope, in ambulatory patients. There is an increased risk in patients whose ability to maintain blood pressure has already been compromised by a reduced blood volume or concurrent administration of certain CNS depressant drugs (e.g., phenothiazines or general anesthetics). Monitor these patients for signs of hypotension after initiating or titrating the dosage of BELBUCA®., In patients with circulatory shock BELBUCA® may cause vasodilation that can further reduce cardiac output and blood pressure. Avoid the use of BELBUCA® in patients with circulatory shock.

Risks of Use in Patients with Increased Intracranial Pressure, Brain Tumors, Head Injury, or Impaired Consciousness

In patients who may be susceptible to the intracranial effects of CO_2 retention (e.g., those with evidence of increased intracranial pressure or brain tumors), BELBUCA® may reduce respiratory drive, and the resultant CO_2 retention can further increase intracranial pressure. Monitor such patients for signs of sedation and respiratory depression, particularly when initiating therapy with BELBUCA®.

Opioids may also obscure the clinical course in a patient with a head injury. Avoid the use of BELBUCA® in patients with impaired consciousness or coma.

Hepatotoxicity

Cases of cytolytic hepatitis and hepatitis with jaundice have been observed in individuals receiving sublingual formulations of buprenorphine for the treatment of opioid dependence, both in clinical trials and in post-marketing adverse events reports. For patients at increased risk of hepatotoxicity (e.g., patients with a history of excessive alcohol intake, intravenous drug abuse or liver disease), obtain baseline liver enzyme levels and monitor periodically during treatment with BELBUCA®.

Risk of Overdose in Patients With Moderate or Severe Hepatic Impairment

In a pharmacokinetic study of subjects dosed with buprenorphine sublingual tablets, buprenorphine plasma levels were found to be higher and the half-life was found to be longer in subjects with moderate and severe hepatic impairment but not in subjects with mild hepatic impairment. For patients with severe hepatic impairment, a dose adjustment is recommended, and patients with moderate or severe hepatic impairment should be monitored for signs and symptoms of toxicity or overdose caused by increased levels of buprenorphine.

Anaphylactic/Allergic Reactions

Cases of acute and chronic hypersensitivity to buprenorphine have been reported both in clinical trials and in post-marketing experience. The most common signs and symptoms include rashes, hives, and pruritus. Cases of bronchospasm, angioneurotic edema, and anaphylactic shock have been reported.

Risk of Use in Patients with Gastrointestinal Conditions

BELBUCA® is contraindicated in patients with known or suspected gastrointestinal obstruction, including paralytic ileus.

BELBUCA® may cause spasm of the sphincter of Oddi. Opioids may cause increases in the serum amylase. Monitor patients with biliary tract disease, including acute pancreatitis, for worsening symptoms.

Increased Risk of Seizures in Patients with Seizure Disorders

The buprenorphine in BELBUCA® may increase the frequency of seizures in patients with seizure disorders and may increase the risk of seizures occurring in other clinical settings associated with seizures. Monitor patients with a history of seizure disorders for worsened seizure control during BELBUCA® therapy.

Risks of Use in Cancer Patients with Oral Mucositis

Cancer patients with oral mucositis may absorb buprenorphine more rapidly than intended and are likely to experience transiently higher plasma levels of the opioid. A dose reduction is recommended in these patients. Monitor carefully for signs and symptoms of toxicity or overdose caused by increased levels of buprenorphine.

Risks of Driving and Operating Machinery

BELBUCA® may impair the mental and physical abilities needed to perform potentially hazardous activities such as driving a car or operating machinery. Warn patients not to drive or operate dangerous machinery unless they are tolerant to side effects of BELBUCA® and know how they will react to the medication.

ADVERSE REACTIONS

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.

Please see full Prescribing Information, including Boxed Warning and Medication Guide, for BELBUCA®.

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

BioDelivery Sciences International, Inc. (NASDAQ: BDSI) is a specialty pharmaceutical company with a focus in the areas of pain management and addiction medicine. 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 breakthrough cancer pain, chronic pain and opioid dependence. BDSI's headquarters is in Raleigh, North Carolina.

For more information, please visit or follow us:	
Internet:	www.bdsi.com
Facebook:	Facebook.com/BioDeliverySI
Twitter:	@BioDeliverySI

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Cautionary Note on Forward-Looking Statements

This press release and any statements of employees, representatives and partners of BioDelivery Sciences International, Inc. (the "Company") 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 Company'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 Company's management and are subject to significant risks and uncertainties, including those detailed in the Company's filings with the Securities and Exchange Commission. Actual results (including, without limitation, the anticipated Canadian launch timeframe for BELBUCA in Canada and the results of the Company's commercialization programs for BELBUCA, including in Canada 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 Company's control). The Company 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.

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