

## **Positive Phase II Study of Pacira's EXPAREL™ (DepoBupivacaine) in Total Knee Arthroplasty Presented at International College of Surgeons World Congress**

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### **New Sustained-Release Analgesic Significantly Reduces Postop Pain, Opioid Use, and Reduces Opioid Related Adverse Events Compared to Gold Standard Pain Medication**

Parsippany, NJ, Dec. 6, 2008 - A Phase II dose escalation study of a single intraoperative administration of EXPAREL™ (DepoBupivacaine) in patients who underwent total knee arthroplasty, or TKA, showed that the novel, sustained-release analgesic effectively and safely controlled moderate-to-severe postoperative pain for over 72 hours, it was reported today in a poster at the Biennial World Congress of the International College of Surgeons in Vienna, Austria. Commenting on the results, Kenneth W. Bramlett, MD, Orthopedic Department, West Alabama Research in Birmingham, Alabama concluded EXPAREL significantly reduced postoperative pain, decreased the use of opioids (therefore lowering associated side effects), and allowed some patients to avoid the use of opioids altogether.

EXPAREL, a proprietary product from Pacira Pharmaceuticals, Inc., is a novel long-acting, sustained-release formulation of bupivacaine, a local anesthetic widely used for treating postoperative pain.

Dr. Bramlett said, "EXPAREL effectively controlled moderate to severe pain for more than 72 hours, with better relief achieved with higher doses and a dose-dependent effect in both analgesia and reduction in opioid rescue." He pointed out the clinical importance of the study outcomes noting that EXPAREL efficacy was statistically significant against bupivacaine, the gold standard of local anesthetics, rather than simply placebo, concluding, "EXPAREL may provide safe and effective, prolonged pain relief and an opioid-sparing alternative to currently available local analgesics."

Findings as reported in the poster include:

- Statistically significant reduction in pain versus Bup/epi in patients receiving EXPAREL 450mg at the end of general anesthesia, 5.0 vs. 7.0 pain intensity ( $P < 0.05$ ).
- Statistically significant reduction in pain at the time of first opioid use in both EXPAREL 300mg and 450mg patient groups versus active control, 6.4 vs. 7.8 pain intensity and 6.1 vs. 7.8 pain intensity respectively ( $P < 0.05$ ).
- Pain intensity was also lower with EXPAREL than with Bup/epi during activity at all postoperative intervals evaluated.
- EXPAREL 450mg also significantly decreased the use of opioid rescue medications throughout the entire evaluation period plus postoperative nausea and vomiting occurrence was 40% lower than in the active control group.
  - Approximately 8% of patients in the EXPAREL 450mg group avoided all opioid use versus zero percent (0%) of patients in the active control group.
- No differences were found in the safety profile of EXPAREL compared with bupivacaine. There were no clinical signs of either cardiac or central nervous system adverse events.

The multi-center, double-blind, randomized Phase II study used a parallel-group, active-control format to evaluate the efficacy and safety of EXPAREL for prolonged postoperative analgesia. Either a single intraoperative administration of EXPAREL or active control was given via local infiltration to 103 adult patients undergoing TKA in 5 centers across the U.S. and Europe.

TKA is the leading orthopedic surgery in the U.S. with approximately 534,000 procedures performed annually according to the National Center for Health Statistics. It is expected that the number of total knee replacement procedures will increase as our population continues to age.

#### **The Potential for EXPAREL**

EXPAREL is a novel formulation of bupivacaine designed to provide effective, safe, prolonged (72 hours) postoperative pain relief in a single administration. Currently available local anesthetics typically have short (about 6 to 8 hours) duration of action resulting in limited pain relief in the first few days following surgery when pain is the most intense.

"The results of this study clearly demonstrate the potential of EXPAREL in fulfilling this unmet need," said Ronald Burch, M.D, PhD, Chief Medical Officer, Pacira. "EXPAREL represents an important advance in pain control that allows for extended delivery of bupivacaine, a well-characterized analgesic with a long-established efficacy and safety record. We look forward to sharing the results of multiple phase II and III clinical trials across a broad range of surgical procedures."

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. It is the latest product to benefit from Pacira Pharmaceutical's **proprietary sustained-release DepoFoam® technology**. DepoFoam technology is designed to address the limitations of widely known and used drugs 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™ (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® and DepoCyt/DepoCyte® -- 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 [www.pacira.com](http://www.pacira.com).

*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 intraoperatively provides analgesia and reduction in use of rescue opiates compare with bupivacaine HCL in patients undergoing Total Knee Arthroplasty" poster presented at the Biennial World Congress of the International College of Surgeons in Vienna, Austria on Dec. 6, 2008 is available at [www.pacira.com](http://www.pacira.com).
- Pacira Pharmaceuticals executives are available for interviews upon request.

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