Pacira Pharmaceuticals, Inc.
Form 10-K
March 27, 2012
Table of Contents

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended: December 31, 2011

Or

o TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from to

Commission file number: 001-35060

PACIRA PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	**51-0619477**
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)

5 Sylvan Way, Suite 100

Parsippany, New Jersey 07054

(Address of Principal Executive Offices) (zip code)

Registrant s telephone number, including area code **(973) 254-3560**

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Name of each exchange on which registered**
Common Stock, $0.001 par value	The NASDAQ Global Market

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes o No x

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes o No x

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes x No o

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes x No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405) is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. o

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See definitions of large accelerated filer, accelerated filer, and smaller reporting company in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer o	Accelerated filer o
Non-accelerated filer o (Do not check if a smaller reporting company)	Smaller reporting company x

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes o No x

The aggregate market value of 5,490,450 shares of voting stock held by non-affiliates of the registrant, based upon the closing sale price of the common stock on June 30, 2011, the last business day of the registrant s most recently completed second fiscal quarter, of $12.00 per share as reported on Nasdaq was $65,885,400. Shares of common stock held by each director and executive officer and by each person who owns 10 percent or more of the outstanding common stock or who is otherwise believed by the registrant to be in a control position have been excluded. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of March 23, 2012, 25,410,791 shares of the registrant s common stock, $0.001 par value per share, were outstanding.

Table of Contents

Table of contents

Table of Contents

References

Pacira Pharmaceuticals, Inc. is the holding company for our California operating subsidiary of the same name, which we refer to as PPI-California. In March 2007, we acquired PPI-California from SkyePharma Holding, Inc. (referred to in this Annual Report on Form 10-K as the Acquisition). Unless the context requires otherwise, references to Pacira, we, the company, us and our in this Annual Report on Form refers to Pacira Pharmaceuticals, Inc., and its subsidiaries. In addition, references in this Annual Report on Form 10-K to DepoCyt(e) mean DepoCyt when discussed in the context of the United States and Canada and DepoCyte when discussed in the context of Europe.

Forward-Looking Statements

This Annual Report on Form 10-K and certain other communications made by us contain forward-looking statements within the meaning of Section 21E of the Securities Exchange of 1934 (the Exchange Act), including statements about our growth and future operating results, discovery and development of products, strategic alliances and intellectual property. For this purpose, any statement that is not a statement of historical fact should be considered a forward-looking statement. We often use the words believe, anticipate, plan, expect, intend, may, will and similar expressions to help identify forward-looking statements. We cannot assure you that our assumptions and expectations will prove to have been correct. These forward-looking statements include, among others, statements about: the company s plans to develop, manufacture, and commercialize EXPAREL; the Company s plans to continue to manufacture and provide support services for its commercial partners who have licensed DepoCyt(e) and DepoDur; the timing of the Company s 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 the Company s ability to serve those markets; the Company s plans to expand the indications of EXPAREL to include nerve block; and our manufacturing, commercialization and marketing capabilities. Important factors could cause our actual results to differ materially from those indicated or implied by forward-looking statements, including those discussed below. We undertake no intention or obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise and readers should not rely on the forward looking statements as representing the company s views as of any date subsequent to the date of the filing of this Annual Report on Form 10-K.

PART I

Item 1. Business

Overview

We are an emerging specialty pharmaceutical company focused on the development, commercialization and manufacture of proprietary pharmaceutical products, based on our proprietary DepoFoam drug delivery technology, for use in hospitals and ambulatory surgery centers.

On October 28, 2011, the United States Food and Drug Administration, or FDA, approved our New Drug Application, or NDA, for our lead product candidate, EXPAREL, a liposome injection of bupivacaine, an amide local anesthetic, indicated for single-dose infiltration into the surgical site to produce postsurgical analgesia.

Our clinical data demonstrates that EXPAREL provides analgesia for up to 72 hours post-surgery, compared with approximately eight hours or less for bupivacaine. Bupivacaine and other shorter acting local anesthetics of the amide type such as mepivacaine and lidocaine are commonly used as the first line of treatment, pre- and post-operatively, of a multimodal postsurgical pain treatment regimen. Because bupivacaine, mepivacaine and lidocaine last eight hours or less, administration of these local anesthetics is commonly followed by the systemic administration of opioids, such as morphine. Together, these drugs form the foundation of the multimodal postsurgical pain treatment regimen for the treatment of extended duration pain. Opioids are associated with a variety of significant adverse events leading to unfavorable hospital economics and healthcare practioners seeking opioid-sparing strategies for their patients.

We believe EXPAREL addresses a significant unmet medical need for a long-acting non-opioid postsurgical analgesic, resulting in simplified postsurgical pain management and reduced opioid consumption, leading to improved patient outcomes and enhanced hospital economics. We estimate there are approximately 39 million opportunities annually in the United States for EXPAREL to be used.

EXPAREL is being launched by certain members of our management team who have successfully launched multiple products in the hospital market. Our commercial team has executed on a full range of pre-launch activities for EXPAREL including: (i) publications and abstracts for the EXPAREL clinical program efficacy and safety, health outcomes studies, and review articles on postsurgical pain management; (ii) health outcomes studies which provide retrospective and prospective analyses for our hospital customers using their own hospital data to demonstrate the true cost of opioid-based postsurgical pain

Table of Contents

management; (iii) key opinion leader, or KOL, development programs and advisory boards to address topics of best practice techniques, guidelines and protocols for the use of EXPAREL, educational needs of our physician, pharmacist and registered nurse customers, nerve block clinical studies and additional indications for the future development of EXPAREL and (iv) education initiatives such as center of excellence programs, preceptorship programs, pain protocols and predictive models for enhanced patient care, web-based training and virtual launch programs.

We have developed a sales force entirely dedicated to commercializing EXPAREL comprised of approximately 60 representatives, seven regional managers and a national sales manager. We have developed this sales force pursuant to a contract with Quintiles Commercial US, Inc., a division of Quintiles, Inc., or Quintiles, and under the terms of this contract we have the flexibility to hire all or a portion of the sales force dedicated to commercializing EXPAREL as full-time employees of Pacira, upon 60 day s notice to Quintiles. We expect to have successfully resolved the commercial manufacturing challenges for EXPAREL to allow product to be commercially available in April 2012, and we believe that our pre-launch activities including significant personal interactions with our hospital customers, position us for a successful launch of EXPAREL.

EXPAREL consists of bupivacaine encapsulated in DepoFoam, both of which are used in FDA-approved products. DepoFoam, our extended release drug delivery technology, is the basis for our two additional FDA-approved commercial products: DepoCyt(e) and DepoDur, which we manufacture for our commercial partners. DepoFoam-based products have been manufactured for over a decade and have an extensive safety record and regulatory approvals in the United States, European countries and other territories. Bupivacaine, a well-characterized, FDA-approved anesthetic/analgesic, has an established safety profile and over 20 years of use in the United States.

The FDA-approved label for EXPAREL includes a broad label for postsurgical analgesia by local administration into the surgical site, or infiltration, a procedure commonly employing bupivacaine. The approved indication states EXPAREL is a liposome injection of bupivacaine, an amide local anesthetic, indicated for single-dose infiltration into the surgical site to produce postsurgical analgesia . We also currently plan to expand the indications of EXPAREL to include nerve block administration, where bupivacaine is also used routinely.

Our current product portfolio and product candidate pipeline is summarized in the table below:

Product(s)/ Product Candidate(s)	Primary Indication(s)	Status	Commercialization Rights
EXPAREL	Postsurgical analgesia by infiltration	Approved by FDA	Pacira (worldwide)
	Postsurgical analgesia -nerve block	Phase 2 (completed)	Pacira (worldwide)
DepoCyt(e)	Lymphomatous meningitis	Marketed	Sigma-Tau Pharmaceuticals Mundipharma International
DepoDur	Post-operative pain	Marketed	EKR Therapeutics (1) Flynn Pharmaceuticals
DepoNSAID	Acute pain	Preclinical	Pacira (worldwide)
DepoMethotrexate	Rheumatoid arthritis Oncology	Preclinical Preclinical	Pacira (worldwide) Pacira (worldwide)

(1) On January 3, 2012, EKR exercised its right to terminate the agreement and delivered a notice of termination. Pursuant to the terms of the agreement, the termination of the licensing, distribution and marketing agreement will be effective 180 days from the date of the notice or July 1, 2012.

Our Strategy

Our goal is to be a leading specialty pharmaceutical company focused on the development, commercialization and manufacture of proprietary pharmaceutical products principally for use in hospitals and ambulatory surgery centers. We plan to achieve this by:

Table of Contents

- commercializing EXPAREL in the United States for postsurgical analgesia by infiltration;

- building a streamlined commercial organization concentrating on major hospitals and ambulatory surgery centers in the United States and targeting surgeons, anesthesiologists, pharmacists and nurses;

- working directly with managed care payers, quality improvement organizations, KOLs in the field of postsurgical pain management and leading influence hospitals with Phase 4 retrospective and prospective trials to demonstrate the economic benefits of EXPAREL;

- securing commercial partnerships for EXPAREL in regions outside of the United States;

- obtaining FDA approval for nerve block indication for EXPAREL;

- manufacturing all our DepoFoam-based products, including EXPAREL, in our current Good Manufacturing Practices, or cGMP, compliant facilities;

- continuing to expand our marketed product portfolio through development of additional DepoFoam-based hospital products utilizing a 505(b)(2) strategy, which permits us to rely upon the FDA s previous findings of safety and effectiveness for an approved product. A 505(b)(2) strategy may not succeed if there are successful challenges to the FDA s interpretation of Section 505(b)(2); and

- continuing research and development partnerships to provide DepoFoam-based products to enhance the duration of action and patient compliance for partner products.

Postsurgical Pain Market Overview

According to Thomson Reuters, roughly 45 million surgical procedures were performed in the United States during the twelve months ending in October 2007. We estimate there are approximately 39 million opportunities annually in the United States where EXPAREL could be used to improve patient outcomes and enhance hospital economics. Postsurgical pain is a response to tissue damage during surgery that stimulates peripheral nerves, which signal the brain to produce a sensory and psychological response. Numerous studies reveal that the incidence and severity of postsurgical pain is primarily determined by the type of surgery, duration of surgery and the pain treatment choice following surgery. Postsurgical pain is usually the most severe the first few days after the completion of a surgical procedure.

Limitations of Current Therapies for Postsurgical Pain

Substantially all surgical patients experience postsurgical pain, with approximately 50% reporting inadequate pain relief according to certain epidemiological studies. Unrelieved acute pain causes patient suffering and can lead to other health problems, which delays recovery from surgery and may result in higher healthcare costs. According to the Agency for Healthcare Research and Quality, aggressive prevention of pain is better than treatment of pain because, once established, pain is more difficult to suppress. Current multimodal therapy for postsurgical pain includes wound infiltration with local anesthetics combined with the systemic administration of opioid and non-steroidal anti-inflammatory drug, or NSAID, analgesics.

Local Anesthetics

Treatment of postsurgical pain typically begins at the end of surgery, with local anesthetics, such as bupivacaine, administered by local infiltration. Though this infiltration provides a base platform of postsurgical pain management for the patient, efficacy of conventional bupivacaine and other available local anesthetics is limited, lasting approximately eight hours or less. As local infiltration is not practical after the surgery is complete, and as surgical pain is greatest in the first few days after surgery, additional therapeutics are required to manage postsurgical pain.

Opioids

Opioids, such as morphine, are the mainstay of postsurgical pain management but are associated with a variety of unwanted and potentially severe side effects, leading healthcare practitioners to seek opioid-sparing strategies for their patients. Opioid side effects include sedation, nausea, vomiting, urinary retention, headache, itching, constipation, cognitive impairment,

Table of Contents

respiratory depression and death. Side effects from opioids have been demonstrated to reduce the patient s quality of life and result in suboptimal pain relief. These side effects may require additional medications or treatments and prolong a patient s stay in the post-anesthesia care unit and the hospital or ambulatory surgery center, thereby increasing costs significantly.

PCA and Elastomeric Bag Systems

Opioids are often administered intravenously through patient controlled analgesia, or PCA, systems in the immediate postsurgical period. The total cost of PCA postsurgical pain management for three days can be up to $500, not including the costs of treating any opioid complications. In an attempt to reduce opioid usage, many hospitals employ elastomeric bag systems designed to deliver bupivacaine to the surgical area through a catheter over a period of time. This effectively extends the duration of bupivacaine in the postsurgical site but has significant shortcomings.

PCA systems and elastomeric bag systems are clumsy and difficult to use, which may delay patient ambulation and introduce catheter-related issues, including infection. In addition, PCA systems and elastomeric bags require significant hospital resources to implement and monitor.

NSAIDs

NSAIDs are considered to be useful alternatives to opioids for the relief of acute pain since they do not produce respiratory depression or constipation. Despite these advantages, the use of injectable NSAIDs, such as ketorolac and ibuprofen, is severely limited in the postsurgical period because they increase the risk of bleeding and gastrointestinal and renal complications.

Our Solution EXPAREL

EXPAREL provides continuous and extended postsurgical analgesia for up to 72 hours and reduces the consumption of supplemental opioid medications. We believe this will simplify postsurgical pain management, minimize breakthrough episodes of pain and result in improved patient outcomes and enhanced hospital economics.

Our EXPAREL strategy has four principal elements:

Replace the use of bupivacaine in postsurgical infiltration. Based on our clinical data, EXPAREL:

- extends postsurgical analgesia for up to 72 hours, from approximately eight hours or less;

- utilizes existing postsurgical infiltration administration techniques;

- dilutes easily with saline to reach desired volume;

- is a ready-to-use formulation; and

- facilitates treatment of both small and large surgical sites.

Become the foundation of a postsurgical pain management regimen in order to reduce and delay opioid usage. Based on the clinical data from our Phase 3 hemorrhoidectomy trial as well as our retrospective health outcomes studies data, EXPAREL:

- significantly delays and reduces opioid usage while improving postsurgical pain management:

- delays first opioid usage to approximately 14 hours post-surgery, compared to approximately one hour for placebo;

- significantly increases the percentage of patients requiring no opioid rescue medication through 72 hours post-surgery, to 28% compared to 10% for placebo;

Table of Contents

- results in 45% less opioid usage at 72 hours post-surgery compared to placebo; and

- increases the percentage of patients who are pain free at 24 hours post-surgery compared to placebo.

Improve patient satisfaction. We believe EXPAREL:

- provides effective pain control without the need for expensive and difficult to use delivery technologies which extend the duration of action for bupivacaine, such as elastomeric bags, or opioids administered through patient controlled analgesia, or PCA, when considered as part of a multimodal postsurgical pain regimen with an NSAID and acetaminophen and morphine rescue;

- reduces the need for patients to be constrained by elastomeric bags and PCA systems, which are clumsy, difficult to use and may introduce catheter-related issues, including infection;

- promotes maintenance of early postsurgical pain management, thereby reducing the time spent in the intensive care unit; and

- promotes early ambulation, which potentially reduces the risk of life-threatening blood clots, and allows quicker return of bowel function, thereby leading to a faster switch to oral nutrition and medicine, and thus a faster discharge from the hospital.

Develop and seek approval of EXPAREL for nerve block administration. We believe this additional indication for EXPAREL:

- presents a low-risk, low-cost opportunity for clinical development; and

- enables us to fully leverage our manufacturing and sales infrastructure.

EXPAREL Development Program

EXPAREL has demonstrated efficacy and safety in two multicenter, randomized, double-blind, placebo-controlled, pivotal Phase 3 clinical trials in patients undergoing soft tissue surgery (hemorrhoidectomy) and orthopedic surgery (bunionectomy). At a pre-NDA meeting in

February 2010, the FDA acknowledged that the two pivotal Phase 3 clinical trials conducted by us, in patients undergoing hemorrhoidectomy and bunionectomy surgeries, appeared to be appropriately designed to evaluate the safety and efficacy of EXPAREL. Both trials met their primary efficacy endpoints in demonstrating statistically significant analgesia through 72 hours for the hemorrhoidectomy trial and 24 hours for the bunionectomy trial. Both trials also met multiple secondary endpoints, including decreased opioid use and delayed time to first opioid use. These two pivotal Phase 3 clinical trials formed the basis of the evidence for efficacy in the NDA for EXPAREL.

The safety of EXPAREL has been demonstrated in 21 clinical trials consisting of nine Phase 1 trials, seven Phase 2 trials and five Phase 3 trials. EXPAREL was administered to over 1,300 human patients at doses ranging from 10 mg to 750 mg administered by local infiltration into the surgical site, and by subcutaneous, perineural, epidural and intraarticular administration. In all 21 clinical trials, EXPAREL was well tolerated. The most common treatment emergent adverse events in the EXPAREL and placebo groups were nausea and vomiting and occurred with similar frequency across the EXPAREL and placebo groups. No signal of any of the central nervous system or cardiovascular system adverse events typically observed with high doses of bupivacaine has been observed with EXPAREL. We conducted two thorough QTc studies that demonstrated that EXPAREL did not cause significant QTc prolongation (a measure of cardiac safety mandated by the FDA for all new products) even at the highest dose evaluated. No events of destruction of articular cartilage, or chondrolysis, have been reported in any of the EXPAREL trials. EXPAREL did not require dose adjustment in patients with mild to moderate liver impairment.

Pivotal Phase 3 Clinical Trials

Hemorrhoidectomy. Our pivotal Phase 3 hemorrhoidectomy clinical trial was a multicenter, randomized, double-blind, placebo-controlled trial conducted in 189 patients at 14 sites in Europe. The study enrolled patients 18 years of age or older undergoing a two or three column excisional hemorrhoidectomy under general anesthesia using the Milligan-Morgan technique, a

commonly used method for surgically removing hemorrhoids. We studied a 266 mg dose of EXPAREL with a primary endpoint of pain control for up to 72 hours with morphine rescue medication available to both trial groups. Additional endpoints included the proportion of pain-free patients, proportion of patients requiring opioid rescue medication, total opioid usage, time to first use of opioid rescue medication and patient satisfaction.

Table of Contents

The 266 mg dose of EXPAREL provided a statistically significant 30% reduction in pain (p<0.0001), as measured by the area under the curve, or AUC, of the NRS-R pain scores at 72 hours and all additional time points measured up to 72 hours. The numeric rating scale at rest score, or the NRS-R, is a commonly used patient reported measurement of pain. Under the NRS-R, severity of pain is measured on a scale from 0 to 10, with 10 representing the worst possible pain. The AUC of the NRS-R pain score represents a sum of the patient s pain measured at several time points using the NRS-R, from time of surgery to the specified endpoint. A lower number indicates less cumulative pain. The p-value is a measure of probability that the difference between the placebo group and the EXPAREL group is due to chance (e.g., p = 0.01 means that there is a 1% (0.01 = 1.0%) chance that the difference between the placebo group and EXPAREL group is the result of random chance as opposed to the EXPAREL treatment). A p-value less than or equal to 0.05 (0.05 = 5%) is commonly used as a criterion for statistical significance.

Phase 3 Hemorrhoidectomy Clinical Trial: AUC of NRS-R Pain Intensity Scores from Initial Infiltration Timepoint, EXPAREL Compared to Placebo

In referencing our pivotal Phase 3 hemorrhoidectomy clinical trial, the FDA-approved label EXPAREL noted there was a significant treatment effect for EXPAREL compared to placebo treatment over the first 72 hour period.