Pacira Announces Topline Phase 3 Results for EXPAREL® as a Single-dose Nerve Block

July 25, 2017

Upper extremity study showed that EXPAREL significantly reduces pain scores and opioid use

Lower extremity study defined safety and pharmacokinetic profile through 120 hours

Timing for resubmission of supplemental New Drug Application remains on track

Conference call scheduled for today at 8:30 AM ET

PARSIPPANY, N.J., July 25, 2017 (GLOBE NEWSWIRE) -- Pacira Pharmaceuticals, Inc. (NASDAQ:PCRX) today announced the completion of two Phase 3 placebo-controlled studies evaluating the efficacy, safety and pharmacokinetics of EXPAREL® (bupivacaine liposome injectable suspension) as a single-dose nerve block for prolonged regional analgesia. The first study evaluated EXPAREL administered as a brachial plexus block for patients undergoing one of two upper extremity surgeries (total shoulder arthroplasty or rotator cuff repair), and the second study evaluated EXPAREL administered as a femoral nerve block for patients undergoing a lower extremity surgical procedure (total knee arthroplasty, or TKA).

“These new data add to the growing body of evidence supporting EXPAREL in the nerve block setting,” said Dave Stack, chairman and chief executive officer. “We believe we are well positioned to satisfy all of the FDA requests and resubmit our sNDA to expand the EXPAREL label. Because a single-dose nerve block of EXPAREL offers prolonged regional analgesia, it has the potential to replace cumbersome devices like pumps and catheters. In addition, the nerve block indication will allow many orthopedic procedures, such as surgeries of the shoulder, hand, foot and ankle, to shift from hospitals to ambulatory surgery centers.”

Upper Extremity Study

EXPAREL demonstrated statistical significance for the primary endpoint of cumulative pain scores over 48 hours as measured by the area under the curve ($p<0.0001$). EXPAREL also achieved statistical significance versus placebo for the study’s key secondary endpoints as follows: total postsurgical opioid consumption through 48 hours ($p<0.0001$); opioid-free subjects through 48 hours ($p<0.01$); and time to first opioid rescue through 48 hours ($p<0.0001$).

The study randomized 156 patients across 17 sites in a 1:1 ratio to receive a single dose of either EXPAREL 133 mg in 10 mL expanded in volume with 10 mL of normal saline for a total volume of 20 mL or placebo 20 mL. EXPAREL was administered as a single-dose brachial plexus block under ultrasound guidance at least one hour prior to surgery. All patients were eligible to receive postsurgical rescue opioids upon request for pain control.

The study captured pharmacokinetic data through 120 hours to determine the median time to maximum plasma concentration (Tmax) for EXPAREL.

The preliminary safety analysis was consistent with previously reported studies of brachial plexus nerve blocks with bupivacaine.

Lower Extremity Study

EXPAREL did not demonstrate statistical significance in the femoral nerve block study ($p>0.05$) due to a significant deviation from protocol identified at a single center. When these patients were excluded from the analyses, patients receiving 266 mg EXPAREL achieved statistical significance versus placebo for the study’s primary endpoint of cumulative pain scores over 72 hours as measured by the area under the curve ($p<0.03$).

The study randomized 232 patients across 14 sites in a 1:1:1 ratio to receive a single dose of either EXPAREL 133 mg in 10 mL expanded in volume with 10 mL of normal saline for a total volume of 20 mL; EXPAREL 266 mg in 20 mL; or placebo 20 mL. Study drug was administered as a single-dose femoral nerve block under ultrasound guidance at least one hour prior to surgery. In addition to study drug, prior to placement of the prosthesis, 8 mL of bupivacaine HCl (0.5%) diluted with 8 mL of normal saline was administered as a periarticular infiltration to the posterior capsule of the knee. All patients were eligible to receive postsurgical rescue opioids upon request for pain control.

The study captured pharmacokinetic data through 120 hours to determine the median time to Tmax for EXPAREL.

The preliminary safety analysis was consistent with previously reported studies of femoral nerve blocks with bupivacaine.

Nerve Block Development Program

In 2014, Pacira submitted a supplemental New Drug Application (sNDA) to the U.S. Food and Drug Administration (FDA) based on positive data from a Phase 3 study of EXPAREL in femoral nerve block for TKA. The study evaluated 278 patients who received either a femoral nerve block with EXPAREL or a placebo. EXPAREL demonstrated statistical significance for the primary endpoint of cumulative pain scores over 72 hours ($p<0.0001$). The EXPAREL group also had lower mean total opioid use (76 vs. 103 mg morphine; $p = 0.0016$). The results of the femoral nerve block study were published in the peer-reviewed journal, *Anesthesiology* (Hadzic et al. Liposome Bupivacaine Femoral Nerve Block for Postsurgical Analgesia after Total Knee Arthroplasty *Anesthesiology* 2016; 124:00-00).

In 2015, the company received a complete response letter (CRL) from the FDA. A CRL is issued when the review of an application is complete, but there are one or more reasons that preclude the approval of the application. The FDA requested an additional clinical trial to establish the efficacy of EXPAREL in an additional clinical setting beyond femoral nerve block for TKA. The FDA also requested a study following safety outcomes through the time to reach maximum concentration of EXPAREL.

The company believes the results from these studies will support the resubmission of its sNDA to the FDA seeking expansion of the EXPAREL label to

include administration via nerve block to produce regional analgesia. The sNDA will be based on the positive data from the original Phase 3 study of EXPAREL in femoral nerve block for TKA (lower extremity) and the Phase 3 study of EXPAREL in brachial plexus block for shoulder surgeries (upper extremity). It will also include safety and pharmacokinetic data from the Phase 3 brachial plexus block study and the second Phase 3 study of EXPAREL in femoral nerve block, as well as data from other peripheral nerve block comparative studies.

Pacira plans to submit the full results from the Phase 3 studies for presentation at future scientific conferences and for publication in peer-reviewed journals.

Conference Call

The Pacira management team will host a call today at 8:30 AM ET. The call can be accessed by dialing 1-877-845-0779 (domestic) or 1-720-545-0035 (international) ten minutes prior to the start of the call and providing the Conference ID 61158003. A replay of the call will be available approximately two hours after the completion of the call and can be accessed by dialing 1-855-859-2056 (domestic) or 1-404-537-3406 (international) and providing the Conference ID 61158003. The replay of the call will be available for one week from the date of the live call.

The live, listen-only webcast of the conference call can also be accessed by visiting the “Investors & Media” section of the company’s website at investor.pacira.com. A replay of the webcast will be archived on the Pacira website for two weeks following the call.

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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