Pacira Announces Publication of Pivotal Study of EXPAREL as a Single-Dose Interscalene Brachial Plexus Nerve Block in Patients Undergoing Shoulder Surgery

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Results, which included significant reductions in pain and opioids, published in Pain Medicine

PARSIPPANY, N.J., June 04, 2019 (GLOBE NEWSWIRE) -- Pacira BioSciences, Inc. (NASDAQ: PCRX) today announced the publication of its multinational Phase 3 study supporting the efficacy and safety of EXPAREL® (bupivacaine liposome injectable suspension) as a single-injection interscalene brachial plexus nerve block (ISNB) in patients undergoing total shoulder arthroplasty or rotator cuff repair. The results demonstrate that EXPAREL significantly improved pain control and reduced opioid consumption through 48 hours compared with placebo and a standardized pain management protocol alone. The data, which provided the basis for FDA approval for this indication, were published in *Pain Medicine.*

The study's primary endpoint was pain intensity scores through 48 hours; secondary endpoints included total postsurgical opioid consumption, percentage of opioid-free patients; and time to first opioid rescue.

A total of 140 patients enrolled across 16 surgical centers in the United States, Belgium, and Denmark were randomized to receive an ultrasound-guided single-dose ISNB with either EXPAREL 133 mg (n=69) or saline placebo (n=71). Compared to patients receiving placebo, patients in the EXPAREL group demonstrated a statistically significant:

- **Reduction in pain scores** measured using the area under the curve of the visual analog scale pain intensity scores through 48 hours (least squares mean [SE], 136.4 [12.09] vs 254.1 [11.77], respectively; *P*<0.0001)
- **Decrease in total postsurgical opioid consumption**, converted to intravenous morphine equivalents, by 78 percent through 48 hours, (least squares mean [SE], 12.0 mg [2.27] vs 54.3 mg [10.05], respectively; *P*<0.0001)
- **Higher percentage of opioid-free patients** at both 24 hours (23% vs 1%, respectively; *P*<0.0001) and 48 hours (13% vs 1%, respectively; *P*=0.008)
- **Prolonged time to first use of rescue opioid**, with median time to rescue medication of 4.2 hours with EXPAREL vs 0.6 hours with placebo (*P*<0.0001)

"Traditionally, clinicians seeking regional pain control have been forced to choose between single-injection blocks with a duration of efficacy that does not match analgesic requirements or continuous blocks that are long-lasting but hinder patient mobility due to cumbersome catheters and pumps. Results from this study illustrate the clinical effectiveness of an interscalene brachial plexus nerve block with EXPAREL, which provides prolonged pain control in a single dose without the need for additional equipment," said Manish Patel, orthopedic surgeon at Eastern Virginia Medical School in Franklin, VA who was also a study investigator and is lead author on the publication. "Further, robust pain control coupled with a reduction or total elimination of opioid requirements, as EXPAREL demonstrated in this study, are two critical factors toward the increasing clinical goal of moving inpatient procedures to an outpatient setting."

Participants in this study were required to remain in the hospital through 72 hours. A standardized pain management protocol was implemented for all patients who were required to remain at the hospital through 72 hours postsurgery. Preoperative analgesics were limited to oral or IV acetaminophen and low-dose aspirin. Intraoperative medication was limited to short-acting opioids. After surgery, patients received up to 1000 mg of oral or IV acetaminophen every eight hours, unless contraindicated. Postsurgical pain rescue medication was limited to oral oxycodone (10 mg every 4 hours as needed) or IV morphine (2.5-5 mg) or hydromorphone (0.5-1 mg).

Incidence of adverse events (AEs) was comparable between groups, and most AEs were mild to moderate in severity. No clinically significant between-group differences in laboratory values, vital signs, or electrocardiograms were observed.

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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