Phase 4 Study Shows EXPAREL® Versus an Active Comparator Significantly Reduces Opioid Consumption and Postsurgical Pain in Patients Undergoing Total Knee Arthroplasty

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Multicenter randomized study serves as unequivocal evidence of EXPAREL as an opioid minimizing agent in a complex and painful surgical procedure

Protocol's best practice infiltration technique for the use of EXPAREL will be focus of educational programs at American Academy of Orthopaedic Surgeons Annual Meeting

PARSIPPANY, N.J. , March 14, 2017 (GLOBE NEWSWIRE) -- Pacira Pharmaceuticals, Inc. (NASDAQ:PCRX) announced that its Phase 4 study of EXPAREL® (bupivacaine liposome injectable suspension) in patients undergoing total knee arthroplasty (TKA) achieved statistical significance for its co-primary endpoints for postsurgical pain and opioid reduction. EXPAREL also achieved statistical significance for certain key secondary endpoints, including time to first opioid use and the percentage of patients who did not require any opioid to treat their postsurgical pain. The company is completing its analyses of additional secondary endpoints. The results from the study will be submitted as a series of publications in the peer-reviewed medical literature later this year.

The co-primary efficacy endpoints were the area under the curve (AUC) of the pain intensity scores measured on a visual analog scale (VAS) from 12 to 48 hours after surgery and the total opioid consumption expressed as morphine equivalents from zero to 48 hours after surgery. The EXPAREL group achieved a statistically significant reduction in pain scores compared to the group who did not receive EXPAREL (p=0.0381). Additionally, patients who received EXPAREL consumed significantly fewer opioids than patients who did not receive EXPAREL during the 48 hours that followed surgery (p=0.0048).

Sixteen centers participated in this trial with 139 patients randomized to an EXPAREL-based or a bupivacaine-based multimodal pain regimen of oral acetaminophen, celecoxib and pregabalin. In addition, all patients received intravenous tranexamic acid at the beginning of surgery or intra-operatively.

The study showed the EXPAREL group achieved statistically significant differences compared to the group who did not receive EXPAREL for the following key secondary endpoints:

- The percentage of patients who were opioid-free through 48 hours
- The average time to first use of an opioid rescue medication

"The operating room is the gateway to opioid abuse and places patients at serious risk for addiction and dependence," said Dave Stack, chairman and chief executive officer of Pacira. "The results of this study provide further evidence that EXPAREL effectively reduces, and in some cases, eliminates the use of opioids while providing prolonged postsurgical pain relief to patients undergoing complex and painful knee replacement surgery with a simple inexpensive multimodal design. A recent survey determined that one in 10 opioid naïve patients are opioid dependent six months after opioid-driven postsurgical pain management – we believe EXPAREL can play a critical role in taking on this national issue."[1]

This Phase 4 study was a multicenter, randomized, double-blind, controlled, parallel group study. Patients were randomized to receive local infiltration analgesia with 266 mg of EXPAREL admixed with bupivacaine and expanded in volume to 120 mL (20 mL EXPAREL vial admixed with 20 mL standard bupivacaine 0.5% and expanded with 80 mL normal saline) to local infiltration analgesia with bupivacaine expanded in volume to 120 mL (20 mL standard bupivacaine 0.5% and expanded with 100 mL normal saline). Investigators administered study drug using six 20 mL prefilled syringes.

To support optimal and replicable outcomes in TKA, this study used a standardized infiltration protocol designed by experienced clinicians to define best practice technique for administering EXPAREL. Key features of the infiltration protocol include 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.

Pacira and its partner, DePuy Synthes companies of Johnson and Johnson, are supporting a number of educational programs for best practice EXPAREL technique in orthopedic procedures. At the American Academy of Orthopaedic Surgeons Annual Meeting taking place in San Diego March 14-18, the companies will host innovative virtual reality experiences for clinicians to enhance their infiltration technique based on the protocol from the Phase 4 study of EXPAREL in 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 http://www.exparel.com/hcp/pdf/EXPAREL_Prescribing_Information.pdf.

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 plans to continue to manufacture and provide support services for our commercial partners who have licensed DepoCyt(e); 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.

References

1. "Volleyball Legend Gabrielle Reece on Knee Replacement, Managing Pain, Olympics and More." USA Today, 28 September 2016.

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