# Positive Phase II Study of Pacira's EXPAREL<sup>TM</sup> (DepoBupivacaine) in Hernia Repair Presented at the Postgraduate Assembly in Anesthesiology (PGA)

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## Novel Local Analgesic Results in Sustained Plasma Concentrations Significantly Reducing Postoperative Pain

Parsippany, NJ, Dec. 14, 2008 - A Phase II trial of a single intraoperative administration of EXPAREL (DepoBupivacaine) resulted in significantly reduced pain with activity in the first 8 to 24 hours following surgery, when pain is generally greatest, compared to conventional treatment. The results of the multicenter, randomized, double-blind study were presented in a poster at the Annual Postgraduate Assembly in Anesthesiology in New York City today, by lead investigator Richard Langford, MD, FRCA, Pain and Anaesthesia Research Centre, St. Bartholomew's Hospital, London, UK.

Dr. Langford indicated that EXPAREL provided safe and well-tolerated analgesia with normal wound healing in all patients and noted that the study also showed:

- Significant reductions in pain with activity in EXPAREL treated patients compared to active control
- A positive trend toward lower opioid use in all EXPAREL groups compared to active control
- More patients who received EXPAREL avoided opioids altogether, compared to active control.

In addition, the study demonstrated dose-proportional sustained plasma concentrations which support the prolonged local release of bupivacaine.

Presenting the results, Dr. Langford stated, "In addition to significantly lowering pain scores with activity during the 8 to 24 hours after administration, EXPAREL also showed trends of decrease in the number of patients using opioids and a decrease in total opioid consumption. This is an important finding as lowering opioid usage can spare patients from side effects, such as sedation, nausea, vomiting and respiratory depression, that can adversely affect their recovery."

EXPAREL, a proprietary product of Pacira Pharmaceuticals, Inc., is a novel long-acting, sustained-release formulation of bupivacaine HCL, a local anesthetic widely used for treating postoperative pain. The dose-escalating study evaluated the efficacy, safety, and pharmacokinetics of EXPAREL compared to bupivacaine HCL in 76 adult male patients (age ranges 48 to 63) in 10 hospitals in the UK and Australia. Subjects were randomized into one of four cohorts and intraoperatively administered either 175mg, 225mg, 300mg or 325mg of EXPAREL or 100mg bupivacaine HCL around the surgical wound by infiltration immediately before closure.

- There was a statistically significant reduction in pain intensity with activity across all EXPAREL doses during the first 8 to 24 hours after surgery compared to bupivacaine HCL (P<0.05). Each patient's pain intensity score after surgery ranged from 21 31 across all EXPAREL groups compared to 45 48 for bupivacaine as measured by the Visual Analogue Scale (VAS) at 8, 12 and 24 hours.
- The research also showed a trend toward lower opioid use in all EXPAREL groups compared to active control.
- More patients in the EXPAREL groups completely avoided opioids 71% to 83% across doses, versus 50% for the bupivacaine groups.
- Pharmacokinetic findings showed that a single intraoperative infiltration of EXPAREL resulted in dose-proportional sustained (72 hours) plasma concentrations of bupivacaine (>100mg/mL).

Safety assessments reported in the poster found EXPAREL to be safe and well-tolerated. Wound healing was normal in all EXPAREL subjects with no significant differences between cohorts. Adverse events were generally mild to moderate with no significant differences between cohorts and no serious adverse events were attributed to the study drug.

Inguinal hernia repair is one of the most common operations in routine surgical practice. In the U.S., more than 600,000 procedures are performed annually with a majority performed on an out-patient basis, according to the National Center for Health Statistics.

The Potential of EXPAREL

"The anesthesiology and surgical community recognizes the need for new approaches to postoperative pain management and welcomes the potential advance EXPAREL presents in overcoming limitations of conventional bupivacaine formulations," said Ronald Burch, M.D, PhD, Chief Medical Officer, Pacira. "EXPAREL, currently in late Phase III clinical development, is being studied in several different types of surgical procedures where postoperative pain management is especially problematic and where the need for prolonged analgesia via a single administration can provide a significant improvement in pain relief, especially during the first 72-hours following surgery when pain is the most intense."

EXPAREL is the latest product to benefit from Pacira's proprietary sustained-release DepoFoam<sup>®</sup> technology. DepoFoam technology is designed to address the limitations of widely used medications by enhancing their dosing and/or administration profile. It achieves this by encapsulating the drug in multivesicular liposomal particles which then release the drug over a desired period of time without altering the drug molecule. DepoFoam is a proven technology that is already used in two commercially available products in the U.S. and Europe.

### About Pacira

Pacira Pharmaceuticals, Inc. is an acute care specialty pharmaceutical company founded in March, 2007 through the acquisition of the former SkyePharma PLC injectable business, for which an experienced management team was assembled to address the needs of the acute care market. The company's most advanced product, EXPAREL<sup>™</sup> (DepoBupivacaine), a bupivacaine-based product intended to deliver postoperative pain relief by infiltration, is in late Phase III clinical development. Pacira will also study EXPAREL for nerve block, non-surgical pain such as long bone fracture and for intraarticular injection. EXPAREL benefits from the proprietary DepoFoam Technology owned by Pacira. Two other DepoFoam-based products -- DepoDur<sup>®</sup> and DepoCyt/DepoCyte<sup>®</sup> -- are marketed by partners in several global territories. The DepoFoam technology also forms the basis of multiple development projects providing Pacira an opportunity to expand its pipeline. Pacira owns two cGMP production facilities which produce the two approved products, EXPAREL clinical development and all pipeline materials. Additional information about Pacira is available at <u>www.pacira.com</u>.

This news release and the anticipated presentation contain forward-looking statements that involve risks and uncertainties, including statements relating to initiation and progress of the Company's clinical trial programs and the preliminary results from the clinical trials. Actual results could differ materially from those projected and the Company cautions readers not to place undue reliance on the forward-looking statements contained in the release and anticipated presentation.

### **Editor's Notes:**

- "A single administration of DepoBupivacaine<sup>™</sup> intraoperative results in prolonged detectable plasma bupivacaine and analgesia in patients undergoing inguinal hernia repair" by Richard M. Langford, FRCA; G.M Chappell, FRACS; Jeff A. Karrasch, FRACP, poster presented December 14, 2008 at the PostGraduate Assembly in Anesthesiology (PGA) of the New York State Society of Anesthesiologists, is available at www.pacira.com
- Pacira Pharmaceuticals executives are available for interviews upon request.

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