Pacira Announces Publication of Phase 4 Study of EXPAREL in Patients Undergoing Total Knee Replacement in The Journal of Arthroplasty

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PILLAR study demonstrated a 78 percent decrease in opioid consumption and significantly better pain control with infiltration of EXPAREL plus bupivacaine versus bupivacaine alone

Ten percent of patients in the EXPAREL arm required no opioids for pain control

PARSIPPANY, N.J., July 26, 2017 (GLOBE NEWSWIRE) -- Pacira Pharmaceuticals, Inc. (NASDAQ:PCRX) today announced the publication of its Phase 4 PILLAR study of EXPAREL® (bupivacaine liposome injectable suspension) in total knee arthroplasty (TKA). The results, which demonstrate a statistically significant reduction in opioid requirements and pain scores for EXPAREL admixed with bupivacaine HCl versus bupivacaine HCl alone, were published in *The Journal of Arthroplasty*.

The study's co-primary efficacy endpoints compared the magnitude and duration of postsurgical analgesia and associated impact on opioid consumption for 139 TKA patients randomized into two groups at 16 centers across the United States. Seventy patients received surgical site infiltration with EXPAREL admixed with bupivacaine HCl; 69 patients received infiltration with bupivacaine HCl alone. Patients in both groups received an identical oral, cost-effective multimodal pain management protocol before and after surgery and had access to rescue opioids as needed. Patients in the EXPAREL arm demonstrated a statistically significant:

- **Decrease in total opioid consumption** by 78 percent (18.7 mg versus 84.9 mg in the bupivacaine group; *P*=0.0048) expressed as morphine equivalents from zero to 48 hours after surgery.
- **Reduction in pain scores** (180.8 versus 209.3 in the bupivacaine group; *P*=0.0381), measured using the area under the curve of the pain intensity scores measured on a visual analog scale from 12 to 48 hours after surgery.

Importantly, EXPAREL also achieved statistical significance for the study's key secondary endpoints related to opioid reduction. Patients in the EXPAREL arm required 77.6 percent fewer opioids through 72 hours than those in the bupivacaine arm (20.9 mg versus 93.6 mg, respectively; *P*=0.0108), with 10 percent remaining opioid-free through 48 and 72 hours (compared to zero patients in the bupivacaine arm; *P*<0.01). Time to first opioid rescue was analyzed using logistic regression and Kaplan-Meier methods, with a significant difference between the EXPAREL group versus the bupivacaine group; *P*=0.0230.

EXPAREL and bupivacaine infiltrations both were well tolerated throughout the study duration. The most common treatment-emergent adverse events (TEAEs) in each group were nausea, dizziness and muscle spasms; all were mild to moderate in severity. No patients discontinued the study because of a TEAE.

"The PILLAR study provides robust evidence of the efficacy and safety of EXPAREL as an integral component of multimodal therapy to effectively control pain and substantially reduce, and in some cases completely eliminate, opioid requirements following total knee arthroplasty," said Michael A. Mont, Chairman of Orthopaedic Surgery at Cleveland Clinic and lead author on the study publication. "These results clearly demonstrate the importance of utilizing a meticulous and standardized infiltration technique on achieving optimal and replicable results for patients."

In order to ensure consistent results, study investigators utilized a standardized infiltration protocol designed by experienced clinicians. Key features included proper volume expansion to ensure full coverage of the nerve fibers responsible for sending pain signals to the brain, admixing with free bupivacaine to provide sufficient immediate pain relief, and a clear definition of the sites for infiltration and administration technique to ensure adequate coverage of the impacted nerve fibers.

Patients in the EXPAREL group were administered EXPAREL 266 mg/20 mL expanded to a total volume of 120 mL with 20 mL of 0.5% bupivacaine and 80 mL of saline. Patients randomized to receive bupivacaine HCl were administered 20 mL of 0.5% bupivacaine expanded to a total volume of 120 mL with 100 mL of saline. Investigators administered study drug using six 20 mL prefilled syringes.

"We are pleased to present the marketplace with confirmatory data demonstrating the significant positive impact EXPAREL can make on postsurgical recovery by sizably reducing opioid requirements while still providing superior pain control compared to bupivacaine alone," said Dave Stack, chairman and chief executive officer of Pacira. "In light of the growing body of evidence that connects postsurgical opioids with long-term use, abuse and addiction, this study underscores the importance of EXPAREL as a non-opioid option that can reduce patient exposure to potentially tragic consequences."

Pacira and its partner in the orthopaedic and spine markets, DePuy Synthes Companies, part of the Johnson & Johnson Family of Companies, aim to raise awareness among health care professionals as well as patients of the importance of utilizing alternative options to opioids for postsurgical pain. Collaborative education and commercial efforts will emphasize best practice techniques related to the infiltration of EXPAREL in orthopaedic procedures and the positive outcomes that were obtained for TKA patients where the PILLAR protocol was employed.

About PILLAR
The **P**ostsurgical **I**nfiltration With EXPARE**L** For **L**ong-Lasting Analgesia In Total Knee **AR**throplasty (PILLAR) study was a Phase 4 multicenter, randomized, double-blind, controlled parallel-group study conducted between April 25, 2016 and January 19, 2017. To date, it is the largest multicenter study comparing an EXPAREL-based multimodal pain management regimen to an identical bupivacaine-based regimen for TKA.

About Pacira

Pacira Pharmaceuticals, Inc. (NASDAQ:PCRX) is a specialty pharmaceutical company focused on the clinical and commercial development of new products that meet the needs of acute care practitioners and their patients. The company's flagship product, EXPAREL® (bupivacaine liposome injectable suspension), indicated for single-dose infiltration into the surgical site to produce postsurgical analgesia, was commercially launched in the United States in April 2012. EXPAREL and two other products have successfully utilized 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. Additional information about Pacira is available at www.pacira.com.

About EXPAREL®

EXPAREL (bupivacaine liposome injectable suspension) is currently indicated for single-dose infiltration into the surgical site to produce postsurgical analgesia. The product combines bupivacaine with DepoFoam®, a proven product delivery technology that delivers medication over a desired period of time. 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 score with up to a 45 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. EXPAREL has not been studied for use in patients younger than 18 years of age. Non-bupivacaine-based local anesthetics, including lidocaine, may cause an immediate release of bupivacaine from EXPAREL if administered together locally. The administration of EXPAREL may follow the administration of lidocaine after a delay of 20 minutes or more. Other formulations of bupivacaine should not be administered within 96 hours following administration of EXPAREL. Monitoring of cardiovascular and neurological status, as well as vital signs should be performed during and after injection of EXPAREL as with other local anesthetic products. Because amide-type local anesthetics, such as bupivacaine, are metabolized by the liver, EXPAREL should be used cautiously in patients with hepatic disease. Patients with severe hepatic disease, because of their inability to metabolize local anesthetics normally, are at a greater risk of developing toxic plasma concentrations. In clinical trials, the most common adverse reactions (incidence greater-than or equal to 10%) following EXPAREL administration were nausea, constipation, and vomiting.

Please see the full Prescribing Information for more details available at: http://www.exparel.com/hcp/pdf/EXPAREL_Prescribing_Information.pdf.

Forward Looking Statements

Any statements in this press release about our future expectations, plans, outlook and prospects, and other statements containing the words "believes," "anticipates," "plans," "estimates," "expects," "intends," "may" and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including risks relating to: the success of our sales and manufacturing efforts in support of the commercialization of EXPAREL; the rate and degree of market acceptance of EXPAREL and our other products; the size and growth of the potential markets for EXPAREL and our ability to serve those markets; our plans to expand the use of EXPAREL to additional indications and opportunities, and the timing and success of any related clinical trials; the related timing and success of United States Food and Drug Administration supplemental New Drug Applications; the outcome of the U.S. Department of Justice inquiry; our plans to evaluate, develop and pursue additional DepoFoam-based product candidates; clinical trials in support of an existing or potential DepoFoam-based product; our commercialization and marketing capabilities; our and Patheon UK Limited's ability to successfully and timely construct dedicated EXPAREL manufacturing suites; and other factors discussed in the "Risk Factors" of our most recent Annual Report on Form 10-K for the fiscal year ended December 31, 2016 and in other filings that we periodically make with the SEC. In addition, the forward-looking statements included in this press release represent our views as of the date of this press release. Important factors could cause our actual results to differ materially from those indicated or implied by forward-looking statements, and as such we anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we specifically disclaim any obligation to do so. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this press release.

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