# Pacira Pharmaceuticals, Inc. Announces New Data Demonstrating Longer Time to First Opioid Use and Reduction in Opioid-Related Adverse Events With EXPAREL™ Compared to Bupivacaine HCl

October 19, 2011

**Pooled Analysis Findings Presented at American College of Clinical Pharmacy Annual Meeting; Data Demonstrating Sustained-Release Properties of EXPAREL also Presented**

PARSIPPANY, N.J., Oct. 19, 2011 /PRNewswire via COMTEX/ --

Pacira Pharmaceuticals, Inc. (Nasdaq: PCRX) today announced new data demonstrating a reduction in opioid burdens with EXPAREL™ (bupivacaine liposome extended-release injectable suspension) at doses up to and including 300 mg compared to bupivacaine HCl in a multimodal setting at the 2011 Annual Meeting of the American College of Clinical Pharmacy (ACCP) in Pittsburgh. These data are the result of a pooled analysis of five trials conducted for postsurgical pain management.

Currently under review with the U.S. Food and Drug Administration, EXPAREL is an innovative long-acting bupivacaine that has been evaluated in multiple Phase 2 and Phase 3 clinical studies to assess prolonged postsurgical analgesia for up to 72 hours with a single-dose local administration at the surgical site. The drug combines bupivacaine with DepoFoam®, a proven product delivery technology that encapsulates medications and delivers them over a desired time period.

Joseph F. Dasta, M.Sc.,FCCM, FCCP, adjunct professor at the University of Texas, College of Pharmacy, presented the data, which evaluated the use of EXPAREL at doses up to and including 300 mg compared to bupivacaine HCl at doses up to and including 150 mg administered via wound infiltration across three surgical models including hemorrhoidectomy, total knee arthroplasty and herniorrhaphy. Data pooled from these five active-control, double-blind, randomized, multicenter, parallel-group trials of more than 700 patients demonstrated that across all surgical models, EXPAREL resulted in longer time to first opioid use (TTFO), a reduced overall consumption of opioids, fewer opioid-related adverse events (ORAEs) and better pain control compared to bupivacaine HCl. Each finding was statistically significant ($P<0.0001$).

Specific results include:

- A median TTFO that was 3.5 times longer for patients receiving EXPAREL compared to patients receiving bupivacaine HCl (9.9 hours vs 2.7 hours, respectively).
- A 50% reduction in the total amount of morphine-equivalent opioids consumed for patients receiving EXPAREL compared to patients receiving bupivacaine HCl (7.9 mg vs 15.8 mg, respectively).
- A 46% reduction in the mean number of ORAEs for patients receiving EXPAREL compared to patients receiving bupivacaine HCl (0.25 vs 0.46, respectively).
- Less pain over 72 hours was demonstrated for patients receiving EXPAREL compared to patients receiving bupivacaine HCl, as evidenced by an area under the curve analysis, a measure of pain over time (AUC0-72 315 vs 427, respectively).

"Postsurgical patients often require opioids, which along with pain relief, cause a plethora of costly and sometimes life-threatening side effects," said Dasta. "In this pooled analysis, patients receiving EXPAREL had less opioid consumption and fewer ORAEs over 72 hours. In my experience, patients who have no or few ORAEs are more likely to benefit from an improved recovery experience. Pharmacists should be particularly interested in this unique approach to postsurgical analgesia as it has not only clinical, but potentially economic implications."

Additionally, Deedee Hu, PharmD, clinical specialist in the Department of Critical Care and Cardiology at Memorial Hermann Memorial City Medical Center in Houston, Texas, also presented new data during a poster presentation at ACCP today demonstrating that EXPAREL exhibits pharmacokinetic properties consistent with bimodal and sustained-release formulations. These data were collected from a total of 446 individuals receiving 75 mg to 750 mg of EXPAREL or bupivacaine HCl across 11 studies. Various surgical models (hemorrhoidectomy, herniorrhaphy, bunionectomy or total knee arthroplasty) and routes of administration (wound infiltration, subcutaneous, epidural or nerve block) were studied.

The key findings include:

- EXPAREL exhibited an initial peak in plasma concentration 0.25-2 hours after administration (likely due to the small amount of extraliposomal bupivacaine present in EXPAREL) followed by a second peak at 12-24 hours (due to the slow and prolonged release of bupivacaine from the DepoFoam). Bupivacaine HCl exhibited a single peak in plasma concentration at 0.25-2 hours followed by a rapid decline toward zero.
- Even at doses up to 600 mg, the maximal plasma concentration of EXPAREL was 935 ng/mL, which is 2- to 4-fold below the minimal toxicity threshold for bupivacaine HCl (central nervous system effects are usually first seen at bupivacaine levels of $\geq$2000 ng/mL; cardiac system effects are usually first seen at levels of $\geq$4000 ng/mL).
- Consistent plasma curves were observed for all doses of EXPAREL, suggesting that dosing can safely be adapted to meet the specific needs of each surgical model.

"These data show that EXPAREL delivers bupivacaine over three days with the well-established DepoFoam carrier matrix, providing postsurgical pain relief while extending the traditional duration of action from seven hours to up to 72 hours," said Dr. Hu. "This bimodal release may be beneficial in the multimodal treatment of postsurgical pain."

"The body of clinical evidence that supports the utility of EXPAREL as a postsurgical pain management therapy continues to grow and we believe these data presented at ACCP further support its potential clinical and health economic utility," said Dave Stack, president and chief executive officer of Pacira Pharmaceuticals, Inc. "Based upon the positive feedback we have received from a variety of clinical key opinion leaders and hospital organizations, we believe that EXPAREL may become a valuable therapeutic option for physicians and their patients, should it be approved by the FDA at the end of October."

**About Pacira**

Pacira Pharmaceuticals, Inc. is an emerging specialty pharmaceutical company focused on the development, manufacture and commercialization of novel pharmaceutical products, based on its proprietary DepoFoam drug delivery technology, for use in hospitals and ambulatory surgery centers. In December 2010, Pacira announced that its New Drug Application (NDA) for EXPAREL (bupivacaine liposome extended-release injectable suspension), the company's most advanced investigational product candidate, had been accepted for filing by the U.S. Food and Drug Administration (FDA). The FDA has assigned a Prescription Drug User Fee Act (PDUFA) goal date of October 28, 2011 for the review of the EXPAREL NDA. EXPAREL is a bupivacaine-based product and has completed extensive Phase 3 clinical development for postsurgical analgesia by infiltration. EXPAREL consists of bupivacaine encapsulated in DepoFoam, which is designed to address the limitations of widely used medications by enhancing their dosing and/or administration profile. Additional information about Pacira is available at http://www.pacira.com/.

**About EXPAREL™**

EXPAREL (bupivacaine liposome extended-release injectable suspension) is Pacira's proprietary drug candidate consisting of bupivacaine encapsulated in DepoFoam®, both of which are currently used separately in FDA-approved products. Bupivacaine is a well-characterized anesthetic/analgesic that has an established safety profile with more than 20 years of use in the United States. Market data indicate that there is an unmet medical need for a longer-acting anesthetic/analgesic for postsurgical pain management. Several Phase 2 and Phase 3 clinical trials have been completed for EXPAREL and suggest statistically significant reduction of pain in soft tissue and orthopedic surgery in different surgical models. Clinical data from Phase 3 trial 316 suggest that EXPAREL provides analgesia for up to 72 hours post-surgery, the primary endpoint for the trial. The safety of EXPAREL was evaluated in 10 randomized, double-blind, local administration into the surgical wound clinical studies involving 823 patients; the most common adverse events following EXPAREL administration were nausea, constipation, and vomiting.

**Forward Looking Statements**

*Any statements in this press release about our future expectations, plans and prospects, including statements about EXPAREL's potential, and other statements containing the words "believes," "anticipates," "plans," "expects," 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 timing of, and our ability to obtain regulatory approval of EXPAREL; the timing of our anticipated commercial launch of EXPAREL; the rate and degree of market acceptance of EXPAREL; the size and growth of the potential markets for EXPAREL and our ability to serve those markets; our commercialization and marketing capabilities; and other factors discussed in the "Risk Factors" section of our Annual Report on Form 10-K for the year ended December 31, 2010, 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. 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.*

**Contacts:**

James S. Scibetta
Chief Financial Officer
Pacira Pharmaceuticals, Inc.
(973) 254-3570

Dan Budwick
Vice President, Media Relations
Pure Communications, Inc.
(973) 271-6085

SOURCE Pacira Pharmaceuticals, Inc.