Pacira Announces Publication of Phase 4 Study of EXPAREL in Cesarean Section Procedures in Anesthesia & Analgesia

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– Results show an opioid-reducing benefit of adding EXPAREL to bupivacaine transversus abdominis plane (TAP) blocks for cesarean delivery –

PARSIPPANY, N.J., Aug. 05, 2020 (GLOBE NEWSWIRE) -- Pacira BioSciences, Inc. (NASDAQ: PCRX) today announced that full results its Phase 4 study of EXPAREL® (bupivacaine liposome injectable suspension) administered via transversus abdominis plane (TAP) field block in patients undergoing Cesarean section (C-section) have been published in *Anesthesia and Analgesia*. In this study, EXPAREL achieved its primary endpoint with a statistically significant reduction in total postsurgical opioid consumption through 72 hours. EXPAREL also achieved statistical significance for reduction in percentage of opioid-spared patients through 72 hours.

This was a multicenter, randomized, double-blind study across 13 clinical sites in the United States, in patients undergoing elective C-section and receiving spinal anesthesia and a multimodal analgesic regimen. Patients were randomized (1:1) to receive EXPAREL 266 mg plus bupivacaine HCl 50 mg or bupivacaine HCl 50 mg alone administered via TAP field block after delivery. Effectiveness was evaluated in a pre-specified modified intent-to-treat (mITT) population which met the study criteria regarding proper administration of TAP and multimodal regimen (N=136). Key findings include:

- **Significant reduction in total opioid consumption** with EXPAREL plus bupivacaine HCl versus bupivacaine HCl
  - **52% reduction through 72 hours**, the primary endpoint of the study (least squares mean [LSM] standard error [SE], 15.5 [6.67] vs 32.0 [6.25] mg, respectively; *P*=0.0117)
  - **49% reduction at one week** (LSM [SE], 23.3 [9.75] vs 45.8 [9.13] mg, respectively; *P*=0.0175)
- **41% reduction of opioid consumption at two weeks,** although results did not reach statistical significance (LSM [SE], 28.2 [11.20] vs 47.8 [10.49] mg, respectively; *P*=0.0542)
- **Significantly higher percentage of opioid-spared patients** with EXPAREL versus bupivacaine HCl, defined as patients who took no more than one oxycodone 10 mg tablet (or equivalent) with no opioid-related side effects through 72 hours
  - **Percentage of opioid-spared patients was 2.2 times higher in the EXPAREL group** vs bupivacaine HCl group (54% vs 25%, respectively; *P*=0.0012)
- **Optimized pain control through 72 hours**, which was comparable in both groups

Patients in the EXPAREL arm of this study were administered a TAP field block with 10 mL EXPAREL admixed with 10 mL 0.25% bupivacaine HCl and 10 mL normal sterile saline injected bilaterally (for a total volume of 60 mL). Patients in the active comparator arm received a TAP field block with 10 mL 0.25% bupivacaine HCl admixed with 20 mL normal sterile saline injected bilaterally (for a total volume of 60 mL).

Research shows nearly nine in 10 mothers and mothers-to-be have concerns about taking opioids during and after childbirth, yet 51% of all C-section patients are prescribed an opioid to manage postsurgical pain.

“With C-sections being one of the most common surgeries in the United States, and data showing that one out of 300 opioid naïve women become persistent opioid users following cesarean delivery, it’s critical we evaluate our approach to postsurgical pain management,” said Ashraf Habib, MD, Chief, Division of Women’s Anesthesia and Professor of Anesthesiology at Duke University and study investigator. “The data from this Phase 4 study demonstrate that an EXPAREL-based multimodal regimen has the potential to optimize postoperative analgesia for C-section patients.”

Prior to C-section, all patients in this study received an intrathecal injection of 150 mcg preservative-free morphine for spinal injection in conjunction with single-shot spinal anesthesia using 1.4-1.6 mL bupivacaine HCl 0.75% and 15 mcg fentanyl. Following C-section, patients also received an opioid-sparing multimodal analgesic regimen which consisted of 15 mg of intravenous (IV) ketorolac, 1000 mg of IV acetaminophen at the time of skin incision closure, and scheduled oral acetaminophen and ibuprofen beginning 6 hours after skin incision closure for up to 72 hours following surgery. Rescue medication was available upon request and postsurgical opioid consumption was collected.

Safety was comparable between study groups, with 64 percent of patients in the EXPAREL group experiencing a treatment-emergent adverse event (TEAE) versus 56 percent of patients in the bupivacaine HCl group. The most common TEAEs include pruritus (itching) and nausea; serious TEAEs were rare (approximately three percent in both groups). There were no fatal TEAEs.

Earlier this year, Pacira announced positive topline results for CHOICE, a next-generation C-section trial designed to eliminate the use of spinal morphine in the EXPAREL arm. In the study, EXPAREL achieved its primary endpoint with a statistically significant reduction in total opioid consumption while maintaining pain scores through 72 hours (*P*≤0.001), and demonstrated statistical significance for the key secondary endpoint of a reduction in the incidence and severity of itching for 72 hours after surgery (*P*≤0.05).

About Pacira BioSciences
Pacira BioSciences, Inc. (NASDAQ: PCRX) is a leading provider of non-opioid pain management and regenerative health solutions dedicated to advancing and improving outcomes for health care practitioners and their patients. The company’s long-acting local analgesic, 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. In April 2019, the company acquired the iovera° system, a handheld cryoanalgesia device used to deliver precise, controlled doses of cold temperature only to targeted nerves. 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. Safety and efficacy have not been established in other nerve blocks. 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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