Endo Pharmaceuticals and BioDelivery Sciences Present New Data on Investigational Product Buprenorphine HCl Buccal Film for Chronic Pain Management

September 9, 2015

Data demonstrate ability to convert from an opioid full agonist like morphine and oxycodone to buprenorphine HCl buccal film

DUBLIN and RALEIGH, N.C., Sept. 9, 2015 /PRNewswire/ -- Endo Pharmaceuticals Inc., a subsidiary of Endo International plc (NASDAQ: ENDP) (TSX: ENL), and BioDelivery Sciences International, Inc. (NASDAQ: BDSI) today presented data from a Phase 2 study for the investigational drug buprenorphine HCl buccal film utilizing BDSI's patented BioErodible MucoAdhesive (BEMA®) drug delivery technology. The findings, presented in a poster session at PAINWeek 2015 in Las Vegas, showed that study participants receiving around-the-clock therapy with an opioid full agonist (morphine or oxycodone) could be switched to buprenorphine HCl buccal film, at approximately half the full agonist dose, without increasing the risk of experiencing opioid withdrawal or a loss of pain relief. These findings also will be presented later this month at the 26th Annual Meeting of the American Academy of Pain Management in National Harbor, MD.

Buprenorphine HCl buccal film is being developed under the proprietary name BELBUCA™ (buprenorphine HCl) buccal film and is currently under review by the U.S. Food and Drug Administration (FDA) for use in patients with pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. The PDUFA action date is in October 2015.

"This study demonstrated that study participants on a full agonist were successfully switched to buprenorphine HCl buccal film, an opioid partial agonist, at approximately 50 percent of the full agonist dose, without the need for an opioid taper and without increasing the risk of withdrawal or loss of pain control," said Lynn Webster, M.D., Vice President of Scientific Affairs, PRA Health Sciences, lead study investigator, and former President of the American Academy of Pain Medicine. "Our findings could have important implications for future strategies to broaden the treatment options for patients living with pain who require around-the-clock opioid treatment."

Buprenorphine HCl buccal film provides buprenorphine in an optimally-designed delivery system, which efficiently and conveniently delivers buprenorphine across the buccal mucosa (inside lining of the cheek). Buprenorphine is a Schedule III controlled substance, meaning that it has been designated as having lower abuse potential than Schedule II drugs, a category which includes most opioid analgesics.

Switching from an Opioid Full to Partial Agonist
The Phase 2, randomized, double-blind, active controlled, 2-period crossover study included 39 chronic pain sufferers who were receiving 80 mg to 220 mg (80-160 mg, n=33; 161-220 mg, n=6) daily around-the-clock therapy of an opioid full agonist (either morphine sulfate or oxycodone HCl), and were confirmed to be opioid dependent. Approximately eight to 12 hours after the last full agonist dose, study subjects received buprenorphine HCl buccal film 300 or 400 mcg, which was calculated to be equivalent to 50 percent of their full agonist dose. The study also included an active-control group, who remained on 50 percent of their full agonist dose. The primary endpoint was the proportion of study participants that demonstrated significant withdrawal symptoms (a maximum Clinical Opiate Withdrawal Scale, or COWS, score of ≥13) or required rescue therapy because of these symptoms.

Of the 35 study participants [31 on 80-160 mg and 4 on 161-220 mg morphine sulfate equivalent (MSE)/day] that completed both periods of the study, significant withdrawal was experienced in one study participant on buprenorphine HCl buccal film and two participants on the full agonist treatment arm. Mean maximum COWS scores were comparable for participants in the buprenorphine HCl buccal film group versus the full agonist group [in the 80-160mg MSE dose group: Mean (SD) 4.6 (3.15) vs. 5.3 (4.42), respectively; p=0.79; in the 161-220 mg MSE dose group, 5.5 (1.91) vs. 6.3 (2.50), p=0.62]. There was no significant difference in pain ratings between the buprenorphine and full agonist treatment groups for patients in the 80-160 mg MSE dose group. The sample size for patients in the higher dose (161 to 220 mg) group was too small to permit a rigorous statistical analysis or conclusions from the data.

The COWS total scores indicate that these subjects were successfully switched between around-the-clock (ATC) opioid and buprenorphine in the dose range (80-220 mg MSE) without precipitating withdrawal issues. There was no evidence of a difference in precipitated opioid withdrawal following buprenorphine and ATC opioid administered 12 hours after a therapeutic dose of ATC opioid.

"We are excited by these new findings as they add to the growing body of evidence supporting the potential of buprenorphine HCl buccal film as an appropriate, effective pain relief option with a low incidence of typical opioid-like side effects," said Sue Hall, Ph.D., Executive Vice President, Chief Scientific Officer and Global Head of Research & Development and Quality at Endo. "Endo has been a long-standing leader in pain. Through our strong scientific expertise and established infrastructure, we are eager to continue researching potential options to address the growing and unique needs of the pain patient community."

Overall, adverse events (AEs) were reported in 20 study participants (60.6 percent) in the 80-160 mg MSE group and 1 patient (16.7 percent) in the 161-220 mg dose group. For the 80-160 mg MSE group, 18 participants (56.3 percent) had at least one AE during buprenorphine HCl buccal film treatment and 13 participants (40.6 percent) had at least one AE during mu-opioid full agonist therapy. The most common AEs reported in the buprenorphine HCl buccal film group included headache (18.8 percent), vomiting (12.5 percent), and nausea, diarrhea, and drug withdrawal syndrome (9.4 percent for each). In the group continuing on the opioid full agonist (50 percent dose, opioid full agonist treatment), the most frequently reported AEs were headache (15.6 percent), drug withdrawal syndrome (12.5 percent), and nausea (6.3 percent).

"Buprenorphine HCl buccal film represents a novel approach to treating chronic pain and if approved, it will be the first and only pain medicine combining the proven efficacy and safety of buprenorphine with BDSI's unique BEMA® delivery system," said Andrew Finn, Pharm.D., Executive Vice President of Product Development for BDSI. "We believe that buprenorphine HCl buccal film would be an important new therapy for chronic pain, a serious and debilitating condition that may significantly burden the lives of millions of patients."

About Buprenorphine HCl Buccal Film
Buprenorphine is a Schedule III controlled substance, meaning that it has been designated as having lower abuse potential than Schedule II drugs, a category which includes most opioid analgesics. Buprenorphine is a mu-opioid receptor partial agonist and a potent analgesic with a relatively long duration of action. Buprenorphine HCl buccal film is being developed under the proprietary name BELBUCA™ (buprenorphine HCl) buccal film and if approved, will be commercialized through a worldwide license and development agreement between Endo Pharmaceuticals and BDSI.

Last year, Endo Pharmaceuticals submitted a New Drug Application (NDA) for buprenorphine HCl buccal film, which was accepted by the FDA in February 2015. At that time, the FDA also granted conditional acceptance for BELBUCA™ as the proposed proprietary name for buprenorphine HCl buccal film.

About Endo International plc
Endo International plc (NASDAQ: ENDP) (TSX: ENL) is a global specialty pharmaceutical company focused on improving patients' lives while creating shareholder value. Endo develops, manufactures, markets and distributes quality branded pharmaceutical and generic pharmaceutical products as well as over-the-counter medications through its operating companies. Endo has global headquarters in Dublin, Ireland, and U.S. headquarters in Malvern, PA. Learn more at www.endo.com.

About Endo Pharmaceuticals Inc.
Endo Pharmaceuticals Inc. is focused on developing and delivering high-value branded pharmaceutical products that meet the unmet needs of patients. Endo Pharmaceuticals is an operating company of Endo International plc, a global specialty pharmaceutical company focused on improving patients' lives while creating shareholder value. Learn more at www.endo.com or www.endopharma.com.

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 headquarters is located in Raleigh, North Carolina. For more information visit www.bdsi.com.

Cautionary Note Regarding Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and Canadian securities legislation, including the statements by Dr. Webster, Dr. Hall and Dr. Finn, and other statements regarding research and development outcomes, efficacy, adverse reactions, market and product potential, product approval and availability. Statements including words such as "believes," "expects," "anticipates," "intends," "estimates," "plan," "will," "may," "look forward," "intend," "guidance," "future" or similar expressions are forward-looking statements. Because these statements reflect Endo's and BDSI's current views, expectations and beliefs concerning future events, these forward-looking statements involve risks and uncertainties. Although Endo and BDSI believe that these forward-looking statements and information are based upon reasonable assumptions and expectations, readers should not place undue reliance on them, or any other forward-looking statements or information in this news release. Investors should note that many factors, as more fully described in the documents filed by Endo with the Securities and Exchange Commission ("SEC") and with securities regulators in Canada on the System for Electronic Document Analysis and Retrieval ("SEDAR"), and by BDSI with the SEC, including under the caption "Risk Factors" in Endo's Form 10-K, Form 10-Q and Form 8-K filings, and in BDSI's Form 10-K, Form 10-Q and Form 8-K filings, as applicable, and as otherwise enumerated herein or therein, could affect Endo's and/or BDSI's future financial results and could cause Endo's and/or BDSI's actual results to differ materially from those expressed in this communication. The forward-looking statements in this press release are qualified by these risk factors. Neither Endo nor BDSI assume any obligation to publicly update any forward-looking statements, whether as a result of new information, future developments or otherwise, except as may be required under applicable securities law.

To view the original version on PR Newswire, visit:http://www.prnewswire.com/news-releases/endo-pharmaceuticals-and-biodelivery-sciences-present-new-data-on-investigational-product-buprenorphine-hcl-buccal-film-for-chronic-pain-management-300139366.html

SOURCE Endo International plc

Endo International plc: Investors/Media: Keri P. Mattox (484) 216-7912; Investors: Jonathan Neely (484) 216-6645; Media: Heather Zoumas-Lubeski (484) 216-6829 or BioDelivery Sciences International: Investors: Al Medwar, VP, Marketing and Corporate Development (919) 582-9050; Matthew P. Duffy, Managing Director, LifeSci Advisors, LLC, 212-915-0685