Pacira Pharmaceuticals, Inc.
Form 10-K
February 25, 2014
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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, 2013

Or

.. 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 Select 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. x

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

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 20,909,360 shares of voting stock held by non-affiliates of the registrant, based upon the closing sale price of the common stock as reported on the NASDAQ on June 28, 2013, the last business day of the registrant's most recently completed second fiscal quarter, of $29.00 per share was $606,371,440. Shares of common stock held by each director and executive officer (and their respective affiliates) 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 February 14, 2014, 33,714,015 shares of the registrant's common stock, $0.001 par value per share, were outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Part III of this Annual Report on Form 10-K incorporates certain information by reference from the registrant's proxy statement for the 2014 annual meeting of stockholders to be filed no later than 120 days after the end of the registrant's fiscal year ended December 31, 2013.

Table of Contents

Table of Contents

Forward-Looking Statements

This Annual Report on Form 10-K and certain other communications made by us contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act 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,” and similar expressions to help identify forward-looking statements. We cannot assure you that our estimates, assumptions and expectations will prove to have been correct. These forward-looking statements include, among others, statements about: the success of our sales and manufacturing efforts in support of the commercialization 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; the Company’s plans to expand the indications of EXPAREL, including nerve block and the related timing and success of a supplemental U.S. Food and Drug Administration New Drug Application; the Company’s plans to evaluate and pursue additional DepoFoam-based product candidates; clinical studies in support of an existing or potential DepoFoam based product; the Company’s plans to continue to manufacture and provide support services for its commercial partners who have licensed DepoCyt(e); and our 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 in Part I-Item 1A. Risk Factors. 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.
These forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance, or achievements to differ materially from those expressed or implied by these statements. These factors include the matters discussed and referenced in Part I-Item 1A. Risk Factors.

Table of Contents

PART I

Item 1. Business

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 10-K 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.

Corporate Information

We were incorporated in Delaware under the name Blue Acquisition Corp. in December 2006 and changed our name to Pacira, Inc. in June 2007. In October 2010, we changed our name to Pacira Pharmaceuticals, Inc. Our principal executive offices are located at 5 Sylvan Way, Suite 100, Parsippany, New Jersey 07054, and our telephone number is (973) 254-3560.

Pacira®, DepoFoam®, DepoCyt® (U.S. registration), DepoCyte® (EU registration), EXPAREL®, the Pacira logo and other trademarks or service marks of Pacira appearing in this Annual Report on Form 10-K are the property of Pacira. This Annual Report on Form 10-K contains additional trade names, trademarks and service marks of other companies.

Overview

We are a specialty pharmaceutical company focused on the development, commercialization and manufacture of pharmaceutical products, based on our proprietary DepoFoam® drug delivery technology, for use primarily in hospitals and ambulatory surgery centers. We operate in one reportable segment. 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-type local anesthetic indicated for infiltration into the surgical site to produce postsurgical analgesia for up to 72 hours. 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 have developed an internal sales force entirely dedicated to commercializing EXPAREL, which we commercially launched in April 2012. In addition, following a pilot program, effective October 1, 2013, we appointed CrossLink BioScience, LLC, or CrossLink, for a term of five years as the exclusive third-party distributor to promote and sell EXPAREL for orthopedic and spine surgeries in the United States, with the exception of certain geographical areas and accounts subject to change and adjustments by mutual agreement.

Our net sales for EXPAREL in 2013 were $76.2 million, and our net sales for EXPAREL in our fiscal quarter ended December 31, 2013, which was the seventh quarter of our launch, were $30.5 million. A total of 2,106 accounts have ordered EXPAREL since launch through December 31, 2013, with approximately 250 accounts having ordered more than $100,000 of EXPAREL by the end of 2013. During the fourth quarter of 2013, we added 374 new accounts, averaging 29 new accounts per week. We believe EXPAREL will ultimately become a major hospital pharmaceutical brand.

In addition to EXPAREL, DepoFoam is also the basis for our other FDA-approved commercial product, DepoCyt(e), which we manufacture for our commercial partners, as well as our other product candidates. For the years ended December 31, 2013, 2012 and 2011 sales of EXPAREL accounted for 89%, 37% and 0% of total revenues and Depocyt(e) 10%, 15% and 66%, respectively.

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	Marketed in U.S.	Pacira (worldwide)
	Postsurgical analgesia-nerve block	Phase 3	Pacira (worldwide)
		Filed INAD	

Bupivacaine Liposome Injectable Suspension	Veterinary postsurgical analgesia	Aratana Therapeutics, Inc. (worldwide)

Table of Contents

Product(s)/Product Candidate(s)	Primary Indication(s)	Status	Commercialization Rights
DepoCyt(e)	Lymphomatous meningitis	Marketed in U.S.	Sigma-Tau Pharmaceuticals
		Marketed in E.U.	Mundipharma International
DepoNSAID	Acute pain	Preclinical	Pacira (worldwide)
DepoMethotrexate	Oncology	Preclinical	Pacira (worldwide)

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:

- 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;
- demonstrating the economic benefits of EXPAREL, working directly with managed care payers, quality improvement organizations, Key Opinion Leaders, or KOLs, in the field of postsurgical pain management and leading influence hospitals in conducting Phase 4 retrospective and prospective trials and drug utilization evaluations;
- servicing the commercial audiences that are rapidly adopting EXPAREL in local infiltration procedures, including not only the soft tissue surgical audiences that were the focus of the launch, but more recently expanding our education to audiences including the orthopedic, spine, and anesthesia (infiltration into the transverse abdominus plane—iTAP) who require similar education and training to ensure consistent, proper and safe use of the product;
- obtaining FDA approval for nerve block indication for EXPAREL;
- leveraging the development success of EXPAREL in the animal health market through our commercial partner for Bupivacaine Liposome Injectable Suspension to serve the companion animal market;
- manufacturing all our DepoFoam-based products, including EXPAREL, in facilities compliant with current Good Manufacturing Practices, or cGMP;
- 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.

EXPAREL-Our Lead Product

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

Our EXPAREL strategy has several principal elements:

1) Replace the use of bupivacaine via elastomeric pumps as the foundation of a multimodal regimen for long-acting postsurgical pain management. Based on our clinical data, EXPAREL:

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

4

Table of Contents

- 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.

2) Become the foundation of a long- acting 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;
- 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.

3) Improve patient satisfaction and outcomes. We believe EXPAREL:

- provides effective pain control without the need for expensive and difficult-to-use delivery technologies that 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;
- 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, which may reduce the time spent in the intensive care unit; and

4) Develop and seek approval of additional indications for EXPAREL, including for nerve block administration. We believe the nerve block indication for EXPAREL:

- presents a low-cost opportunity for clinical development; and
- enables us to fully leverage our manufacturing and sales infrastructure.

EXPAREL Health Economic Benefits

In addition to being efficacious and safe, we believe that EXPAREL provides health economic benefits that play an important role in formulary decision-making and that these health economic benefits are an often over-looked factor in planning for the commercial success of a pharmaceutical product. Several members of our management team have extensive experience applying health economic outcomes research to support the launch of successful commercial products. Our strategy is to work directly with our hospital C-suite customers, group purchasing organizations, integrated health networks, quality improvement organizations, KOLs in the field of postsurgical pain management and leading influence hospitals and to provide them with retrospective and prospective studies to demonstrate the economic benefits of EXPAREL.

Our national, regional, and local analyses assessing retrospective health outcomes, conducted in conjunction with hospital customer groups utilizing their own hospital databases, revealed that the use of opioids for postsurgical pain control is a significant driver of hospital resource consumption, including higher hospitalization costs, longer length of stay, and higher readmission rates.

Table of Contents

Phase 4 Clinical Studies

We recently completed our IMPROVE program, a series of open-label prospective Phase 4 clinical studies evaluating the differences in postsurgical opioid use and health economic outcomes in patients undergoing open colectomy, ileostomy reversal, and lap colectomy. Findings consistently showed reduction in median length of hospital stay, mean hospitalization costs, and mean opioid consumption.

Additionally, we conducted a Phase 4 study (the "TRANSCEND" trial) in patients undergoing gynecologic or colorectal surgery. Prior to surgery, patients received either EXPAREL or sham (normal saline) iTAP as part of a multimodal pain regimen. The study goal was to demonstrate the utility of EXPAREL by achieving either co-primary endpoint of Day 3 Overall Benefit of Analgesia Score (OBAS) or total opioid rescue. A pre-planned interim analysis was performed on the first 39 patients recruited, which revealed a signal in one of the co-primary endpoints (OBAS), but poor compliance with the algorithm for total opioid rescue in the protocol and no signal for that co-primary endpoint. As a result, the decision was made not to continue the trial, but rather to analyze all of the patients recruited up to that point (n=67). In this analysis, the total opioid rescue continued to show no signal (with only 35 percent of patients protocol compliant), while the OBAS demonstrated an advantage for EXPAREL ($P<0.05$) compared to the sham-treated group.

EXPAREL Regulatory Plan

The NDA for EXPAREL was approved on October 28, 2011, using a 505(b)(2) application. The initial FDA approval of EXPAREL is for single-dose infiltration into the surgical site to produce postsurgical analgesia.

EXPAREL consists of bupivacaine encapsulated in DepoFoam, both of which are used in FDA-approved products:

- Bupivacaine, a well-characterized generic anesthetic/analgesic, has an established safety profile and over 20 years of use in the United States.

- DepoFoam, modified to meet the requirements of each product, is used to extend the release of the active drug substances in the products DepoCyt(e) and the no-longer marketed DepoDur.

The FDA, as a condition of EXPAREL approval, has required us to study EXPAREL in pediatric patients. We have agreed to a trial timeline where, over several years, we will study pediatric patient populations in descending order starting with 12 to 18 year olds and ending with children under two years of age.

Additional Indications

We are pursuing several additional indications for EXPAREL and expect to submit a supplemental U.S. Food and Drug Administration New Drug Application, or sNDA, for nerve block administration. We believe that this additional indication for EXPAREL presents a low-cost opportunity for clinical development and will allow us to fully leverage our manufacturing and commercial infrastructure.

Nerve block is a general term used to refer to the injection of local anesthetic onto or near nerves for control of pain. Nerve blocks can be single injections but have limited duration of action. When extended pain management is required, a catheter is used to deliver bupivacaine continuously using an external pump. According to Thomson Data, over eight million nerve block procedures were conducted in the United States in 2008, with over four million of these procedures utilizing bupivacaine. EXPAREL is designed to provide extended pain management with a single injection utilizing a narrow gauge needle.

In 2012, we initiated two pivotal nerve block trials comparing the effect of EXPAREL versus placebo through a femoral nerve block study for total knee arthroplasty and an intercostal block study for posterolateral thoracotomy procedures. In May 2013, we reported positive findings from the first part of our femoral nerve block study for total knee arthroplasty; the final part of this study is still ongoing. In August 2013, we reported that the intercostal nerve block study for posterolateral thoracotomy did not achieve its primary endpoint. The FDA has previously indicated to us at its end of Phase 2 meeting that a single pivotal trial meeting its primary endpoint would be sufficient to gain approval for the nerve block indication, assuming demonstration of adequate safety. We plan to submit data from the ongoing femoral nerve block study to demonstrate efficacy and safety, as well as safety data from the intercostal nerve block study, for an sNDA, anticipated in early 2014. We believe that this new indication will present an alternative long-term method of pain control with a single injection, replacing the costly and cumbersome standard of care

requiring a perineural catheter, drug reservoir and pump needed to continuously deliver bupivacaine.

Table of Contents

Sales and Marketing

We have built our marketing and sales organization to commercialize EXPAREL and our product candidates in the United States. We intend to out-license commercialization rights for other territories. Our goal is to retain significant control over the development process and commercial execution for our product candidates, while participating in a meaningful way in the economics of all products that we bring to the market.

Our commercial team, consisting of both sales representatives and scientific and medical affairs professionals, executes on a full range of activities for EXPAREL, including:

- providing publications and abstracts showing the EXPAREL clinical program efficacy and safety, health outcomes program and review articles on pain management;

- working in tandem with hospital staff, such as registered nurses, surgeons, heads of quality, pharmacists and C-level executives, to provide access and resources for drug utilization (DUE) or medication use evaluations (MUE), and 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 control;

- working with KOLs and advisory boards to address topics of best practice techniques as well as guidelines and protocols for the use of EXPAREL, meeting the educational and training needs of our physician, surgeon, anesthesiologist, pharmacist and registered nurse customers; and

- undertaking education initiatives such as center of excellence programs, preceptorship programs, pain protocols and predictive models for enhanced patient care, interactive discussion forums, web-based training and virtual launch programs.

Initially at launch, we outsourced our dedicated commercial sales force through our relationship with Quintiles Commercial US, Inc., or Quintiles. On January 28, 2013, this sales force transitioned from Quintiles employees to Pacira employees. They are supported by our current marketing team as well as teams of healthcare professionals, including medical affairs, scientific affairs and nursing teams, who support our formulary approval and customer education initiatives. Additionally, on October 1, 2013, we entered into an agreement with CrossLink to act as a local agent and lead partner in collaboration with additional distributors to promote and sell EXPAREL in select territories in the United States for postsurgical pain management following orthopedic and spine procedures.

In order to increase the speed with which we address market segments, or to increase our access to market segments that we are currently not addressing, we may expand our sales resources in the future directly or by developing additional relationships with third parties that agree to sell our product.

The primary target audience for EXPAREL is healthcare practitioners who influence pain management decisions, including surgeons, anesthesiologists, pharmacists and nurses.

DepoFoam-Our Proprietary Drug Delivery Technology

Our current product development activities utilize our proprietary DepoFoam drug delivery technology. DepoFoam consists of microscopic spherical particles composed of a honeycomb-like structure of numerous internal aqueous chambers containing an active drug ingredient. Each chamber is separated from adjacent chambers by lipid membranes. Following injection, the DepoFoam particles release drug over an extended period of time by erosion and/or reorganization of the particles' lipid membranes. Release rates are determined by the choice and relative amounts of lipids in the formulation.

We believe DepoFoam formulation provides several technical, regulatory and commercial advantages over competitive technologies, including:

- Convenience. Our DepoFoam products are ready to use and do not require reconstitution or mixing with another solution, and can be used with patient-friendly narrow gauge needles and pen systems;

- Multiple regulatory precedents. Our current and past DepoFoam products, including DepoCyt(e) and DepoDur, have been approved in the United States and Europe, making regulatory authorities familiar with our DepoFoam

technology;

Table of Contents

- Extensive safety history. Our DepoFoam products have over ten years of safety data as DepoCyt(e) has been sold in the United States since 1999;

- Proven manufacturing capabilities. We make the DepoFoam-based products, EXPAREL and DepoCyt(e) in our cGMP facilities;

- Flexible time release. Encapsulated drug releases over a desired period of time, from 1 to 30 days;

- Favorable pharmacokinetics. Decrease in adverse events associated with high peak blood levels, thereby improving the utility of the product;

- Shortened development timeline. Does not alter the native molecule, potentially enabling the filing of a 505(b)(2) application; and

- Aseptic manufacturing and filling. Enables use with proteins, peptides, nucleic acids, vaccines and small molecules.

Other Products

DepoCyt(e)

DepoCyt(e) is a sustained-release liposomal formulation of the chemotherapeutic agent cytarabine utilizing our DepoFoam technology. DepoCyt(e) is indicated for the intrathecal treatment of lymphomatous meningitis, a life-threatening complication of lymphoma, a cancer of the immune system. Lymphomatous meningitis can be controlled with conventional cytarabine, but because of the drug's short half-life, a spinal injection is required twice per week, whereas DepoCyt(e) is dosed once every two weeks in an outpatient setting. DepoCyt(e) was granted accelerated approval by the FDA in 1999 and full approval in 2007. We recognized revenue from DepoCyt(e) of $8.4 million from our commercial partners in 2013.

Product Candidates

DepoNSAID

Our preclinical product candidates, extended release formulations of NSAIDs, are designed to provide the benefits of injectable NSAIDs with a prolonged duration of action in order to improve patient care and ease of use in the acute pain environment. Currently available injectable systemic products provide a four to six hour duration of action. We believe that there is an unmet medical need for a product which could provide a local infiltration since the mode of action for NSAIDs is by local activity. A product developed for local infiltration should provide pain relief with a much lower dose of NSAID and potentially avoid the side effects commonly associated with the systemic use of these agents. We have DepoFoam formulations for several NSAIDs, and we expect to select a lead product candidate in 2014.

Commercial Partners and Agreements

SkyePharma Holdings, Inc.

In connection with the stock purchase agreement related to the Acquisition, we agreed to pay SkyePharma Holdings, Inc., or Skyepharma, specified contingent milestone payments related to EXPAREL sales as set forth below:

(i)$10.0 million upon first commercial sale in the United States;
(ii)$4.0 million upon first commercial sale in a major EU country (United Kingdom, France, Germany, Italy and Spain);
(iii)$8.0 million when annual net sales collected reach $100.0 million;
(iv)$8.0 million when annual net sales collected reach $250.0 million; and
(v)$32.0 million when annual net sales collected reach $500.0 million.

The first contingency was resolved in April 2012, resulting in a $10.0 million payment to Skyepharma. Additionally, we agreed to pay to Skyepharma 3% of net sales of EXPAREL collected in the United States, Japan, the United Kingdom, France, Germany, Italy and Spain. Such obligations to make percentage payments will continue for

the term in which such sales related to EXPAREL are covered by a valid claim in certain patent rights related to EXPAREL and other

Table of Contents

biologics products. The expiration date of the last valid claim will occur in 2018. Cumulatively through December 31, 2013, Skyepharma has earned $2.4 million of percentage payments on net sales of EXPAREL collected. We have the right to cease paying the 3% percentage payments in the event that Skyepharma breaches certain covenants not to compete contained in the stock purchase agreement. In the event that we cease to sell EXPAREL and begin marketing a similar replacement product for EXPAREL, we would no longer be obligated to make percentage payments, but we may be required to make certain milestone payments upon reaching certain sales milestones.

For additional information related to the Skyepharma agreement, please refer to Note 6, Goodwill and Intangible Assets, in the Consolidated Financial Statements.

Research Development Foundation

Pursuant to an agreement with one of our stockholders, the Research Development Foundation, or RDF, we are required to pay RDF a low single-digit royalty on the collection of revenues from our DepoFoam-based products, for as long as certain patents assigned to us under the agreement remain valid. RDF has the right to terminate the agreement for an uncured material breach by us, in connection with our bankruptcy or insolvency or if we directly or indirectly oppose or dispute the validity of the assigned patent rights.

Sigma-Tau Pharmaceuticals, Inc.

In December 2002, we entered into a supply and distribution agreement with Enzon Pharmaceuticals Inc. regarding the sale of DepoCyt. Pursuant to the agreement, Enzon was appointed the exclusive distributor of DepoCyt in the United States and Canada for a ten-year term. In January 2010, Sigma-Tau Pharmaceuticals, Inc., or Sigma-Tau, acquired the rights to sell DepoCyt from Enzon Pharmaceuticals for the United States and Canada. Under the supply and distribution agreement, we supply unlabeled DepoCyt vials to Sigma-Tau for finished packaging. Under these agreements, we receive a fixed payment for manufacturing the vials of DepoCyt and an additional royalty payment, if Sigma-Tau's quarterly net sales exceed a certain amount, which brings total payments in the thirty percent range on sales by Sigma-Tau in the United States and Canada.

We and Sigma-Tau have the right to terminate the agreement for an uncured material breach by the other party or in the event that a generic pharmaceutical product that is therapeutically equivalent to DepoCyt is commercialized. We may terminate the agreement if certain minimum sales targets are not met by Sigma-Tau. Sigma-Tau may terminate the agreement if, as a result of a settlement or a final court or regulatory action, the manufacture, use or sale of DepoCyt in the United States is prohibited.

Mundipharma International Holdings Limited

In June 2003, we entered into an agreement granting Mundipharma International Holdings Limited, or Mundipharma, exclusive marketing and distribution rights to DepoCyte in the European Union and certain other European countries. This agreement has a term of 15 years, and after that term expires, continues year to year unless terminated by us or by Mundipharma upon no less than 12 months written notice.

Under the agreement, as amended, and a separate supply agreement, we receive a fixed payment for manufacturing the vials of DepoCyte, as well as a royalty in addition to the fixed sum per vial supplied to Mundipharma, if Mundipharma's quarterly net sales exceed a certain amount, and a mid single-digit royalty on all annual sales exceeding a certain amount. We are also entitled to receive up to €10.0 million in milestone payments from Mundipharma upon the achievement by Mundipharma of certain milestone events, of which we have already received €2.5 million and we do not expect to receive the remaining €7.5 million.

We and Mundipharma have the right to terminate the agreement for an uncured material breach by the other party, in connection with the other party's bankruptcy or insolvency or the repossession of all or any material part of the other party's business or assets. Mundipharma has the right to terminate the agreement if its marketing authorization is cancelled or withdrawn for a certain period, or if it is prevented from selling DepoCyte in any three countries in the territory covered in the agreement by a final non-appealable judgment in respect of infringement by DepoCyte of any third party intellectual property rights.

Paul Capital Advisors LLC

On March 23, 2007, we entered into an amended and restated royalty interests assignment agreement with Paul Capital Advisors LLC, or Paul Capital, pursuant to which we assigned to Paul Capital the right to receive a portion of our

9

Table of Contents

royalty payments from DepoCyt(e) and DepoDur. The original agreement was entered into prior to the Acquisition by Skyepharma in order to monetize certain royalty payments from DepoCyt(e) and DepoDur. In connection with the Acquisition, the original agreement with Paul Capital was amended and restated and the responsibility to pay the royalty interest in product sales of DepoCyt(e) and DepoDur was transferred to us and we were required to make payments to Paul Capital upon the occurrence of certain events. For additional information, see "Management's Discussion and Analysis of Financial Condition and Results of Operations-Liquidity and Capital Resources-Royalty Interests Assignment Agreement" and "Risk Factors-Risks Related to Our Financial Condition and Capital Requirements." Under our financing arrangement with Paul Capital, upon the occurrence of certain events, Paul Capital may require us to repurchase the right to receive royalty payments that we assigned to it, or may foreclose on certain assets that secure our obligations to Paul Capital. Any exercise by Paul Capital of its right to cause us to repurchase the assigned right or any foreclosure by Paul Capital would adversely affect our results of operations and our financial condition. This financing arrangement terminates on December 31, 2014.

Aratana Therapeutics, Inc.

On December 5, 2012 we entered into an Exclusive License, Development and Commercialization Agreement and related Supply Agreement with Aratana Therapeutics, Inc. or Aratana. Under the agreements, we granted Aratana an exclusive royalty-bearing license, including the limited right to grant sublicenses, for the development and commercialization of our bupivacaine liposome injectable suspension product for animal health indications. Under the agreement, Aratana will develop and seek approval for the use of the product in veterinary surgery to manage postsurgical pain, focusing initially on developing it for cats, dogs and other companion animals.

In connection with our entry into the agreement, we received a one-time payment of $1.0 million and are eligible to receive up to an additional aggregate $42.5 million upon the achievement of development and commercial milestones, of which we received $0.5 million in 2013. Once the product has been approved by the Food and Drug Administration for sale in the United States, Aratana will pay us a tiered double digit royalty on net sales made in the United States. If the product is approved by foreign regulatory agencies for sale outside of the United States, Aratana will pay us a tiered double digit royalty on such net sales. Royalty rates will be reduced by a certain percentage upon the entry of a generic competitor for animal health indications into a jurisdiction or if Aratana must pay royalties to third parties under certain circumstances.

Either party has the right to terminate the license agreement in connection with (i) an insolvency event involving the other party that is not discharged in a specified period of time, (ii) a material breach of the agreement by the other party that remains uncured for a specified cure period or (iii) the failure to achieve a minimum annual revenue as set forth in the agreement, all on specified notice. We may terminate the agreement in connection with (i) Aratana's failure to pay any amounts due under the agreement, (ii) Aratana's failure to achieve regulatory approval in a particular jurisdiction with respect to such jurisdiction or (iii) Aratana's failure to achieve its first commercial sale within a certain amount of time on a country by country basis after receiving regulatory approval, all on specified notice. Aratana may terminate the license agreement (i) upon the entry of a generic competitor for animal health indications on a country by country basis or (ii) at any time on a country by country basis except with respect to the United States and any country in the European Union, all on specified notice. The parties may also terminate the license agreement by mutual consent. The license agreement will terminate automatically if we terminate the supply agreement. In the event that the License Agreement is terminated, all rights to the product (on a jurisdiction by jurisdiction basis) will be terminated and returned to us.

Unless terminated earlier pursuant to its terms, the license agreement is effective until December 5, 2027, after which Aratana has the option to extend the agreement for an additional five (5) year term, subject to certain requirements.

CrossLink BioScience, LLC

Effective October 1, 2013, we and CrossLink commenced a five-year arrangement for the promotion and sale of EXPAREL, pursuant to the terms of a Master Distributor Agreement (as amended, the "Agreement"). We entered into the Agreement on March 11, 2013, which provided for an initial small-scale pilot period commencing on April 1, 2013 and ending on September 30, 2013 (the "Pilot Period"), during which CrossLink was appointed as the exclusive distributor of EXPAREL for certain specified accounts. The Agreement permitted either party to terminate the Agreement within 15 days prior to the expiration of the Pilot Period, and unless such termination was effected, the

Agreement would automatically renew for a term of five years, commencing on October 1, 2013 and ending on September 30, 2018 (the “Term”). Neither party provided notice of termination, and upon the commencement of the Term, certain performance metrics and payment terms became effective, and CrossLink’s distribution territory expanded.

Under the Agreement, we appointed CrossLink as the exclusive third-party distributor during the Term to promote and sell EXPAREL for orthopedic and spine surgeries in the United States, with the exception of certain geographical areas and

Table of Contents

accounts (the "Territory"). The prices and purchasing terms related to sales of EXPAREL are determined by us, and all orders are subject to acceptance or rejection by us. CrossLink is entitled to receive commissions on its sales of EXPAREL in the Territory, subject to certain conditions and adjustments. CrossLink may receive additional performance-based payments if it achieves certain sales goals, and we may terminate the Agreement if CrossLink fails to meet certain minimum performance metrics.

CrossLink and any sub-distributors engaged by CrossLink pursuant to the terms of the Agreement are subject to certain obligations and restrictions, including required compliance with certain laws and regulations, confidentiality obligations and our policies. The Agreement contains customary representations and warranties and mutual indemnification obligations. In addition, CrossLink and its sub-distributors are prohibited from promoting, selling or distributing any competitive products during the Term.

Pacira and CrossLink have mutual termination rights under the Agreement, and we have additional unilateral termination rights under certain circumstances. The Agreement also permits us to terminate the Agreement without cause effective September 30, 2016, subject to certain terms and conditions set forth in the Agreement.

Significant Customers

We had three customers each comprising 10% or more of our total revenue for the year ended December 31, 2013. AmerisourceBergen Health Corporation, Cardinal Health, Inc. and McKesson Drug Company accounted for 33%, 28%, and 18% of our revenues, respectively. These customers are wholesalers that process orders for EXPAREL under a drop-ship program.

Manufacturing

We manufacture EXPAREL and DepoCyt(e) in two manufacturing facilities that we refer to as the Science Center Campus in San Diego, California. These facilities are designated as Building 1 and Building 6 and are located within two miles of each other on two separate and distinct sites. Our facilities are inspected regularly and approved for pharmaceutical manufacturing by the FDA, the European Medicines Agency, or the EMA, the Medicines and Healthcare Products Regulatory Agency, or the MHRA, the Drug Enforcement Administration, or the DEA, and the Environmental Protection Agency, or the EPA.

We purchase raw materials and components from third party suppliers in order to manufacture EXPAREL. In most instances, alternative sources of supply are available, although switching to an alternative source would, in some instances, take time and could lead to delays in manufacturing our drug candidates. We also purchase raw materials and equipment from third party suppliers, for the manufacture of DepoCyt(e). While we have not experienced shortages of our raw materials in the past, such suppliers may not sell these raw materials to us at the times that we need them or on commercially reasonable terms and we do not have any control over the process or timing of the acquisition of these raw materials from our suppliers.

All manufacturing of products, initial product release and stability testing are conducted by us in accordance with cGMP.

Building 1 is an approximately 84,000 square foot concrete structure located on a five acre site. It was custom built as a pharmaceutical R&D and manufacturing facility in August 1995. Activities in this facility include the manufacture of EXPAREL bulk pharmaceutical product candidate in a dedicated production line and its fill/finish into vials, microbiological and quality control testing, product storage, development of analytical methods, research and development, the coordination of clinical and regulatory functions, and general administrative functions. To date, the bulk manufacturing of all EXPAREL product sold to the marketplace has occurred in a manufacturing line housed in what we refer to as Suite A. We are currently working to expand our manufacturing capacity and anticipate receiving FDA approval for our newly installed manufacturing line, referred to as Suite C, in the second quarter of 2014. Combined with Suite A, we expect Suite C to significantly increase our manufacturing capacity and ability to meet the growing demand for EXPAREL. We plan to further expand our manufacturing capacity either directly or through

third parties as demand for EXPAREL increases.

Building 6 is located in a 17-acre pharmaceutical industrial park. It is a two story concrete masonry structure built in 1977 that we and our predecessors have leased since August 1993. We occupy approximately 22,000 square feet of the first floor. Building 6 houses the current manufacturing process for DepoCyt(e), the fill/finish of DepoCyt(e) into vials, a pilot plant suite for new product development and early stage clinical product production, a microbiology laboratory and miscellaneous support and maintenance areas.

Table of Contents

Distribution of our DepoFoam products, including EXPAREL, requires cold-chain distribution, whereby a product must be maintained between specified temperatures. We have validated processes for continuous monitoring of temperature from manufacturing through delivery to the end-user. We and our partners utilize similar cold-chain processes for DepoCyt(e).

Intellectual Property and Exclusivity

We seek to protect our product candidates and our technology through a combination of patents, trade secrets, proprietary know-how, regulatory exclusivity and contractual restrictions on disclosure.

Patents and Patent Applications

We seek to protect the proprietary position of our product candidates by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development of our business. As of December 31, 2013, there are over 14 families of patents and patent applications relating to various aspects of the DepoFoam delivery technology. Patents have been issued in numerous countries, with an emphasis on the North American, European and Japanese markets. These patents generally have a term of 20 years from the date of the nonprovisional filing unless referring to an earlier filed application. Some of our U.S. patents have a term from 17 years from the grant date. Our issued patents expire at various dates in the future, with the last currently issued patent expiring in 2019.

In regards to patents providing protection for EXPAREL, issued patents in the United States relating to the composition of the product candidate and methods for modifying the rate of drug release of the product candidate expire in September 2018 and January 2017, respectively. A patent relating to compositions including EXPAREL, but not EXPAREL specifically, expired in November 2013. Pending U.S. applications relating to the composition of the product candidate and the process for making the product candidate, if granted, would expire in September 2018 and November 2018, respectively. In Europe, granted patents related to the composition of the product candidate expire in November 2014 and September 2018. Pending applications in Europe relating to methods of modifying the rate of drug release of the product candidate and the process for making the product candidate, if granted, would expire in January 2018 and November 2018, respectively. In April 2010, a provisional patent was filed relating to a new process to manufacture EXPAREL and other DepoFoam-based products. The process offers many advantages to the current process, including larger scale production and lower manufacturing costs. In April 2011, we filed a non-provisional patent application which, if granted, could prevent others from using this process until 2031. Furthermore, a non-exclusively licensed patent of ours relating to EXPAREL was allowed in Europe with an expiration date in October 2021 and was extended in the United States until October 2023.

Trade Secrets and Proprietary Information

Trade secrets play an important role in protecting DepoFoam-based products and provide protection beyond patents and regulatory exclusivity. The scale-up and commercial manufacture of DepoFoam products involves processes, custom equipment and in-process and release analytical techniques that we believe are unique to us. The expertise and knowledge required to understand the critical aspects of DepoFoam manufacturing steps requires knowledge of both traditional and non-traditional emulsion processing and traditional pharmaceutical production, overlaid with all of the challenges presented by aseptic manufacturing. We seek to protect our proprietary information, including our trade secrets and proprietary know-how, by requiring our employees, consultants and other advisors to execute proprietary information and confidentiality agreements upon the commencement of their employment or engagement. These agreements generally provide that all confidential information developed or made known during the course of the relationship with us be kept confidential and not be disclosed to third parties except in specific circumstances. In the case of our employees, the agreements also typically provide that all inventions resulting from work performed for us, utilizing our property or relating to our business and conceived or completed during employment shall be our exclusive property to the extent permitted by law. Where appropriate, agreements we obtain with our consultants also typically contain similar assignment of invention obligations. Further, we require confidentiality agreements from third parties that receive our confidential data or materials.

Competition

The pharmaceutical and biotechnology industries are intensely competitive and subject to rapid and significant technological change. Our competitors include organizations such as major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies and generic drug companies. Many of our competitors have greater financial and other resources than we have, such as more commercial resources, larger research and development staffs and more extensive marketing and manufacturing organizations. As a result, these companies may obtain marketing approval more rapidly than we are able and may be more effective in selling and marketing their products. Smaller

Table of Contents

or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies.

Our competitors may succeed in developing, acquiring or licensing on an exclusive basis technologies and drug products that are more effective or less costly than EXPAREL or any other products that we are currently selling through partners or developing or that we may develop, which could render our products obsolete and noncompetitive. We expect any products that we develop and commercialize to compete on the basis of, among other things, efficacy, safety, convenience of administration and delivery, price and the availability of reimbursement from government and other third-party payers. We also expect to face competition in our efforts to identify appropriate collaborators or partners to help commercialize our product candidates in our target commercial markets.

EXPAREL is competing with elastomeric pump/catheter devices intended to provide bupivacaine over several days. I-FLOW Corporation (acquired by Kimberly-Clark Corporation in 2009) has marketed these medical devices in the United States since 2004. In addition, we anticipate that EXPAREL will compete with currently marketed bupivacaine and opioid analgesics such as morphine.

Government Regulation

Federal Food, Drug and Cosmetic Act

Prescription drug products are subject to extensive pre- and post-market regulation by the FDA, including regulations that govern the testing, manufacturing, distribution, safety, efficacy, approval, labeling, storage, record keeping, reporting, advertising and promotion of such products under the Federal Food, Drug and Cosmetic Act, or FDCA, and its implementing regulations, and by comparable agencies and laws in foreign countries. Failure to comply with applicable FDA or other regulatory requirements may result in, among other things, warning letters, clinical holds, civil or criminal penalties, recall or seizure of products, injunction, debarment, partial or total suspension of production or withdrawal of the product from the market. The FDA must approve any new drug, including a new dosage form or new use of a previously approved drug, prior to marketing in the United States. All applications for FDA approval must contain, among other things, information relating to safety and efficacy, pharmaceutical formulation, stability, manufacturing, processing, packaging, labeling and quality control.

New Drug Applications

Generally, the FDA must approve any new drug before marketing of the drug occurs in the United States. This process generally involves:

- completion of preclinical laboratory and animal testing and formulation studies in compliance with the FDA's Good Laboratory Practice, or GLP, regulations;

- submission to the FDA of an IND application for human clinical testing, which must become effective before human clinical trials may begin in the United States;

- approval by an independent institutional review board, or IRB, at each clinical trial site before each trial may be initiated;

- performance of human clinical trials, including adequate and well-controlled clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each intended use;

- submission of an NDA to the FDA;

- satisfactory completion of an FDA pre-approval inspection of the product's manufacturing facility or facilities to assess compliance with the FDA's cGMP regulations, and to ensure that the facilities, methods and controls are adequate to preserve the drug's identity, quality and purity;

- satisfactory completion of an FDA advisory committee review, if applicable; and

- approval by the FDA of the NDA.

13

Table of Contents

The preclinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that the FDA will grant approvals for any of our product candidates on a timely basis, if at all. Preclinical tests include laboratory evaluation of product chemistry, formulation and stability, as well as studies to evaluate toxicity in animals. The results of preclinical tests, together with manufacturing information, analytical data and a proposed clinical trial protocol and other information, are submitted as part of an IND application to the FDA. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, places the trial on a clinical hold because of, among other things, concerns about the conduct of the clinical trial or about exposure of human research subjects to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Our submission of an IND may not result in FDA authorization to commence a clinical trial. In addition, the FDA requires to amend an existing IND for each successive clinical trial conducted during product development. Further, an independent institutional review board, or IRB, covering each medical center proposing to conduct the clinical trial must review and approve the plan for any clinical trial and informed consent information for subjects before the clinical trial commences at that center, and it must monitor the clinical trial until completed. The FDA, the IRB or the sponsor may suspend a clinical trial at any time, or from time to time, on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. For purposes of an NDA submission and approval, typically, the conduct of human clinical trials occurs in the following three pre-market sequential phases, which may overlap:

- Phase 1: sponsors initially conduct clinical trials in a limited population to test the product candidate for safety, dose tolerance, absorption, metabolism, distribution and excretion in healthy humans or, on occasion, in patients, such as cancer patients.

- Phase 2: sponsors conduct clinical trials generally in a limited patient population to identify possible adverse effects and safety risks, to determine the efficacy of the product for specific targeted indications and to determine dose tolerance and optimal dosage. Sponsors may conduct multiple Phase 2 clinical trials to obtain information prior to beginning larger and more extensive Phase 3 clinical trials.

- Phase 3: these include expanded controlled and uncontrolled trials, including pivotal clinical trials. When Phase 2 evaluations suggest the effectiveness of a dose range of the product and acceptability of such product's safety profile, sponsors undertake Phase 3 clinical trials in larger patient populations to obtain additional information needed to evaluate the overall benefit and risk balance of the drug and to provide an adequate basis to develop labeling.

In addition, sponsors may elect to conduct, or be required by the FDA to conduct, post-approval clinical trials to further assess the drug's safety or effectiveness after NDA approval. Such post approval trials are typically referred to as Phase 4 clinical trials.

Sponsors submit the results of product development, preclinical studies and clinical trials to the FDA as part of an NDA. NDAs must also contain extensive information relating to the product's pharmacology, chemistry, manufacture, controls and proposed labeling, among other things. In addition, 505(b)(2) applications must contain a patent certification for each patent listed in FDA's "Orange Book" that covers the drug referenced in the application and upon which the third-party studies were conducted. For some drugs, the FDA may require risk evaluation and mitigation strategies, or REMS, which could include medication guides, physician communication plans, or restrictions on distribution and use, such as limitations on who may prescribe the drug or where it may be dispensed or administered. Upon receipt, the FDA has 60 days to determine whether the NDA is sufficiently complete to initiate a substantive review. If the FDA identifies deficiencies that would preclude substantive review, the FDA will refuse to accept the NDA and will inform the sponsor of the deficiencies that must be corrected prior to resubmission. If the FDA accepts the submission for substantive review, the FDA typically reviews the NDA in accordance with established

timeframes. Under PDUFA, the FDA agrees to specific goals for NDA review time through a two-tiered classification system, Priority Review and Standard Review. A Priority Review designation is given to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists. For a Priority Review application, the FDA aims to complete the initial review cycle for New Molecular Entities , or NMEs, within six months of the 60 day filing date, and for Non-NMEs within six months of the date of receipt. Standard Review applies to all applications that are not eligible for Priority Review. The FDA aims to complete Standard Review NDAs for NMEs within ten-months of the 60 day filing date, and for Non-NMEs within ten months of the date of receipt. Review processes often extend significantly beyond anticipated completion dates due to FDA requests for additional information or clarification, difficulties scheduling an advisory committee meeting, negotiations regarding REMS, or FDA workload issues. The FDA may refer the application to an advisory committee

Table of Contents

for review, evaluation and recommendation as to the application's approval. The recommendations of an advisory committee do not bind the FDA, but the FDA generally follows such recommendations.

Under PDUFA, NDA applicants must pay significant NDA user fees upon submission. In addition, manufacturers of approved prescription drug products must pay annual establishment and product user fees.

Before approving an NDA, the FDA may inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and are adequate to ensure consistent production of the product within required specifications. Additionally, the FDA will typically inspect one or more clinical sites to ensure compliance with GCP before approving an NDA.

After the FDA evaluates the NDA and the manufacturing facilities, it may issue an approval letter or a Complete Response Letter, or CRL, to indicate that the review cycle for an application is complete and that the application is not ready for approval. CRLs generally outline the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. Even if such additional information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data from clinical trials are not always conclusive and the FDA may interpret data differently than we do. The FDA could also require a REMS plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling, a commitment to conduct one or more post-market studies or clinical trials and the correction of identified manufacturing deficiencies, including the development of adequate controls and specifications. If and when the deficiencies have been addressed to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Section 505(b)(2) New Drug Applications

As an alternate path to FDA approval, particularly for modifications to drug products previously approved by the FDA, an applicant may submit an NDA under Section 505(b)(2) of the FDCA. Section 505(b)(2) was enacted as part of the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, and permits the submission of an NDA where at least some of the information required for approval comes from clinical trials not conducted by or for the applicant and for which the applicant has not obtained a right of reference. The FDA interprets Section 505(b)(2) of the FDCA to permit the applicant to rely upon the FDA's previous findings of safety and effectiveness for an approved product. The FDA may also require companies to perform additional clinical trials or measurements to support any change from the previously approved product. The FDA may then approve the new product candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

Section 505(b)(2) applications are subject to any non-patent exclusivity period applicable to the referenced product, which may delay approval of the 505(b)(2) application even if FDA has completed its substantive review and determined the drug should be approved. In addition, 505(b)(2) applications must include patent certifications to any patents listed in the Orange Book as covering the referenced product. If the 505(b)(2) applicant seeks to obtain approval before the expiration of an applicable listed patent, the 505(b)(2) applicant must provide notice to the patent owner and NDA holder of the referenced product. If the patent owner or NDA holder bring a patent infringement lawsuit within 45 days of such notice, the 505(b)(2) application cannot be approved for 30 months or until the 505(b)(2) applicant prevails, whichever is sooner. If the 505(b)(2) applicant loses the patent infringement suit, FDA may not approve the 505(b)(2) application until the patent expires, plus any period of pediatric exclusivity.

In the NDA submissions for our product candidates, we intend to follow the development and approval pathway permitted under the FDCA that we believe will maximize the commercial opportunities for these product candidates.

Post-Approval Requirements

After approval, the NDA sponsor must comply with comprehensive requirements governing, among other things, drug listing, recordkeeping, manufacturing, marketing activities, product sampling and distribution, annual reporting and adverse event reporting. There are also extensive U.S. Drug Enforcement Agency, or DEA, regulations applicable to marketed controlled substances.

If new safety issues are identified following approval, the FDA can require the NDA sponsor to revise the approved labeling to reflect the new safety information; conduct post-market studies or clinical trials to assess the new safety

Table of Contents

information; and implement a REMS program to mitigate newly-identified risks. The FDA may also require post-approval testing, including Phase 4 studies, and surveillance programs to monitor the effect of approved products which have been commercialized, and the FDA has the authority to prevent or limit further marketing of a product based on the results of these post-marketing programs. Drugs may be marketed only for approved indications and in accordance with the provisions of the approved label. Further, if we modify a drug, including any changes in indications, labeling or manufacturing processes or facilities, the FDA may require us to submit and obtain FDA approval of a new or supplemental NDA, which may require us to develop additional data or conduct additional preclinical studies and clinical trials.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and any third-party manufacturers that we may decide to use.

If after approval the FDA determines that the product does not meet applicable regulatory requirements or poses unacceptable safety risks, the FDA may take other regulatory actions, including initiating suspension or withdrawal of the NDA approval. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. These regulations include standards and restrictions for direct-to-consumer advertising, industry-sponsored scientific and educational activities, promotional activities involving the internet, and off-label promotion. While physicians may prescribe for off-label uses, manufacturers may only promote for the approved indications and in accordance with the provisions of the approved label. The FDA has very broad enforcement authority under the FDCA, and failure to abide by these regulations can result in penalties, including the issuance of a warning letter directing entities to correct deviations from FDA standards, a requirement that future advertising and promotional materials be pre-cleared by the FDA, and state and federal civil and criminal investigations and prosecutions.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution, including a drug pedigree which tracks the distribution of prescription drugs.

International Regulation

In addition to regulations in the United States, we are subject to a variety of foreign regulations governing clinical trials and the commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of foreign countries before we can

commence clinical trials or marketing of the product in those countries. The approval process varies from country to country, and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country.

Table of Contents

For example, in the European Economic Area, or EEA (which is comprised of the 27 Member States of the EU plus Norway, Iceland and Liechtenstein), medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations:

- The Community MA, which is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the EMA, and which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, and medicinal products containing a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA (the Reference Member State, or RMS), this National MA can be recognized in other Member States (the Concerned Member States, or CMS) through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure, an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the RMS. The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics, or SPC, and a draft of the labeling and package leaflet, which are sent to the CMS for their approval. If the CMS raise no objections, based on a potential serious risk to public health, to the assessment, SPC, labeling, or packaging proposed by the RMS, the product is subsequently granted a national MA in all the Member States (i.e. in the RMS and the CMS). If one or more CMS raise objections based on a potential serious risk to public health, the application is referred to the Coordination group for Mutual recognition and Decentralized procedure for human medicinal products, or CMDh, which is composed of representatives of the EEA Member States. If a consensus cannot be reached within the CMDh the matters is referred for arbitration to the CHMP, which can reach a final decision binding on all EEA Member States. A similar process applies to disputes between the RMS and the CMS in the Mutual Recognition Procedure.

As with FDA approval, we may not be able to secure regulatory approvals in Europe in a timely manner, if at all. Additionally, as in the United States, post-approval regulatory requirements, such as those regarding product manufacture, marketing, or distribution, would apply to any product that is approved in Europe, and failure to comply with such obligations could have a material adverse effect on our ability to successfully commercialize any product.

The conduct of clinical trials in the EU is governed by the EU Clinical Trials Directive (Directive 2001/20/EC of 4 April 2001, of the European Parliament and of the Council on the approximation of the laws, regulations and administrative provisions of the Member States relating to implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use). The provisions of the EU Clinical Trials Directive were required to be implemented and applied by the EEA Member States before May 2004. The EU Clinical Trials Directive harmonizes the regulatory requirements of the Member States of the EEA for the conduct of clinical trials in their respective territories. The EU Clinical Trials Directive requires sponsors of clinical trials to submit formal applications to, and to obtain the approval of, national ethics committees and regulatory authorities prior to the initiation of clinical trials.

In addition to regulations in Europe and the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial distribution of any future products.

Third Party Payer Coverage and Reimbursement

The commercial success of our products and product candidates will depend, in part, upon the availability of coverage and reimbursement from third-party payers at the federal, state and private levels. Government payer programs, including Medicare and Medicaid, private health care insurance companies and managed care plans may deny

coverage or reimbursement for a product or therapy in whole or in part if they determine that the product or therapy is not medically appropriate or necessary. Also, third-party payers have attempted to control costs by limiting coverage and the amount of reimbursement for particular procedures or drug treatments. The United States Congress and state legislatures from time to time propose and adopt

Table of Contents

initiatives aimed at cost containment, which could impact our ability to sell our products at a price level high enough to realize an appropriate return on our investment.

For example, in March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, which we refer to collectively as the Health Care Reform Law, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. The Health Care Reform Law revised the definition of "average manufacturer price" for reporting purposes, which could increase the amount of Medicaid drug rebates owed to states by pharmaceutical manufacturers for covered outpatient drugs. The Health Reform Law also established a new Medicare Part D coverage gap discount program, in which drug manufacturers must provide 50% point-of-sale discounts on products covered under Part D beginning in 2011. Further, also beginning in 2011, the new law imposed a significant annual, nondeductible fee on companies that manufacture or import branded prescription drug products. Substantial new provisions affecting compliance have also been enacted, which may require us to modify our business practices with healthcare practitioners. Some details of the Health Care Reform Law are yet to be determined, as applicable federal and state agencies must issue regulations or guidance under the new law. Although it is too early to determine the effect of the Health Care Reform Law, the new law appears likely to continue the pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs. Moreover, in the coming years, additional changes could be made to governmental healthcare programs that could significantly impact the success of our products.

In addition, other legislative changes have been proposed and adopted since the Health Care Reform Law was enacted, which could result in reductions in Medicare payments to providers. The full impact on our business of these legislative actions is uncertain. Nor is it clear whether other legislative changes will be adopted, if any, or how such changes would affect the demand for our products.

The cost of pharmaceuticals continues to generate substantial governmental and third-party payer interest. We expect that the pharmaceutical industry will experience pricing pressures due to the trend toward managed healthcare, the increasing influence of managed care organizations and additional legislative proposals. Our results of operations could be adversely affected by current and future healthcare reforms. Ongoing federal and state government initiatives directed at lowering the total cost of health care will likely continue to focus on health care reform, the cost of prescription pharmaceuticals and on the reform of the Medicare and Medicaid payment systems. Examples of how limits on drug coverage and reimbursement in the United States may cause reduced payments for drugs in the future include:

- changing Medicare reimbursement methodologies;
- fluctuating decisions on which drugs to include in formularies;
- revising covered outpatient drug rebate calculations under the Medicaid program; and
- reforming drug importation laws.

Some third-party payers also require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers that use such therapies or place limits on the amount of reimbursement. While we cannot predict whether any proposed cost-containment measures will be adopted or otherwise implemented in the future, the announcement or adoption of these proposals could have a material adverse effect on our ability to obtain adequate prices for our product candidates and to operate at a reasonable return on investment.

In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. There can be no assurance that our products will be considered medically reasonable and necessary for a specific indication, that our products will be considered cost-effective by third-party payers, or that an adequate level or reimbursement will be available so that the third-party

payers' reimbursement policies will not adversely affect our ability to sell our products profitably.

Marketing/Data Exclusivity

The FDA may grant three or five years of marketing exclusivity in the United States for the approval of new or supplemental NDAs, including Section 505(b)(2) NDAs, for, among other things, new indications, dosages or dosage forms of an existing drug, if new clinical investigations that were conducted or sponsored by the applicant are essential to the approval

Table of Contents

of the application. Additionally, six months of marketing exclusivity in the United States is available under Section 505A of the FDCA if, in response to a written request from the FDA, a sponsor submits and the agency accepts requested information relating to the use of the approved drug in the pediatric population. This six month pediatric exclusivity period is not a standalone exclusivity period, but rather is added to any existing patent or non-patent exclusivity period for which the drug product is eligible. Based on our clinical trial program for EXPAREL, FDA granted three years of marketing exclusivity to EXPAREL, which expires on October 28, 2014.

Manufacturing Requirements

We must comply with applicable FDA regulations relating to the FDA's cGMP regulations. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and drug product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports, and returned or salvaged products. The manufacturing facilities for our products must meet cGMP requirements to the satisfaction of the FDA pursuant to a pre-approval inspection before we can use them to manufacture our products. We and any third-party manufacturers are also subject to periodic inspections of facilities by the FDA and other authorities, including procedures and operations used in the testing and manufacture of our products to assess our compliance with applicable regulations. Failure to comply with these and other statutory and regulatory requirements subjects a manufacturer to possible legal or regulatory action, including warning letters, the seizure or recall of products, injunctions, consent decrees placing significant restrictions on or suspending manufacturing operations and civil and criminal penalties. Adverse experiences with the product must be reported to the FDA and could result in the imposition of market restrictions through labeling changes or in product removal. Product approvals may be withdrawn if compliance with regulatory requirements is not maintained or if problems concerning safety or efficacy of the product occur following approval.

Healthcare Fraud and Abuse Laws

We are subject to various federal, state and local laws targeting fraud and abuse in the healthcare industry. For example, in the United States, there are federal and state anti-kickback laws that prohibit the offer, payment or receipt of kickbacks, bribes or other remuneration intended to induce the purchase or recommendation of healthcare products and services or reward purchases or recommendations. Violations of these laws can lead to civil and criminal penalties, including fines, imprisonment and exclusion from participation in federal healthcare programs. These laws are potentially applicable to manufacturers of products regulated by the FDA and reimbursed by federal healthcare programs, such as us, and to hospitals, physicians and other potential purchasers of such products.

In particular, the federal Anti-Kickback Statute prohibits persons from knowingly and willfully soliciting, receiving, offering or providing remuneration, directly or indirectly, to induce either the referral of an individual, or the furnishing, recommending, or arranging for a good or service, for which payment may be made under a federal healthcare program such as the Medicare and Medicaid programs. The term "remuneration" is not defined in the federal Anti-Kickback Statute and has been broadly interpreted to include anything of value, including gifts, discounts, the provision of goods and services, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payments, ownership interests and providing anything at less than its fair market value. In addition, the Health Care Reform Law, among other things, amends the intent requirement of the federal Anti-Kickback Statute and the applicable criminal healthcare fraud statutes contained within 42 U.S.C. § 1320a-7b. Pursuant to the statutory amendment, a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the Health Care Reform Law provides that the federal government may assert that a reimbursement claim for items or services resulting from a violation of 42 U.S.C. § 1320a-7b constitutes a false or fraudulent claim for purposes of the civil False Claims Act (discussed below) or the civil monetary penalties statute, which imposes a penalty of $5,000 against any person who is determined to have presented or caused to be presented claims to a federal health care program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. Moreover, the lack of uniform court interpretation of the Anti-Kickback Statute makes compliance with the law difficult.

Recognizing that the federal Anti-Kickback Statute is broad and may prohibit innocuous or beneficial arrangements within the healthcare industry, the statute establishes certain exemptions from the statutory prohibition and authorizes additional exemptions by regulation. Pursuant to this authority, the U.S. Department of Health and Human Services'

Office of Inspector General, or OIG, issued regulations in July of 1991, and periodically since that time, which the OIG refers to as “safe harbors.” These safe harbor regulations set forth certain provisions which, if met in form and substance, will assure pharmaceutical companies, healthcare providers and other parties that they will not be prosecuted under the federal Anti-Kickback Statute. Although full compliance with these provisions ensures against prosecution under the federal Anti-Kickback Statute, the failure of a transaction or arrangement to fit within a specific safe harbor does not necessarily mean that the transaction or arrangement is illegal or that prosecution under the federal Anti-Kickback Statute will be pursued. However,

Table of Contents

conduct and business arrangements that do not fully satisfy an applicable safe harbor may result in increased scrutiny by government enforcement authorities, such as the OIG or federal prosecutors. Additionally, there are certain statutory exceptions to the federal Anti-Kickback Statute, one or more of which could be used to protect a business arrangement, although we understand that OIG is of the view that an arrangement that does not meet the requirements of a regulatory safe harbor does not satisfy the corresponding statutory exception, if any, under the federal Anti-Kickback Statute.

Additionally, many states have adopted laws similar to the federal Anti-Kickback Statute. Some of these state prohibitions apply to referral of patients for healthcare items or services reimbursed by any third-party payer, not only the Medicare and Medicaid programs, and do not contain identical safe harbors. Government officials have focused their enforcement efforts on marketing of healthcare services and products, among other activities, and have brought cases against numerous pharmaceutical and medical device companies, and certain sales and marketing personnel for allegedly offering unlawful inducements to potential or existing customers in an attempt to procure their business or reward past purchases or recommendations.

Another development affecting the healthcare industry is the increased use of the federal civil False Claims Act and, in particular, actions brought pursuant to the False Claims Act's "whistleblower" or "qui tam" provisions. The civil False Claims Act imposes liability on any person or entity who, among other things, knowingly presents, or causes to be presented, a false or fraudulent claim for payment by a federal healthcare program. The qui tam provisions of the False Claims Act allow a private individual to bring civil actions on behalf of the federal government alleging that the defendant has submitted a false claim to the federal government, and to share in any monetary recovery. In recent years, the number of suits brought by private individuals has increased dramatically. In addition, various states have enacted false claim laws analogous to the False Claims Act. When an entity is determined to have violated the False Claims Act, it may be required to pay up to three times the actual damages sustained by the government, plus civil penalties of $5,500 to $11,000 for each separate false claim. There are many potential bases for liability under the False Claims Act. Liability arises, primarily, when an entity knowingly submits, or causes another to submit, a false claim for reimbursement to the federal government. The False Claims Act has been used to assert liability on the basis of inadequate care, kickbacks and other improper referrals, improperly reported government pricing metrics such as Best Price or Average Manufacturer Price, improper use of Medicare numbers when detailing the provider of services, improper promotion of off-label uses (i.e., uses not expressly approved by the FDA in a drug's label), and allegations as to misrepresentations with respect to the services rendered. Our activities relating to the reporting of discount and rebate information and other information affecting federal, state and third-party reimbursement of our products, and the sale and marketing of our products and our service arrangements or data purchases, among other activities, may be subject to scrutiny under these laws. We are unable to predict whether we would be subject to actions under the False Claims Act or a similar state law, or the impact of such actions. However, the cost of defending such claims, as well as any sanctions imposed, could adversely affect our financial performance.

Also, the Health Insurance Portability and Accountability Act of 1996, or HIPAA, created several new federal crimes, including health care fraud, and false statements relating to health care matters. The health care fraud statute prohibits knowingly and willfully executing a scheme to defraud any health care benefit program, including private third-party payers. The false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for health care benefits, items or services.

In addition, under California law, pharmaceutical companies must adopt a comprehensive compliance program that is in accordance with both the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers, or OIG Guidance, and the Pharmaceutical Research and Manufacturers of America Code on Interactions with Healthcare Professionals, or the PhRMA Code. The PhRMA Code seeks to promote transparency in relationships between health care professionals and the pharmaceutical industry and to ensure that pharmaceutical marketing activities comport with the highest ethical standards. The PhRMA Code contains strict limitations on certain interactions between health care professionals and the pharmaceutical industry relating to gifts, meals, entertainment and speaker programs, among others. Also, certain states, such as Massachusetts, Minnesota, Vermont and others, have imposed restrictions on the types of interactions that pharmaceutical and medical device

companies or their agents (e.g., sales representatives) may have with health care professionals, including bans or strict limitations on the provision of meals, entertainment, hospitality, travel and lodging expenses, and other financial support, including funding for continuing medical education activities.

Healthcare Privacy and Security Laws

We may be subject to, or our marketing activities may be limited by, HIPAA, and its implementing regulations, which established uniform standards for certain “covered entities” (healthcare providers, health plans and healthcare clearinghouses) governing the conduct of certain electronic healthcare transactions and protecting the security and privacy of protected health

Table of Contents

information. The American Recovery and Reinvestment Act of 2009, commonly referred to as the economic stimulus package, included sweeping expansion of HIPAA's privacy and security standards called the Health Information Technology for Economic and Clinical Health Act, or HITECH, which became effective on February 17, 2010. Among other things, the new law makes HIPAA's privacy and security standards directly applicable to "business associates"-independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions.

Environmental Matters

Our research and development processes and our manufacturing processes involve the controlled use of hazardous materials, chemicals and produce waste products. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of hazardous materials and waste products. We do not expect the cost of complying with these laws and regulations to be material. While we believe we are in compliance with applicable environmental regulations, the failure to fully comply with any such regulations could result in the imposition of penalties, fines and/or sanctions which could have a material adverse effect on our business.

Employees

As of December 31, 2013, we had 310 employees, of which two were part-time. All of our employees are located in the United States. None of our employees are represented by a labor union, and we consider our current employee relations to be good.

Available Information

We file reports and other information with the SEC as required by the Exchange Act. We make available free of charge through our website (http://www.pacira.com) our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act. We make these reports available through our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the SEC. In addition, we regularly use our website to post information regarding our business, product development programs and governance, and we encourage investors to use our website, particularly the information in the section entitled "Investors & Media," as a source of information about us. The foregoing references to our website are not intended to, nor shall they be deemed to, incorporate information on our website into this Annual Report on Form 10-K by reference.

Item 1A. Risk Factors

In addition to the other information in this Annual Report on Form 10-K, any of the factors set forth below could significantly and negatively affect our business, financial condition, results of operations or prospects. The trading price of our common stock may decline due to these risks. This section contains forward-looking statements. You should refer to the explanation of the qualifications and limitations on forward-looking statements beginning on page 1.

Risks Related to the Development and Commercialization of Our Product Candidates

Our success depends on our ability to successfully commercialize EXPAREL.

We have invested a significant portion of our efforts and financial resources in the development and commercialization of our lead product, EXPAREL, which was approved by the FDA on October 28, 2011 and commercially launched in April 2012. During 2013, sales of EXPAREL constituted a significant portion of our total revenue, and our success depends on our ability to continue to effectively commercialize EXPAREL. Our ability to effectively generate revenues from EXPAREL will depend on our ability to, among other things:

- create market demand for EXPAREL through our marketing and sales activities and other arrangements established for the promotion of EXPAREL;
- train, deploy and support a qualified sales force;
- secure formulary approvals for EXPAREL at a substantial number of targeted hospitals;
- manufacture EXPAREL in sufficient quantities in compliance with requirements of the FDA and similar foreign regulatory agencies and at acceptable quality and pricing levels in order to meet commercial demand;

21

Table of Contents

- implement and maintain agreements with wholesalers, distributors and group purchasing organizations on commercially reasonable terms;
- receive adequate levels of coverage and reimbursement for EXPAREL from commercial health plans and governmental health programs;
- maintain compliance with regulatory requirements;
- obtain regulatory approvals for additional indications for the use of EXPAREL;
- ensure that our entire supply chain efficiently and consistently delivers EXPAREL to our customers; and
- maintain and defend our patent protection and regulatory exclusivity for EXPAREL.

Any disruption in our ability to generate revenues from the sale of EXPAREL will have a material and adverse impact on our results of operations.

Our efforts to successfully commercialize EXPAREL are subject to many internal and external challenges and if we cannot overcome these challenges in a timely manner, our future revenues and profits could be materially and adversely impacted.

EXPAREL has been a marketed drug for less than two years. As a result, we continue to expend significant time and resources to train the sales force to be credible and persuasive in convincing physicians and hospitals to use EXPAREL. In addition, we also must train the sales force to ensure that a consistent and appropriate message about EXPAREL is delivered to our potential customers. If we are unable to effectively train the sales force and equip them with effective materials, including medical and sales literature to help them inform and educate potential customers about the benefits and risks of EXPAREL and its proper administration, our efforts to successfully commercialize EXPAREL could be put in jeopardy, which could have a material adverse effect on our future revenues and profits.

In addition to our extensive internal efforts, the successful commercialization of EXPAREL will require many third parties, over whom we have no control, to choose to utilize EXPAREL. These third parties include physicians and hospital pharmacy and therapeutics committees, which we refer to as P&T committees. Generally, before we can attempt to sell EXPAREL in a hospital, EXPAREL must be approved for addition to that hospital's list of approved drugs, or formulary list, by the hospital's P&T committee. A hospital's P&T committee typically governs all matters pertaining to the use of medications within the institution, including the review of medication formulary data and recommendations for the appropriate use of drugs within the institution to the medical staff. The frequency of P&T committee meetings at hospitals varies considerably, and P&T committees often require additional information to aid in their decision-making process. Therefore, we may experience substantial delays in obtaining formulary approvals. Additionally, hospital pharmacists may be concerned that the cost of acquiring EXPAREL for use in their institutions will adversely impact their overall pharmacy budgets, which could cause pharmacists to resist efforts to add EXPAREL to the formulary, or to implement restrictions on the usage of EXPAREL in order to control costs. We cannot guarantee that we will be successful in obtaining the approvals we need from enough P&T committees quickly enough to optimize hospital sales of EXPAREL.

Even if we obtain hospital formulary approval for EXPAREL, physicians must still prescribe EXPAREL for its commercialization to be successful. Because EXPAREL is a relatively new drug with a limited track record of sales in the United States, any inability to timely supply EXPAREL to our customers, or any unexpected side effects that develop from use of the drug, particularly early in product launch, may lead physicians to not accept EXPAREL as a viable treatment alternative.

If EXPAREL does not achieve broad market acceptance, the revenues that we generate from its sales will be limited. The degree of market acceptance of EXPAREL also depends on a number of other factors, including:

- changes in the standard of care for the targeted indications for EXPAREL, which could reduce the marketing impact of any claims that we can make;
- the relative efficacy, convenience and ease of administration of EXPAREL;
- the prevalence and severity of adverse events associated with EXPAREL;
- cost of treatment versus economic and clinical benefit, both in absolute terms and in relation to alternative treatments;
- the availability of adequate coverage or reimbursement by third parties, such as insurance companies and other healthcare payers, and by government healthcare programs, including Medicare and Medicaid;
- the extent and strength of our marketing and distribution of EXPAREL;

- the safety, efficacy and other potential advantages over, and availability of, alternative treatments, including, in the case of EXPAREL, a number of products already used to treat pain in the hospital setting; and
- distribution and use restrictions imposed by the FDA or to which we agree as part of a mandatory risk evaluation and mitigation strategy or voluntary risk management plan.

Our ability to effectively promote and sell EXPAREL and any product candidates that we may develop, license or acquire in the hospital marketplace will also depend on pricing and cost effectiveness, including our ability to produce a product at a competitive price and therefore achieve acceptance of the product onto hospital formularies, and our ability to obtain sufficient third-party coverage or reimbursement. Since many hospitals are members of group purchasing organizations, which leverage

Table of Contents

the purchasing power of a group of entities to obtain discounts based on the collective buying power of the group, our ability to attract customers in the hospital marketplace will also depend on our ability to effectively promote our product candidates to group purchasing organizations. We will also need to demonstrate acceptable evidence of safety and efficacy, as well as relative convenience and ease of administration. Market acceptance could be further limited depending on the prevalence and severity of any expected or unexpected adverse side effects associated with our product candidates.

In addition, the labeling approved by the FDA does not contain claims that EXPAREL is safer or more effective than competitive products and does not permit us to promote EXPAREL as being superior to competing products. Further, the availability of inexpensive generic forms of postsurgical pain management products may also limit acceptance of EXPAREL among physicians, patients and third-party payers. If EXPAREL does not achieve an adequate level of acceptance among physicians, patients and third-party payers, we may not generate meaningful revenues from EXPAREL and we may not become profitable.

We face significant competition from other pharmaceutical and biotechnology companies. Our operating results will suffer if we fail to compete effectively.

The pharmaceutical and biotechnology industries are intensely competitive and subject to rapid and significant technological change. Our major competitors include organizations such as major multinational pharmaceutical companies, established biotechnology companies and specialty pharmaceutical and generic drug companies. Many of our competitors have greater financial and other resources than we have, such as larger research and development staff, more extensive marketing, distribution, sales and manufacturing organizations and experience, more extensive clinical trial and regulatory experience, expertise in prosecution of intellectual property rights and access to development resources like personnel and technology. As a result, these companies may obtain regulatory approval more rapidly than we are able to and may be more effective in selling and marketing their products. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Our competitors may succeed in developing, acquiring or licensing on an exclusive basis technologies and drug products that are more effective or less costly than EXPAREL or any product candidate that we are currently developing or that we may develop, which could render our products obsolete and noncompetitive or significantly harm the commercial opportunity for EXPAREL or our product candidates.

As a result of these factors, our competitors may obtain patent protection or other intellectual property rights that may limit our ability to develop other indications for, or commercialize, EXPAREL. Our competitors may also develop drugs that are safer, more effective, useful or less costly than ours and may be more successful than us in manufacturing and marketing their products.

EXPAREL competes with well-established products with similar indications. Competing products available for postsurgical pain management include opioids such as morphine, fentanyl, meperidine and hydromorphone, each of which is available generically from several manufacturers, and several of which are available as proprietary products using novel delivery systems. Ketorolac, an injectable non-steroidal anti-inflammatory drug, or NSAID, is also available generically in the United States from several manufacturers, and Caldolor (ibuprofen for injection), an NSAID, has been approved by the FDA for pain management and fever in adults. In addition, EXPAREL competes with non-opioid products such as bupivacaine, marcaine, ropivacaine and other anesthetics/analgesics, all of which are also used in the treatment of postsurgical pain and are available as either oral tablets, injectable dosage forms or administered using novel delivery systems. Additional products may be developed for the treatment of acute pain, including new injectable NSAIDs, novel opioids, new formulations of currently available opioids and NSAIDs, long-acting local anesthetics and new chemical entities as well as alternative delivery forms of various opioids and NSAIDs.

EXPAREL also competes with elastomeric bag/catheter devices intended to provide bupivacaine over several days. I-FLOW Corporation (acquired by Kimberly-Clark Corporation in 2009) has marketed these medical devices in the United States since 2004.

If we are unable to establish and maintain effective marketing and sales capabilities or enter into agreements with third parties to market and sell EXPAREL, we may be unable to generate product revenues.

We are continuing to build our commercial infrastructure for the marketing, sale and distribution of pharmaceutical products. In order to continue commercializing EXPAREL effectively, we must continue to build our marketing, sales and distribution capabilities. We entered into an agreement with Quintiles for the outsourcing of our specialty sales force, which we then hired as direct employees in January 2013. The establishment, development and training of our sales force and related compliance plans to market EXPAREL is expensive and time consuming. In the event we are not successful in developing our marketing and sales infrastructure, we may not be able to successfully commercialize EXPAREL, which would limit our ability to generate product revenues.

In addition to our internal marketing and sales efforts, we have entered into agreements with third party distributors to promote and sell EXPAREL in certain territories. For example, following a pilot program, effective October 1, 2013, we appointed CrossLink as our exclusive third-party distributor to promote and sell EXPAREL for orthopedic and spine surgeries

Table of Contents

in the U.S., with the exception of certain geographical areas and accounts, for a five year term. We may seek additional distribution arrangements in the future, including arrangements with third party distributors to commercialize and sell EXPAREL in certain foreign countries. The use of distributors involves certain risks, including risks that such distributors will:

- not effectively distribute or support our products;
- not provide us with accurate or timely information regarding their inventories, the number of accounts using our products or complaints about our products;
- fail to comply with their obligations to us;
- fail to comply with laws and regulations to which they are subject, whether in the U.S. or in foreign jurisdictions;
- reduce or discontinue their efforts to sell or promote our products; or
- cease operations.

Any such failure may result in decreased sales, which would have an adverse effect on our business.

We rely on third parties to perform many essential services for EXPAREL and any other products that we commercialize, including services related to customer service support, warehousing and inventory program services, distribution services, contract administration and chargeback processing services, accounts receivable management and cash application services, and financial management and information technology services. If these third parties fail to perform as expected or to comply with legal and regulatory requirements, our ability to commercialize EXPAREL will be significantly impacted and we may be subject to regulatory sanctions.

We have entered into agreements with third-party service providers to perform a variety of functions related to the sale and distribution of EXPAREL, key aspects of which are out of our direct control. These service providers provide key services related to customer service support, warehousing and inventory program services, distribution services, contract administration and chargeback processing services, accounts receivable management and cash application services, and financial management and information technology services. In addition, most of our inventory is stored at a single warehouse maintained by one such service provider. We substantially rely on these providers as well as other third-party providers that perform services for us, including entrusting our inventories of products to their care and handling. If these third-party service providers fail to comply with applicable laws and regulations, fail to meet expected deadlines, or otherwise do not carry out their contractual duties to us, or encounter physical or natural damage at their facilities, our ability to deliver product to meet commercial demand would be significantly impaired. In addition, we may engage third parties to perform various other services for us relating to adverse event reporting, safety database management, fulfillment of requests for medical information regarding our product candidates and related services. If the quality or accuracy of the data maintained by these service providers is insufficient, we could be subject to regulatory sanctions.

Distribution of our DepoFoam-based products, including EXPAREL, requires cold-chain distribution provided by third parties, whereby the product must be maintained between specified temperatures. We and our partners have utilized similar cold-chain processes for DepoCyt(e) and DepoDur. If a problem occurs in our cold-chain distribution processes, whether through our failure to maintain our products or product candidates between specified temperatures or because of a failure of one of our distributors or partners to maintain the temperature of the products or product candidates, the product or product candidate could be adulterated and rendered unusable. We have obtained limited inventory and cargo insurance coverage for our products. However, our insurance coverage may not reimburse us or may not be sufficient to reimburse us for any expenses or losses we may suffer. This could have a material adverse effect on our business, financial condition, results of operations and reputation.

We will need to increase the size of our organization and effectively manage our sales force, and we may experience difficulties in managing growth.

As of December 31, 2013, we had 310 employees. We may need to expand our personnel resources in order to manage our operations and sales of EXPAREL. Our management, personnel, systems and facilities currently in place may not be adequate to support this future growth. In addition, we may not be able to recruit and retain qualified personnel in the future, particularly marketing positions, due to competition for personnel among pharmaceutical businesses, and the failure to do so could have a significant negative impact on our future product revenues and business results. Our need to effectively manage our operations, growth and various projects requires that we:

- continue the hiring and training of an effective commercial organization for the commercialization of EXPAREL, and establish appropriate systems, policies and infrastructure to support that organization;
- continue to establish and maintain effective relationships with distributors and commercial partners for the promotion and sale of our products;
- ensure that our distributors, partners, suppliers, consultants and other service providers successfully carry out their contractual obligations, provide high quality results, and meet expected deadlines;
- manage our development efforts and clinical trials effectively;
- expand our manufacturing capabilities;

Table of Contents

- continue to carry out our own contractual obligations to our licensors and other third parties; and
- continue to improve our operational, financial and management controls, reporting systems and procedures.

We may be unable to successfully implement these tasks on a larger scale and, accordingly, may not achieve our development and commercialization goals. Additionally, these tasks may impose a strain on our administrative and operational infrastructure. If we are unable to effectively manage our growth, our product sales and resulting revenues will be negatively impacted.

We may not be able to manage our business effectively if we are unable to attract and retain key personnel.

We may not be able to attract or retain qualified management and commercial, scientific and clinical personnel due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses, as well as universities, non-profit research organizations and government entities, particularly in the San Diego, California and northern New Jersey areas. If we are not able to attract and retain necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

Our industry has experienced a high rate of turnover of management personnel in recent years. We are highly dependent on the development and manufacturing expertise for our DepoFoam delivery technology and the commercialization expertise of certain members of our senior management. In particular, we are highly dependent on the skills and leadership of our management team, including David Stack, our president, chief executive officer and chairman. If we lose one or more of these key employees, our ability to successfully implement our business strategy could be seriously harmed. Replacing key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize products successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate additional key personnel.

Mr. Stack, our president, chief executive officer and chairman is also a managing director at MPM Capital and a managing partner of Stack Pharmaceuticals, Inc. Although Mr. Stack has devoted substantially all of his business time to our company over the past 12 months, Mr. Stack's responsibilities at MPM Capital and Stack Pharmaceuticals, Inc. might require that he spend less than all his business time managing our company in the future.

Under our consulting agreement with Gary Patou, M.D., our chief medical officer, he is not required to devote all of his business time to our company. We cannot assure you that Dr. Patou's business time commitment to us will be sufficient to perform the duties of our chief medical officer.

We face potential product liability exposure, and if successful claims are brought against us, we may incur substantial liability for DepoCyt(e), EXPAREL or product candidates that we may develop and may have to limit their commercialization.

The use of DepoCyt(e), EXPAREL and any product candidates that we may develop, license or acquire in clinical trials and the sale of any products for which we obtain regulatory approval expose us to the risk of product liability claims. Product liability claims might be brought against us by consumers, health care providers or others using, administering or selling our products. If we cannot successfully defend ourselves against these claims, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- loss of revenue from decreased demand for our products and/or product candidates;
- impairment of our business reputation or financial stability;
- costs of related litigation;
- substantial monetary awards to patients or other claimants;
- diversion of management attention;
- loss of revenues;
- withdrawal of clinical trial participants and potential termination of clinical trial sites or entire clinical programs; and
- the inability to commercialize our product candidates.

We have obtained limited product liability insurance coverage for our products and our clinical trials with a $10.0 million annual aggregate coverage limit. However, our insurance coverage may not reimburse us, or may not be sufficient to reimburse us, for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and, in the future, we may not be able to maintain insurance coverage on acceptable terms, at

a reasonable cost or in sufficient amounts to protect us against losses due to liability. We intend to expand our insurance coverage to include the sale of additional commercial products upon FDA approval for our product candidates in development, but we may be unable to obtain commercially reasonable product liability insurance for any products approved for marketing, or at all. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. A successful product

Table of Contents

liability claim or series of claims brought against us could cause our stock price to fall and, if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

If we fail to manufacture EXPAREL in sufficient quantities and at acceptable quality and pricing levels, or to fully comply with cGMP regulations, we may face delays in the commercialization of this product or be unable to meet market demand, and may lose potential revenues.

The manufacture of EXPAREL requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls, and the use of specialized processing equipment. We must comply with federal, state and foreign regulations, including the FDA's regulations governing cGMP, enforced by the FDA through its facilities inspection program and by similar regulatory authorities in other jurisdictions where we do business. These requirements include, among other things, quality control, quality assurance and the maintenance of records and documentation. The FDA or similar foreign regulatory authorities at any time may implement new standards, or change their interpretation and enforcement of existing standards for manufacture, packaging or testing of our products. Any failure to comply with applicable regulations may result in fines and civil penalties, suspension of production, product seizure or recall, operating restrictions, imposition of a consent decree, modification or withdrawal of product approval, or criminal prosecution, and would limit the availability of our product. Any manufacturing defect or error discovered after products have been produced and distributed also could result in significant consequences, including costly recall procedures, re-stocking costs, damage to our reputation and potential for product liability claims.

If we are unable to produce the required commercial quantities of EXPAREL to meet market demand for EXPAREL on a timely basis or at all, or if we fail to comply with applicable laws for the manufacturing of EXPAREL, we will suffer damage to our reputation and commercial prospects and we will lose potential revenues. We will need to expand our manufacturing operations or outsource such operations to third parties.

To successfully meet future customer demand for EXPAREL, we will need to expand our existing commercial manufacturing facilities or establish large-scale commercial manufacturing capabilities. In addition, as our drug development pipeline increases and matures, we will have a greater need for clinical trial and commercial manufacturing capacity. As a result, we must continue to improve our manufacturing processes to allow us to reduce our drug costs. We may not be able to manufacture our drugs at a cost or in quantities necessary to be commercially successful.

The build-up or other expansion of our internal manufacturing capabilities for EXPAREL production in San Diego, California exposes us to significant up-front fixed costs. If market demand for EXPAREL does not align with our expanded manufacturing capacity, we may be unable to offset these costs and to achieve economies of scale, and our operating results may be adversely affected as a result of high operating expenses. Alternatively, if we experience demand for EXPAREL in excess of our estimates, our facilities may be insufficient to support higher production volumes, which could harm our customer relationships and overall reputation. Our ability to meet such excess demand could also depend on our ability to raise additional capital and effectively scale our manufacturing operations.

In addition, the procurement time for the equipment that we use to manufacture EXPAREL requires long lead times. Therefore, we may experience delays, additional or unexpected costs and other adverse events in connection with our capacity expansion projects, including those associated with potential delays in the procurement of manufacturing equipment required to manufacture EXPAREL.

In addition to expanding our internal manufacturing facilities, we may enter into arrangements with third parties to manufacture, supply, test and/or store EXPAREL or our other products. Entering into such arrangements requires testing and compliance inspections, FDA approvals, and development of the processes necessary for the production of our products. Such arrangements also involve additional risks, many of which would be outside of our control. Such risks include disruptions or delays in production, manufactured products that do not meet our required specifications, the failure of such third party manufacturers to comply with cGMP regulations or other regulatory requirements, protection of our intellectual property and manufacturing process, loss of control of our complex manufacturing process, financial risks in connection with our investment in setting up a third party manufacturing process and inabilities to fulfill our commercial needs.

If we are unable to achieve and maintain satisfactory production yields and quality, whether through our internal manufacturing capabilities or arrangements with contract manufacturers, our relationships with potential customers and overall reputation may be harmed, and our revenues could decrease.

We are currently the sole manufacturer of EXPAREL and DepoCyt(e). Our inability to continue manufacturing adequate supplies of these products could result in a disruption in the supply to our customers and partners, which could have a material adverse impact on our business and results of operations.

We are currently the sole manufacturer of EXPAREL and DepoCyt(e). We develop and manufacture EXPAREL and DepoCyt(e) at our facilities in San Diego, California, which are the only FDA approved sites for manufacturing EXPAREL and DepoCyt(e) in the world. We may experience temporary or prolonged suspensions in production of our products due to issues

Table of Contents

in our manufacturing process that must be remediated or in response to inspections conducted by the FDA or similar foreign regulatory authorities, which could have a material adverse effect on our business, financial position and results of operations.

For example, in 2012 we temporarily ceased the manufacturing of DepoCyt(e) for sales in the European Union to implement a remediation plan to address certain issues noted in an inspection report issued by the the Medicines and Healthcare products Regulatory Agency, or MHRA, in July 2012 regarding our DepoCyt(e) manufacturing facility, which is located in a separate building from our EXPAREL manufacturing facility. The assessment report also recommended a selective recall of DepoCyt(e) in European Union (EU) member states where DepoCyt(e) is not considered to be an "essential medicinal product," which contributed to a reduction in product sales of DepoCyt(e) during fiscal year 2012. Although we received notice from the MHRA in January 2013 that our remediation efforts were successful and that we could resume production of DepoCyt(e) for sale in Europe, we may be required in the future to cease manufacturing operations at our facilities in response to inspection reports or other regulatory actions, and such temporary cessations could result in additional costs or delays in the production and sale of our products.

Our San Diego facilities are also subject to the risks of a natural or man-made disaster, including earthquakes and fires, or other business disruption. In addition, we have obtained limited property and business interruption insurance coverage for our facilities in San Diego. However, our insurance coverage may not reimburse us, or may not be sufficient to reimburse us, for any expenses or losses we may suffer. There can be no assurance that we would be able to meet our requirements for EXPAREL and DepoCyt(e) if there were a catastrophic event or failure of our current manufacturing system. If we are required to change or add a new manufacturer or supplier, the process would likely require prior FDA and/or equivalent foreign regulatory authority approval, and would be very time consuming. An inability to continue manufacturing adequate supplies of EXPAREL and DepoCyt(e) at our facilities in San Diego, California could result in a disruption in the supply of EXPAREL and DepoCyt(e), respectively, to our customers and partners and a breach of our contractual obligations to such counterparties.

We rely on third parties for the timely supply of specified raw materials and equipment for the manufacture of DepoCyt(e) and EXPAREL. Although we actively manage these third-party relationships to provide continuity and quality, some events which are beyond our control could result in the complete or partial failure of these goods and services. Any such failure could have a material adverse effect on our financial condition and operations.

We purchase certain raw materials and equipment from various suppliers in order to manufacture our products. The acquisition of certain of these materials may require considerable lead times, and our ability to source such materials is also dependent on logistics providers. If we are unable to source the required raw materials and equipment from our suppliers on a timely basis and in accordance with our specifications, we may experience delays in manufacturing and may not be able to meet our customers' or partners’ demands for our products. In addition, we and our third-party suppliers must comply with federal, state and foreign regulations, including cGMP regulations, and any failure to comply with applicable regulations, or failure of government agencies to provide necessary authorizations, may harm our ability to manufacture and commercialize our products on a timely and competitive basis, which could result in decreased product sales and lower revenues.

Our future growth depends on our ability to identify, develop, acquire or in-license products and if we do not successfully identify, develop, acquire or in-license related product candidates or integrate them into our operations, we may have limited growth opportunities.

An important part of our business strategy is to continue to develop a pipeline of product candidates by developing, acquiring or in-licensing products, businesses or technologies that we believe are a strategic fit with our focus on the hospital marketplace. However, these business activities may entail numerous operational and financial risks, including:

- significant capital expenditures;
- difficulty or inability to secure financing to fund development activities for such development, acquisition or in-licensed products or technologies;
- incurrence of substantial debt or dilutive issuances of securities to pay for development, acquisition or in-licensing of new products;
- disruption of our business and diversion of our management's time and attention;

- higher than expected development, acquisition or in-license and integration costs;
- exposure to unknown liabilities;
- difficulty and cost in combining the operations and personnel of any acquired businesses with our operations and personnel;
- inability to retain key employees of any acquired businesses;
- difficulty entering markets in which we have limited or no direct experience;
- difficulty in managing multiple product development programs; and
- inability to successfully develop new products or clinical failure.

We have limited resources to identify and execute the development, acquisition or in-licensing of products, businesses and technologies and integrate them into our current infrastructure. We may compete with larger pharmaceutical companies and

Table of Contents

other competitors, including public and private research organizations, academic institutions and government agencies, in our efforts to establish new collaborations and in-licensing opportunities. These competitors likely will have access to greater financial resources, research and development staffs and facilities than us and may have greater expertise in identifying and evaluating new opportunities. We may not be successful in locating and acquiring or in-licensing additional desirable product candidates on acceptable terms or at all. Moreover, we may devote resources to potential development, acquisitions or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts.

Our business involves the use of hazardous materials and we must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

Our manufacturing activities involve the controlled storage, use and disposal of hazardous materials, including the components of our products, product candidates and other hazardous compounds. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling, release and disposal of, and exposure to, these hazardous materials. Violation of these laws and regulations could lead to substantial fines and penalties. Although we believe that our safety procedures for handling and disposing of these materials comply with the standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental contamination or injury from these materials or unintended failure to comply with these laws and regulations. In the event of an accident or failure to comply with these laws and regulations, state or federal authorities may curtail our use of these materials and interrupt our business operations. In addition, we could become subject to potentially material liabilities relating to the investigation and cleanup of any contamination, whether currently unknown or caused by future releases.

Our business and operations would suffer in the event of system failures.

Despite the implementation of security measures, our internal computer systems are vulnerable to damage from computer viruses, human error, unauthorized access, natural disasters, intentional acts of vandalism, terrorism, war and telecommunication and electrical failures. Any system failure, accident or security breach that causes interruptions in our operations could result in a material disruption of our product development programs. For example, the loss of clinical trial data from completed clinical trials for EXPAREL could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we may incur liability and the further development of our product candidates may be delayed.

Any collaboration arrangements that we may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize our product candidates.

Our business model is to commercialize our product candidates in the United States and generally to seek collaboration arrangements with pharmaceutical or biotechnology companies for the development or commercialization of our product candidates in the rest of the world. Accordingly, we may enter into collaboration arrangements in the future on a selective basis. Any future collaboration arrangements that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaboration arrangements.

Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision making authority.

Collaborations with pharmaceutical companies and other third parties often are terminated or allowed to expire by the other party. Any such termination or expiration would adversely affect us financially and could harm our business reputation.

Clinical trials may fail to demonstrate the safety and efficacy of our drug products, which could prevent or significantly delay obtaining regulatory approval.

Prior to receiving approval to commercialize any of our drug products, we must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA, and other regulatory authorities in the U.S. and

other countries, that each of the products is both safe and effective. For each drug product, we will need to demonstrate its efficacy and monitor its safety throughout the process. If such development is unsuccessful, our business and reputation would be harmed and our stock price would be adversely affected.

All of our drug products are prone to the risks of failure inherent in drug development. Clinical trials of new drug products sufficient to obtain regulatory marketing approval are expensive and take years to complete. We may not be able to successfully complete clinical testing within the time frame we have planned, or at all. We may experience numerous unforeseen events during, or as a result of, the clinical trial process that could delay or prevent us from receiving regulatory approval or commercializing our drug products. In addition, the results of pre-clinical studies and early-stage clinical trials of

Table of Contents

our drug products do not necessarily predict the results of later-stage clinical trials. Later-stage clinical trials may fail to demonstrate that a drug product is safe and effective despite having progressed through initial clinical testing. Even if we believe the data collected from clinical trials of our drug products is promising, such data may not be sufficient to support approval by the FDA or any other U.S. or foreign regulatory approval. Pre-clinical and clinical data can be interpreted in different ways.

Accordingly, FDA officials could interpret such data in different ways than we or our partners do which could delay, limit or prevent regulatory approval. The FDA, other regulatory authorities, our institutional review boards, our contract research organizations, or we ourselves may suspend or terminate our clinical trials for our drug products. Any failure or significant delay in completing clinical trials for our drug products, or in receiving regulatory approval for the sale of any drugs resulting from our drug products, may severely harm our business and reputation. Even if we receive FDA and other regulatory approvals, our drug products may later exhibit adverse effects that may limit or prevent their widespread use, may cause the FDA to revoke, suspend or limit their approval, or may force us to withdraw products derived from those drug products from the market.

Our dependence on contract research organizations could result in delays in and additional costs for our drug development efforts.

We may rely on contract research organizations, or CROs, to perform preclinical testing and clinical trials for drug candidates that we choose to develop without a collaborator. If the CROs that we hire to perform our preclinical testing and clinical trials or our collaborators or licensees do not meet deadlines, do not follow proper procedures, or a conflict arises between us and our CROs, our preclinical testing and clinical trials may take longer than expected, may be delayed or may be terminated. If we were forced to find a replacement CRO to perform any of our preclinical testing or clinical trials, we may not be able to find a suitable replacement on favorable terms, if at all. Even if we were able to find another CRO to perform a preclinical test or clinical trial, any material delay in a test or clinical trial may result in significant additional expenditures that could adversely affect our operating results. Events such as these may also delay regulatory approval for our drug candidates or our ability to commercialize our products.

We depend on clinical investigators and clinical sites to enroll patients in our clinical trials and sometimes other third parties to manage the trials and to perform related data collection and analysis, and, as a result, we may face costs and delays outside of our control.

We rely on clinical investigators and clinical sites to enroll patients and sometimes third parties to manage our trials and to perform related data collection and analysis. However, we may be unable to control the amount and timing of resources that the clinical sites that conduct the clinical testing may devote to our clinical trials. If our clinical investigators and clinical sites fail to enroll a sufficient number of patients in our clinical trials or fail to enroll them on our planned schedule, we will be unable to complete these trials or to complete them as planned, which could delay or prevent us from obtaining regulatory approvals for our product candidates.

Our agreements with clinical investigators and clinical sites for clinical testing and for trial management services place substantial responsibilities on these parties, which could result in delays in, or termination of, our clinical trials if these parties fail to perform as expected. For example, if any of our clinical trial sites fail to comply with FDA-approved good clinical practices, we may be unable to use the data gathered at those sites. If these clinical investigators, clinical sites or other third parties do not carry out their contractual duties or obligations or fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to their failure to adhere to our clinical protocols or for other reasons, our clinical trials may be extended, delayed or terminated, and we may be unable to obtain regulatory approval for, or successfully commercialize, our product candidates.

Regulatory Risks

We may not receive regulatory approval for any of our product candidates, or the approval may be delayed for various reasons, including successful challenges to the FDA's interpretation of Section 505(b)(2), which would have a material adverse effect on our business and financial condition.

We may experience delays in our efforts to obtain regulatory approval from the FDA for any of our product candidates, and there can be no assurance that such approval will not be delayed, or that the FDA will ultimately approve these product candidates. Although the FDA's longstanding position has been that the Agency may rely upon prior findings of safety or effectiveness to support approval of a 505(b)(2) application, this policy has been controversial and subject to challenge in the past. If the FDA's policy is successfully challenged administratively or in court, we may be required to seek approval of our products via full NDAs that contain a complete data package demonstrating the safety and effectiveness of our products, which would be time-consuming and expensive and would have a material adverse effect on our business and financial condition.

Table of Contents

The FDA, as a condition of the EXPAREL approval on October 28, 2011, has required us to study EXPAREL in pediatric patients. We have agreed to a trial timeline where, over several years, we will study pediatric patient populations in descending order starting with 12-18 year olds and ending with children under two years of age. These trials will be expensive and time consuming and we will be required to meet the timelines for submission of protocols and data and for completion as agreed with the FDA, and we may be delayed in meeting such timelines. We may be required to conduct these trials even if we believe that the costs and potential benefits of conducting the trials are not warranted from a scientific or financial perspective. The failure to conduct these pediatric trials or to meet applicable deadlines could result in the imposition of sanctions, including, among other things, issuance of warnings letters or imposition of seizures or injunctions.

The FDA may determine that EXPAREL or any of our product candidates have undesirable side effects.

If concerns are raised regarding the safety of a new drug as a result of undesirable side effects identified during clinical testing, the FDA may decline to approve the drug at the end of the NDA review period or issue a letter requesting additional data or information prior to making a final decision regarding whether or not to approve the drug. The number of such requests for additional data or information issued by the FDA in recent years has increased, and resulted in substantial delays in the approval of several new drugs. Undesirable side effects caused by EXPAREL or any product candidate could also result in the inclusion of unfavorable information in our product labeling, imposition of distribution or use restrictions, a requirement to conduct post-market studies or to implement a risk evaluation and mitigation strategy, denial, suspension or withdrawal of regulatory approval by the FDA or other regulatory authorities for any or all targeted indications, and in turn prevent us from commercializing and generating revenues from the sale of EXPAREL or any product candidate.

For example, the side effects observed in the EXPAREL clinical trials completed to date include nausea and vomiting. In addition, the class of drugs that EXPAREL belongs to has been associated with nervous system and cardiovascular toxicities at high doses. We cannot be certain that these side effects and others will not be observed in the future, or that the FDA will not require additional trials or impose more severe labeling restrictions due to these side effects or other concerns. The active component of EXPAREL is bupivacaine and bupivacaine infusions have been associated with the destruction of articular cartilage, or chondrolysis. Chondrolysis has not been observed in clinical trials of EXPAREL, but we cannot be certain that this side effect will not be observed in the future.

Following approval of EXPAREL or any of our product candidates, if we or others later identify previously unknown undesirable side effects caused by such products, if known side effects are more frequent or severe than in the past, or if we or others detect unexpected safety signals for such products or any products perceived to be similar to such products:

- regulatory authorities may require the addition of unfavorable labeling statements, specific warnings or contraindications (including boxed warnings);
- regulatory authorities may suspend or withdraw their approval of the product, or require it to be removed from the market;
- regulatory authorities may impose restrictions on the distribution or use of the product;
- we may be required to change the way the product is administered, conduct additional clinical trials, reformulate the product, change the labeling of the product or change or obtain re-approvals of manufacturing facilities;
- sales of the product may be significantly decreased from projected sales;
- we may be subject to government investigations, product liability claims and litigation; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of EXPAREL or any of our product candidates and could substantially increase our commercialization costs and expenses, which in turn could delay or prevent us from generating significant revenues from its sale.

Regulatory approval for any approved product is limited by the FDA to those specific indications and conditions for which clinical safety and efficacy have been demonstrated.

Any regulatory approval is limited to those specific diseases and indications for which a product is deemed to be safe and effective by the FDA. For example, the FDA-approved label for EXPAREL does not include an indication in obstetrical paracervical block anesthesia. In addition to the FDA approval required for new formulations, any new

indication for an approved product also requires FDA approval. If we are not able to obtain FDA approval for any desired future indications for our products and product candidates, our ability to effectively market and sell our products may be reduced and our business may be adversely affected.

While physicians may choose to prescribe drugs for uses that are not described in the product's labeling and for uses that differ from those tested in clinical studies and approved by the regulatory authorities, our ability to promote the products is limited to those indications that are specifically approved by the FDA. These "off-label" uses are common across medical specialties and may constitute an appropriate treatment for some patients in varied circumstances. Regulatory authorities in the United States generally do not regulate the behavior of physicians in their choice of treatments. Regulatory authorities do, however, restrict communications by pharmaceutical companies on the subject of off-label use. Although recent court decisions

Table of Contents

suggest that certain off-label promotional activities may be protected under the First Amendment, the scope of any such protection is unclear. If our promotional activities fail to comply with the FDA's regulations or guidelines, we may be subject to warnings from, or enforcement action by, these authorities. In addition, our failure to follow FDA rules and guidelines relating to promotion and advertising may cause the FDA to issue warning letters or untitled letters, suspend or withdraw an approved product from the market, require a recall or institute fines or civil fines, or could result in disgorgement of money, operating restrictions, injunctions or criminal prosecution, any of which could harm our business.

If we fail to comply with federal and state healthcare laws, including fraud and abuse and health information privacy and security laws, we could face substantial penalties and our business, results of operations, financial condition and prospects could be adversely affected.

As a pharmaceutical company, even though we do not provide healthcare services or receive payments directly from or bill directly to Medicare, Medicaid or other third-party payers for our products, certain federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. We would be subject to healthcare fraud and abuse and patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which constrains our marketing practices, educational programs, pricing policies and relationships with healthcare providers or other entities, by prohibiting, among other things, soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under federally funded healthcare programs, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims and false statement laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payers that are false or fraudulent or making any materially false statement in connection with the delivery or payment for healthcare benefits, items, or services;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended, which created federal criminal and civil statutes that prohibit executing a scheme to defraud any healthcare benefit program;
- federal physician self-referral laws, such as the Stark law, which prohibit a physician from making a referral to a provider of certain health services with which the physician or the physician's family member has a financial interest, and prohibit submission of a claim for reimbursement pursuant to a prohibited referral;
- HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and its implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information; and
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payer, including commercial insurers, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available under the U.S. federal Anti-Kickback Statute, it is possible that some of our business activities could be subject to challenge under one or more of such laws. Moreover, recent health care reform legislation has strengthened these laws. For example, the Health Care Reform Law, among other things, amends the intent requirement of the federal anti-kickback and criminal health care fraud statutes; a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it. In addition, the Health Care Reform Law provides that the government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the false claims statutes. Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, or causing to be made, a false statement to get a false claim paid. Recently, several pharmaceutical and other healthcare companies have been prosecuted under the federal false claims laws for allegedly inflating drug prices they report to pricing services, which in turn are used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal

programs for the product. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws. To the extent that any product we make is sold in a foreign country, we may be subject to similar foreign laws and regulations.

Further, there has been a recent trend in the increase of federal and state laws and regulations regarding consulting arrangements with physicians. The Health Care Reform Law imposes new requirements to report certain financial arrangements with physicians and others, including reporting any "transfer of value" made or distributed to prescribers and other healthcare providers and reporting any investment interests held by physicians and their immediate family members during each calendar year beginning in 2013, subject to federal implementation and enforcement policies. In addition, some states such as California, Massachusetts and Vermont, mandate that we comply with a state code of conduct, adopt a company code of conduct under state criteria, disclose marketing payments made to physicians, and/or report compliance information to

Table of Contents

the state authorities. Some states, such as Massachusetts, have created an internet database to provide disclosed information on certain transactions with physicians to the public. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply in multiple jurisdictions with different compliance and reporting requirements increases the possibility that a pharmaceutical company may run afoul of one or more of the requirements.

If our past or present operations, or those of our distributors are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in U.S. federal or state health care programs, and the curtailment or restructuring of our operations. Similarly, if the healthcare providers, distributors or other entities with whom we do business are found to be out of compliance with applicable laws and regulations, they may be subject to sanctions, which could also have a negative impact on us. The risk of being found to have violated such laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Any penalties, damages, fines, curtailment or restructuring of our operations could materially adversely affect our ability to operate our business and our financial results. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud laws may prove costly.

The design, development, manufacture, supply, and distribution of EXPAREL and DepoCyt(e) is highly regulated and technically complex.

The design, development, manufacture, supply, and distribution of EXPAREL and DepoCyt(e) is highly regulated and technically complex. We, along with our third-party providers, must comply with all applicable regulatory requirements of the FDA and foreign authorities. In addition, the facilities used to manufacture, store, and distribute our products are subject to inspection by regulatory authorities at any time to determine compliance with applicable regulations.

The manufacturing techniques and facilities used for the manufacture and supply of our products must be operated in conformity with cGMP and other FDA, DEA and MHRA regulations, including potentially prior regulatory approval. In addition, any expansion of our existing manufacturing facilities or the introduction of any new manufacturing facilities would also require conformity with cGMP and other FDA, DEA and MHRA regulations. In complying with these requirements, we, along with our suppliers, must continually expend time, money and effort in production, record keeping, and quality assurance and control to ensure that our products meet applicable specifications and other requirements for safety, efficacy and quality. In addition, we, along with our suppliers, are subject to unannounced inspections by the FDA, MHRA and other regulatory authorities.

Any failure to comply with regulatory and other legal requirements applicable to the manufacture, supply and distribution of our products could lead to remedial action (such as recalls), civil and criminal penalties and delays in manufacture, supply and distribution of our products. For instance, in July 2012, the MHRA issued its inspection report in which the MHRA noted certain critical and major failures to comply with the Principles and Guidelines of Good Manufacturing Practices related to our DepoCyt(e) manufacturing facility. We responded to the MHRA regarding these inspectional observations, completed implementation of our proposed remediation plan and were reinspected by the MHRA in December 2012. In January 2013, we received notice from the MHRA that our remediation efforts were successful and that we could recommence manufacturing DepoCyt(e) for Europe.

If we fail to comply with the extensive regulatory requirements to which we and our products, EXPAREL and DepoCyt(e), are subject, such products could be subject to restrictions or withdrawal from the market and we could be subject to penalties.

The testing, manufacturing, quality control, labeling, safety, effectiveness, advertising, promotion, storage, sales, distribution, import, export and marketing, among other things, of our products EXPAREL and DepoCyt(e) are subject to extensive regulation by governmental authorities in the United States and elsewhere throughout the world. Quality control and manufacturing procedures regarding EXPAREL and DepoCyt(e) must conform to cGMP.

Regulatory authorities, including the FDA and the MHRA, periodically inspect manufacturing facilities to assess compliance with cGMP. Our failure, or the failure of any contract manufacturers with whom we may work in the future, to comply with the laws administered by the FDA, the MHRA or other governmental authorities could result in, among other things, any of the following:

- product recall or seizure;
- suspension or withdrawal of an approved product from the market;
- interruption of production;
- operating restrictions;
- warning letters;
- injunctions;

Table of Contents

- refusal to permit import or export of an approved product;
- refusal to approve pending applications or supplements to approved applications that we submit;
- denial of permission to file an application or supplement in a jurisdiction;
- consent decrees;
- suspension or termination of ongoing clinical trials;
- fines and other monetary penalties;
- criminal prosecutions; and
- unanticipated expenditures.

If the government or third-party payers fail to provide coverage and adequate coverage and payment rates for EXPAREL, DepoCyt(e) or any future products we may develop, license or acquire, if any, are unavailable, or if hospitals choose to use therapies that are less expensive, our revenue and prospects for profitability will be limited.

In both domestic and foreign markets, sales of our existing products and any future products will depend in part upon the availability of coverage and reimbursement from third-party payers. Such third-party payers include government health programs such as Medicare and Medicaid, managed care providers, private health insurers and other organizations. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available. Assuming coverage is approved, the resulting reimbursement payment rates might not be adequate. In particular, many U.S. hospitals receive a fixed reimbursement amount per procedure for certain surgeries and other treatment therapies they perform. Because this amount may not be based on the actual expenses the hospital incurs, hospitals may choose to use therapies which are less expensive when compared to our product candidates. Although hospitals currently receive separate reimbursement for EXPAREL used in the hospital outpatient setting, EXPAREL, DepoCyt(e) or any product candidates that we may develop, in-license or acquire, if approved, will face competition from other therapies and drugs for these limited hospital financial resources. We may need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of any future products to the satisfaction of hospitals, other target customers and their third-party payers. Such studies might require us to commit a significant amount of management time and financial and other resources. Our future products might not ultimately be considered cost-effective. Adequate third-party coverage and reimbursement might not be available to enable us to maintain price levels sufficient to realize an appropriate return on investment in product development.

Third-party payers, whether foreign or domestic, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. For example, third-party payers may limit the indications for which our products will be reimbursed to a smaller set of indications than we believe is appropriate or limit the circumstances under which our products will be reimbursed to a smaller set of circumstances than we believe is appropriate. In addition, in the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payers. Therefore, coverage and reimbursement for drug products can differ significantly from payer to payer.

Further, we believe that future coverage and reimbursement will likely be subject to increased restrictions both in the United States and in international markets, as federal, state, and foreign governments continue to propose and pass new legislation designed to reduce or contain the cost of healthcare. Third-party coverage and reimbursement for our products or product candidates for which we receive regulatory approval may not be available or adequate in either the United States or international markets, which could have a negative effect on our business, results of operations, financial condition and prospects.

We are subject to new legislation, regulatory proposals and healthcare payer initiatives that may increase our costs of compliance and adversely affect our ability to market our products, obtain collaborators and raise capital.

In March 2010, the President signed the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, which we refer to collectively as the Health Care Reform Law. The Health Care Reform Law makes extensive changes to the delivery of health care in the United States. Among the provisions of the Health Care Reform Law of greatest importance to the pharmaceutical industry are the following:

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an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, beginning in 2011;

- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program, retroactive to January 1, 2010, to 23.1% and 13.0% of the average manufacturer price for most branded and generic drugs, respectively;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50.0% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D, beginning in 2011;

Table of Contents

- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations, effective March 23, 2010;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals beginning in April 2010 and by adding new mandatory eligibility categories for certain individuals with income at or below 133.0% of the Federal Poverty Level beginning in 2014, thereby potentially increasing both the volume of sales and manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program, effective in January 2010;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians, effective April 1, 2012, subject to federal implementation and enforcement policies;
- a licensure framework for follow-on biologic products;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- creation of the Independent Payment Advisory Board which, beginning in 2014, will have authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs and those recommendations could have the effect of law even if Congress does not act on the recommendations; and
- establishment of a Center for Medicare Innovation at the Centers for Medicare & Medicaid Services to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending, beginning by January 1, 2011.

These measures could result in decreased net revenues from our pharmaceutical products and decrease potential returns from our development efforts. Congress has also proposed a number of legislative initiatives, including possible repeal of the Health Care Reform Law. At this time, it remains unclear whether there will be any changes made to the Health Care Reform Law, whether to certain provisions or its entirety. In addition, some details regarding the implementation of the Health Care Reform Law are yet to be determined, and at this time, the full effect that the Health Care Reform Law would have on our business remains unclear.

In addition, other legislative changes have been proposed and adopted since the Health Care Reform Law was enacted. For example, on August 2, 2011, the President signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend proposals in spending reductions to Congress. As a result of the failure of the Joint Select Committee to propose, and of Congress to enact, deficit reduction measures of at least $1.2 trillion for the years 2013 through 2021, the Budget Control Act provides for automatic cuts to be made to most federal government programs, which, with respect to Medicare, would include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013. Pursuant to the American Taxpayer Relief Act of 2012, which was enacted by Congress on January 1, 2013, the imposition of these automatic cuts was delayed until March 1, 2013. On March 1, 2013, the President signed an executive order implementing the automatic budget reductions. Pursuant to that order, payments to Medicare providers for services furnished on or after April 1, 2013 were reduced by 2%. In addition, the new law, among other things, reduces Medicare inpatient payment amounts to hospitals and increases the statute of limitations for recovering overpayments from three years to five years. The full impact on our business of this new law, assuming it is implemented, is uncertain. Nor is it clear whether other legislative changes will be adopted or how such changes would affect the demand for our products.

In addition, there have been a number of other legislative and regulatory proposals aimed at changing the pharmaceutical industry. In particular, California has enacted legislation that requires development of an electronic pedigree to track and trace each prescription drug at the saleable unit level through the distribution system. California's electronic pedigree requirement is scheduled to take effect in January 2015. Compliance with California and future federal or state electronic pedigree requirements may increase our operational expenses and impose significant administrative burdens. As a result of these and other new proposals, we may determine to change our current manner of operation, provide additional benefits or change our contract arrangements, any of which could have a material adverse effect on our business, financial condition and results of operations.

In July 2012, the President signed into law the Food and Drug Administration Safety and Innovation Act, or FDASIA. This law makes several significant changes to the Federal Food, Drug, and Cosmetic Act and FDA's processes for reviewing marketing applications that could have a significant impact on the pharmaceutical industry, including, among other things, the following:

- reauthorizes the Prescription Drug User Fee Act, or PDUFA, increases the amount of associated user fees, and, for certain types of applications, increases the expected time frame for FDA review of the application;
- permanently reauthorizes and makes some revisions to the Best Pharmaceuticals for Children Act and the Pediatric Research Equity Act, which provides for pediatric exclusivity and mandated pediatric assessments for certain types of applications, respectively;

Table of Contents

- revises certain standards and requirements for FDA inspections of manufacturing facilities and the importation of drug products from foreign countries;
- creates incentives for the development of certain antibiotic drug products;
- modifies the standards for accelerated approval of certain new medical treatments;
- expands the reporting requirements for potential and actual drug shortages;
- requires the FDA to issue a report on, among other things, ensuring safe use of prescription drugs that have the potential for abuse;
- requires the FDA to hold a public meeting regarding the potential rescheduling of drug products containing hydrocodone, which was held in January 2013; and
- requires electronic submission of certain marketing applications following the issuance of final FDA regulations.

The full impact of FDASIA on our business is uncertain.

Public concern regarding the safety of drug products such as EXPAREL could result in the inclusion of unfavorable information in our labeling, or require us to undertake other activities that may entail additional costs.

In light of widely publicized events concerning the safety risk of certain drug products, the FDA, members of Congress, the Government Accountability Office, medical professionals and the general public have raised concerns about potential drug safety issues. These events have resulted in the withdrawal of drug products, revisions to drug labeling that further limit use of the drug products and the establishment of risk management programs that may, for example, restrict distribution of drug products after approval. The Food and Drug Administration Amendments Act of 2007, or FDAAA, grants significant expanded authority to the FDA, much of which is aimed at improving the safety of drug products before and after approval. In particular, the FDAAA authorizes the FDA to, among other things, require post-approval studies and clinical trials, mandate changes to drug labeling to reflect new safety information and require risk evaluation and mitigation strategies for certain drugs, including certain currently approved drugs. The FDAAA also significantly expands the federal government's clinical trial registry and results databank, which we expect will result in significantly increased government oversight of clinical trials. Under the FDAAA, companies that violate these and other provisions of the new law are subject to substantial civil monetary penalties, among other regulatory, civil and criminal penalties. The increased attention to drug safety issues may result in a more cautious approach by the FDA in its review of data from our clinical trials. Data from clinical trials may receive greater scrutiny, particularly with respect to safety, which may make the FDA or other regulatory authorities more likely to require additional preclinical studies or clinical trials. If the FDA requires us to provide additional clinical or preclinical data for EXPAREL, the indications for which this product candidate was approved may be limited or there may be specific warnings or limitations on dosing, and our efforts to commercialize EXPAREL may be otherwise adversely impacted.

Risks Related to Intellectual Property

The patents and the patent applications that we have covering our products are limited to specific injectable formulations, processes and uses of drugs encapsulated in our DepoFoam drug delivery technology and our market opportunity for our product candidates may be limited by the lack of patent protection for the active ingredient itself and other formulations and delivery technology and systems that may be developed by competitors.

The active ingredients in EXPAREL and DepoCyt(e) are bupivacaine and cytarabine, respectively. Patent protection for the bupivacaine and cytarabine molecules themselves has expired and generic immediate-release products are available. As a result, competitors who obtain the requisite regulatory approval can offer products with the same active ingredients as EXPAREL and DepoCyt(e) so long as the competitors do not infringe any process, use or formulation patents that we have developed for these drugs encapsulated in our DepoFoam drug delivery technology.

For example, we are aware of at least one long-acting injectable bupivacaine product in development which utilizes an alternative delivery system to EXPAREL. Such a product is similar to EXPAREL in that it also extends the duration of effect of bupivacaine, but achieves this clinical outcome using a completely different drug delivery system as compared to our DepoFoam drug delivery technology.

The number of patents and patent applications covering products in the same field as EXPAREL indicates that competitors have sought to develop and may seek to market competing formulations that may not be covered by our

patents and patent applications. The commercial opportunity for EXPAREL could be significantly harmed if competitors are able to develop and commercialize alternative formulations of bupivacaine that are long acting but outside the scope of our patents.

Because EXPAREL has been approved by the FDA, one or more third parties may challenge the patents covering this product, which could result in the invalidation or unenforceability of some or all of the relevant patent claims. For example, if a third party files an Abbreviated New Drug Application, or ANDA, for a generic drug product containing bupivacaine and relies in whole or in part on studies conducted by or for us, the third party will be required to certify to the FDA that either: (1) there is no patent information listed in the FDA's Orange Book with respect to our NDA for EXPAREL; (2) the patents listed in the Orange Book have expired; (3) the listed patents have not expired, but will expire on a particular date and approval is sought after patent expiration; or (4) the listed patents are invalid or will not be infringed by the manufacture, use or sale of the third-

Table of Contents