New Retrospective Analysis Demonstrates Significant Reductions in Postsurgical Pain and Opioid Requirements with EXPAREL in Cesarean Section Patients

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Results show incorporating transversus abdominis plane block with EXPAREL results in significantly improved patient functional recovery and hospital throughput

Twelve percent of patients receiving EXPAREL were opioid-free

PARSIPPANY, N.J., Dec. 12, 2018 (GLOBE NEWSWIRE) -- Pacira Pharmaceuticals, Inc. (NASDAQ: PCRX) today announced the publication of new data from a retrospective investigator-initiated study analyzing the use of EXPAREL® (bupivacaine liposome injectable suspension) administered as a transversus abdominis plane (TAP) block to manage postsurgical pain following cesarean section (C-section) procedures. Findings show that patients receiving EXPAREL had a significant reduction in opioid consumption and pain intensity, as well as significantly improved discharge- and postanesthesia care unit (PACU)-ready times, functional recovery and reduced length of stay (LOS). The study results were published this week in *The Journal of Pain Research.*

Study researchers reviewed the charts of 201 consecutive women who underwent C-section procedures and received a multimodal pain management protocol with or without a TAP block utilizing 266 mg of EXPAREL. The study population included patients who underwent elective, unscheduled waiting list, or emergency cesarean delivery with anesthesia and post-cesarean pain management by one anesthesiologist at Texas Children's Hospital Pavilion for Women between 2012 and 2015.

Compared to patients who received multimodal pain control without the use of EXPAREL, patients who received a TAP block demonstrated a statistically significant:

- **Decrease in postsurgical opioid consumption** by 47%, (79.6 mg vs 41.9 mg, respectively; *P*<0.001) expressed in oral morphine equivalent dosing
- **Decrease in postsurgical pain intensity** by 46% (*P*<0.001) measured using the area under the curve from day 0 to 3 of pain intensity scores assessed on a numeric rating scale
- **Decrease in PACU-ready times** (138 vs 163 minutes; *P*=0.028) **and LOS** (2.9 vs 3.9 days; *P*<0.001)
- **Decrease in average time to ambulation and solid food** by 39% and 31% (*P*<0.01 each), respectively

Additionally, a significantly greater percentage of patients treated with EXPAREL (12%) compared to those without EXPAREL (3%) consumed no opioids after surgery (*P*=0.017) and fewer patients treated with EXPAREL (34%) compared to those without EXPAREL (50%) reported any adverse event (*P*=0.026). Comparable rates of opioid-related adverse events of interest (ie. nausea, pruritus, vomiting) were observed.

"Many women experience moderate to severe post-cesarean pain, and when inadequately managed, this pain can interfere with maternal-infant bonding and can be associated with delayed recovery and postpartum depression," said B. Wycke Baker, MD, Chief of Service, Anesthesiology at Texas Children's Pavilion for Women, Clinical Professor of Anesthesiology, Obstetrics and Gynecology at Baylor College of Medicine and lead author on the study publication. "Our findings suggest that the addition of a TAP block with EXPAREL to a multimodal pain management protocol provides effective and improved pain control without the need for high volumes of opioids for women undergoing C-sections."

Research reveals that women far outpace men in their use of opioids. Studies have shown that 30 percent more opioid prescriptions were written for women than for men,[1] and women are 40 percent more likely than men to become newly persistent opioid users (using these medications three to six months after surgery), placing them at risk for dependence and addiction.[2]

"Prescribing data continues to show us that postsurgical opioids pose a great risk to women, and it's critical we minimize their exposure to opioids in the surgical setting," said Dave Stack, Chairman and Chief Executive Officer of Pacira. "This study demonstrates that EXPAREL can have a measurable impact on reducing or eliminating the use of opioids while providing superior pain control, and should play a key role in multimodal pain management protocols."

Cesarean delivery was the most common U.S. operating room procedure in 2014, accounting for 9% of such procedures[3] and 32% of all births.[4] Additional research shows that 9 in ten mothers have concerns about taking opioids after childbirth, and despite these concerns, 51 percent of C-section patients are still prescribed an opioid.[5]

About Pacira
Pacira Pharmaceuticals, Inc. (NASDAQ: PCRX) is a specialty pharmaceutical company dedicated to advancing and improving postsurgical outcomes for acute care practitioners and their patients. The company's flagship product, EXPAREL ® (bupivacaine liposome injectable suspension) was commercially launched in the United States in April 2012. EXPAREL utilizes DepoFoam®, a unique and proprietary product delivery technology that encapsulates drugs without altering their molecular structure, and releases them over a desired period of time. To learn more about Pacira, including the corporate mission to reduce overreliance on opioids, visit www.pacira.com.

About EXPAREL®
EXPAREL (bupivacaine liposome injectable suspension) is indicated for single-dose infiltration in adults to produce postsurgical local analgesia and as an interscalene brachial plexus nerve block to produce postsurgical regional analgesia. The product combines bupivacaine with DepoFoam®, a

proven product delivery technology that delivers medication over a desired time period. EXPAREL represents the first and only multivesicular liposome local anesthetic that can be utilized in the peri- or postsurgical setting. By utilizing the DepoFoam platform, a single dose of EXPAREL delivers bupivacaine over time, providing significant reductions in cumulative pain scores with up to a 78 percent decrease in opioid consumption; the clinical benefit of the opioid reduction was not demonstrated. Additional information is available at www.EXPAREL.com.

Important Safety Information
EXPAREL is contraindicated in obstetrical paracervical block anesthesia. Adverse reactions reported with an incidence greater than or equal to 10% following EXPAREL administration via infiltration were nausea, constipation, and vomiting; adverse reactions reported with an incidence greater than or equal to 10% following EXPAREL administration via interscalene brachial plexus nerve block were nausea, pyrexia, and constipation. If EXPAREL and other non-bupivacaine local anesthetics, including lidocaine, are administered at the same site, there may be an immediate release of bupivacaine from EXPAREL. Therefore, EXPAREL may be administered to the same site 20 minutes after injecting lidocaine. EXPAREL is not recommended to be used in the following patient population: patients <18 years old and/or pregnant patients. Because amide-type local anesthetics, such as bupivacaine, are metabolized by the liver, EXPAREL should be used cautiously in patients with hepatic disease. Warnings and Precautions Specific to EXPAREL: Avoid additional use of local anesthetics within 96 hours following administration of EXPAREL.EXPAREL is not recommended for the following types or routes of administration: epidural, intrathecal, regional nerve blocks other than interscalene brachial plexus nerve block, or intravascular or intra-articular use. The potential sensory and/or motor loss with EXPAREL is temporary and varies in degree and duration depending on the site of injection and dosage administered and may last for up to 5 days, as seen in clinical trials.Warnings and Precautions for Bupivacaine-Containing Products: Central Nervous System (CNS) Reactions: There have been reports of adverse neurologic reactions with the use of local anesthetics. These include persistent anesthesia and paresthesia. CNS reactions are characterized by excitation and/or depression. Cardiovascular System Reactions: Toxic blood concentrations depress cardiac conductivity and excitability which may lead to dysrhythmias, sometimes leading to death. Allergic Reactions: Allergic-type reactions (eg, anaphylaxis and angioedema) are rare and may occur as a result of hypersensitivity to the local anesthetic or to other formulation ingredients. Chondrolysis: There have been reports of chondrolysis (mostly in the shoulder joint) following intra-articular infusion of local anesthetics, which is an unapproved use.
Methemoglobinemia: Cases of methemoglobinemia have been reported with local anesthetic use. Full Prescribing Information is available at www.EXPAREL.com.

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[1] Pacira. *United States for Non-Dependence: An Analysis of the Impact of Opioid Overprescribing in America.* September 2017. [Analysis in the report was based on research conducted by the QuintilesIMS Institute.]

[2] Pacira. *Exposing A Silent Gateway to Persistent Opioid Use: A Choices Matter Status Report.* October 2018. [Analysis in the report was based on research conducted by IQVIA.]

[3] McDermott K, Freeman W, Elixhauser A. Overview of operating room procedures during inpatient stays in U.S. hospitals, 2014. *HCUP Statistical Brief*. 2017;233:1–18.

[4] Martin JA, Hamilton BE, Osterman MJ, Driscoll AK, Mathews TJ. Births: final data for 2015. *Natl Vital Stat Rep*. 2017;66(1):1.

[5] *Moms Meet* Member Survey of 1,452 members. Responses collected from 3/16/2018 to 3/30/2018.

Pacira Pharmaceuticals, Inc.