SECURITIES AND EXCHANGE COMMISSION

# FORM 8-K

Current report filing

Filing Date: 2013-01-15 | Period of Report: 2013-01-15 SEC Accession No. 0001104659-13-002659

(HTML Version on secdatabase.com)

### **FILER**

#### Pacira Pharmaceuticals, Inc.

CIK:1396814| IRS No.: 000000000 | State of Incorp.:DE | Fiscal Year End: 1231 Type: 8-K | Act: 34 | File No.: 001-35060 | Film No.: 13530654 SIC: 2834 Pharmaceutical preparations Mailing Address 5 SYLVAN WAY SUITE 100 PARSIPPANY NJ 07054 Business Address 5 SYLVAN WAY SUITE 100 PARSIPPANY NJ 07054 973-254-3560

### UNITED STATES SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

### FORM 8-K

#### CURRENT REPORT Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 15, 2013

### PACIRA PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Charter)

Delaware (State or Other Jurisdiction of Incorporation) **001-35060** (Commission File Number) **51-0619477** (IRS Employer Identification No.)

5 Sylvan Way, Suite 100, Parsippany, New Jersey (Address of Principal Executive Offices) **07054** (Zip Code)

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

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (*see* General Instruction A.2. below):

□ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

□ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

□ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

□ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

#### Item 2.02 Results of Operations and Financial Condition.

In connection with the Private Placement, the Company is providing the following updated disclosures with respect to recent developments.

#### **Recent Developments**

#### Estimated 2012 Results

The Company is in the process of finalizing its results of operations and other financial and operating data for the year ended and quarter ended December 31, 2012. While the Company's full financial information and operating data for such periods are not available, the information below is based on management's preliminary estimates from currently available information.

For the quarter ended December 31, 2012, the Company currently expects to report net sales of EXPAREL of approximately \$7.8 million, and currently expects to report total revenues of approximately \$10.5 million as compared to total revenues of \$4.2 million for the quarter ended December 31, 2011. For the year ended December 31, 2012, the Company currently expects to report net sales of EXPAREL of approximately \$14.6 million, and currently expects to report total revenues of approximately \$39.1 million as compared to total revenues of \$15.7 million for the year ended December 31, 2011. The expected increase in total revenues for the year ended and quarter ended December 31, 2012 as compared to the corresponding period in the preceding year is primarily attributable to EXPAREL sales since the launch in April 2012 as well as the increase in our collaborative licensing and development revenue relating to the recognition of deferred revenue in connection with the termination of certain license agreements.

The average daily box sales of EXPAREL increased month over month, from September 2012 through December 2012, by approximately 13%, 23%, 26% and 39%, respectively. Average daily box sales is the total boxes sold in the applicable month, divided by the business days in such month, excluding holidays when product cannot be shipped. The Company sold an estimated 5,497 total boxes of EXPAREL during the period from its commercial launch in April 2012 through December 31, 2012.

As of December 31, 2012, the Company currently expects to have cash, cash equivalents, restricted cash and short-term investments of \$42.6 million.

Because the reporting period ended December 31, 2012 has recently ended, the unaudited financial information presented above for the year ended and quarter ended December 31, 2012 reflects estimates based only upon preliminary information available to the Company as of the date hereof, is subject to change pending finalization and is not a comprehensive statement of the Company's financial results or position as of or for the year ended and quarter ended December 31, 2012. The Company's independent registered public accounting firm, CohnReznick LLP, has not audited, reviewed, compiled or performed any procedures with respect to the above preliminary estimated financial information, and, accordingly, does not express an opinion or provide any form of assurance with respect thereto. During the course of the Company's financial statement closing process or the audit of its financial statements, the Company may identify items that would require it to make adjustments to its preliminary operating results described above.

As a result, the foregoing discussion constitutes forward-looking statements and, therefore, the Company cautions investors that these statements are subject to risks and uncertainties, including possible adjustments to the Company's preliminary operating results and the risk factors highlighted in the Company's filings with the Securities and Exchange Commission. The Company's consolidated financial statements and operating data as of and for the year ended and quarter ended December 31, 2012 will not be available until after the Private Placement is completed and may vary materially from the preliminary estimated financial information the Company has provided. Accordingly, investors should not place undue reliance on these preliminary estimates. The estimates as of and for the year

ended and quarter ended December 31, 2012 are not necessarily indicative of any future period and should be read together with the attached 'Risk Factors,' which are updated from the "Risk Factors" included in the Company's Annual Report on Form 10-K for the year ended December 31, 2011 and the "Risk Factors" included in the Company's quarterly reports on Form 10-Q for the quarters ended June 30, 2012 and September 30, 2012. The Company's updated "Risk Factors" are filed herewith as Exhibit 99.2 and incorporated by reference herein.

#### Item 7.01 Regulation FD Disclosure.

The information disclosed in Item 2.02 above is incorporated by reference herein.

On January 15, 2013, Pacira Pharmaceuticals, Inc. (the "Company") announced its intention to offer \$100 million aggregate principal amount of convertible senior notes due 2019 (plus up to an additional \$10 million aggregate principal amount if the initial purchasers exercise their option to purchase additional notes in full), subject to market conditions and other factors (the "Private Placement"). The materials filed herewith as Exhibit 99.1 hereto and incorporated by reference in this Item 7.01 have been excerpted from materials made available to potential investors in connection with the Private Placement.

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#### Safe Harbor

Certain of the statements made in this Current Report on Form 8-K are forward-looking statements for purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995, such as those, among others, relating to the Company's business, including plans to manufacture and commercialize EXPAREL, the success of our commercialization of EXPAREL, the future development of product candidates and the timing thereof, the timing and results of our clinical trials, potential indications for our product candidates and the timing thereof, the timing and results of additional products and future financial results. Actual results or developments may differ materially from those projected or implied in these forward-looking statements. Factors that may cause such a difference include the impact of general economic, industry or political conditions in the United States or internationally; 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 potential markets for EXPAREL and our ability to serve those markets; our commercialization and marketing capabilities; and other factors discussed in the "Risk Factors" set forth in Exhibit 99.2 of this Current Report on Form 8-K and in other filings that we periodically make with the SEC. In addition, the forward-looking statements included in this Current Report on Form 8-K represent our views as of the date of this Current Report on Form 8-K. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this Current Report on Form 8-K.

#### Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exh	ibit				
No.		Description			
	99.1*	Excerpted Investor Material			
	99.2*	Updated Risk Factors			
*	Deemed	filed under the Exchange Act			

#### SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: January 15, 2013

#### PACIRA PHARMACEUTICALS, INC.

By: /s/ James Scibetta James Scibetta

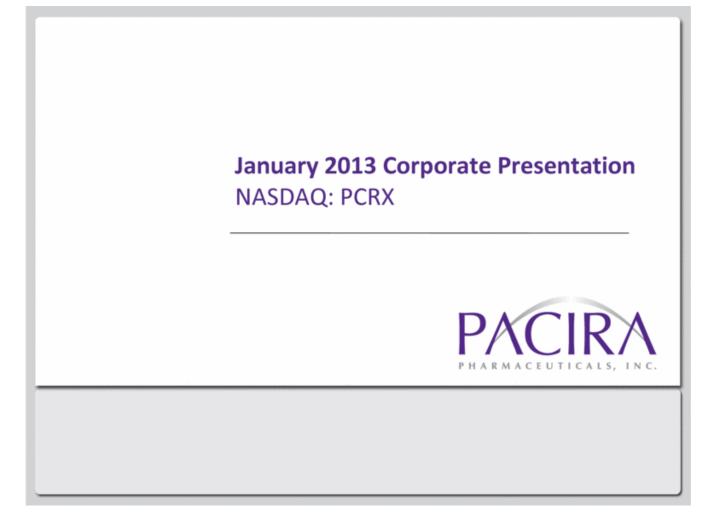
Chief Financial Officer

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#### EXHIBIT INDEX

0.		Description
99.1*	Excerpted Investor Material	
99.2*	Updated Risk Factors	
Deemed	filed under the Exchange Act	

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### **Forward-Looking Statements**

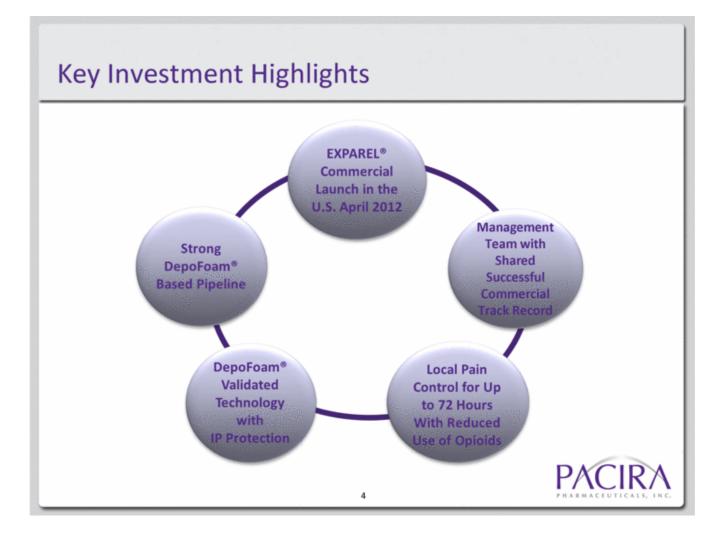
This presentation contains forward-looking statements, within the meaning of Section 21E of the Securities Exchange Act of 1934 (collectively, forward-looking statements), about our business, including statements related to our expectations regarding completion of the proposed notes offering, plans to manufacture and commercialize EXPAREL, the success of our commercialization of EXPAREL, the future development of product candidates and the timing thereof, the timing and results of our clinical trials, potential indications for our product candidates and the timing and likelihood of the commercialization of additional products and future financial results. Actual results or developments may differ materially from those projected or implied in these forward-looking statements. Factors that may cause such a difference include, whether or not we will offer the notes or consummate the offering; the anticipated terms of the notes and the offering; the impact of general economic, industry or political conditions in the United States or internationally; 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 potential markets for EXPAREL and our ability to serve those markets; our commercialization and marketing capabilities; and other factors discussed in the "Risk Factors" section of our most recent Annual Report on Form 10-K for the fiscal year ended December 31, 2011; our Quarterly Reports on Form 10-Q for the quarters ended June 30, 2012 and September 30, 2012; and in other filings that we periodically make with the SEC. In addition, the forward-looking statements included in this presentation represent our views as of the date of this presentation. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we specifically disclaim any obligation to do so. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this presentation.



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# Highly Experienced Management Team With Shared Successful Commercial Track Record





# EXPAREL Uses DepoFoam<sup>®</sup> to Release Bupivacaine Over Time

- By utilizing the DepoFoam product delivery platform, EXPAREL delivers therapeutic levels of bupivacaine up to 72 hours\*
- DepoFoam is a multivesicular liposomal product delivery technology that encapsulates drugs without altering their molecular structure and then releases them over a desired period of time<sup>1</sup>

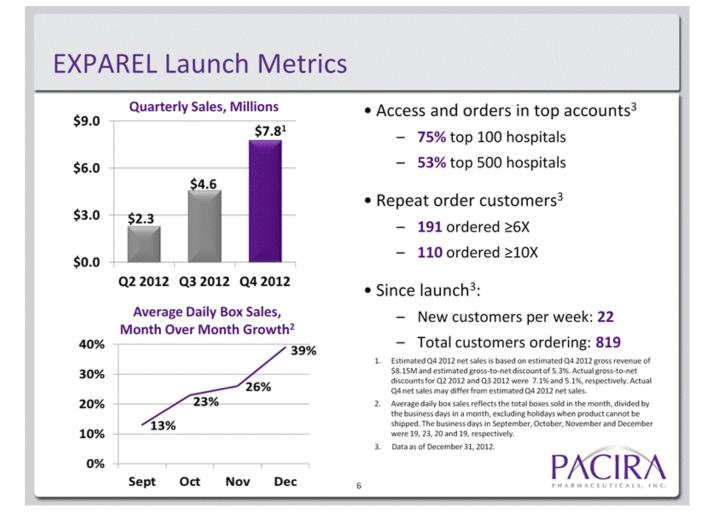


- DepoFoam utilizes membrane components that are based on natural and well tolerated sources and are cleared by normal metabolic pathways
- As incorporated in EXPAREL, DepoFoam is <3% lipid, biodegradable, and biocompatible
- No DepoFoam competitor No Near Term IP Cliff

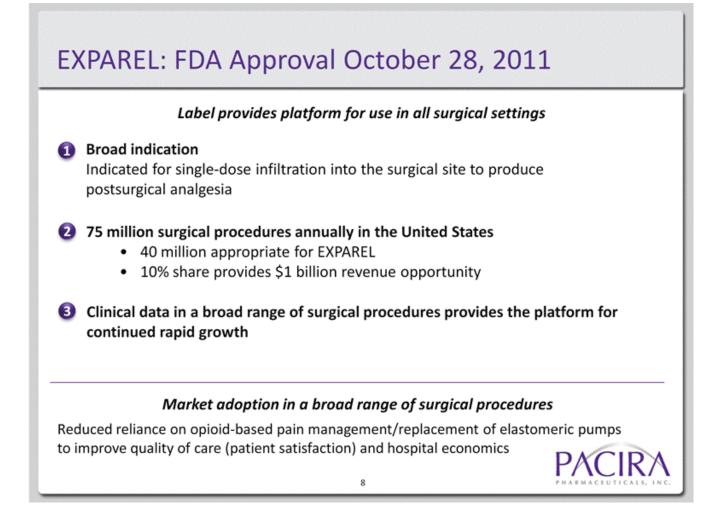
PACIRA

 Lambert WJ, Los K. DepoFoam multivesicular liposomes for the sustained release of macromolecules. In: Rathbone MJ, Hadgraft J, Roberts MS, Lane ME, eds. *Modified release drug delivery technology*. 2nd ed. New York: Informa Healthcare; 2008.
 \*As demonstrated in a pivotal soft tissue trial (hemorrhoidectomy) with a 72-hour endpoint.

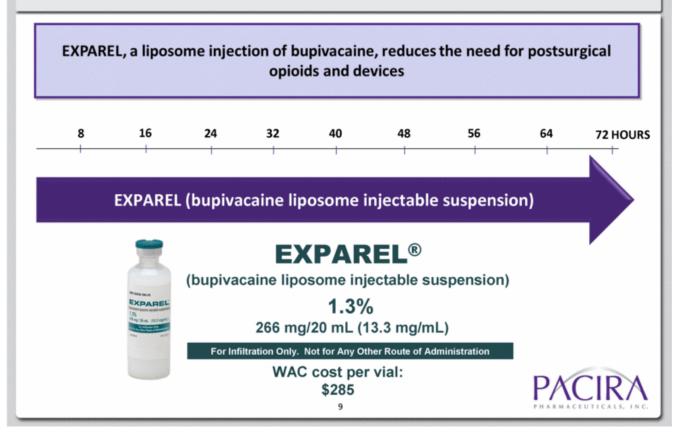
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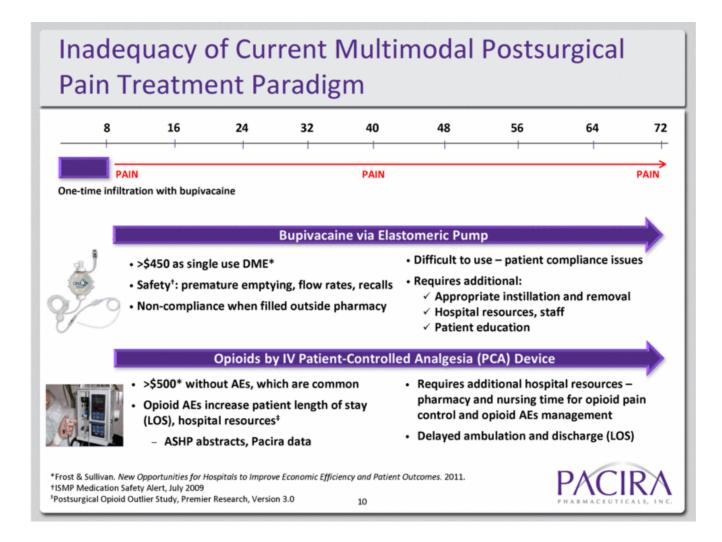












# EXPAREL Value Proposition Addresses a Significant Market Need

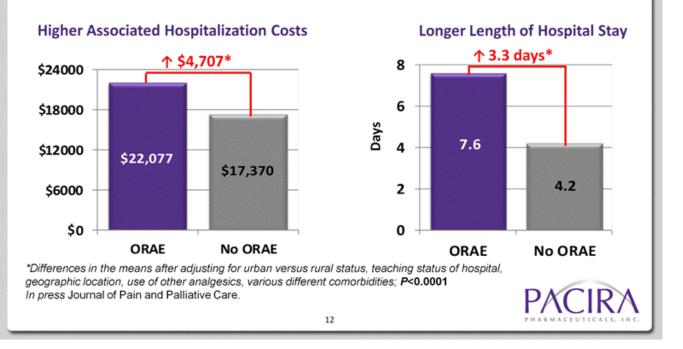
- FDA Approval
  - Efficacy and safety, P=0.0007 for patient satisfaction
- Quantify the true cost of opioids as the platform for postsurgical pain control
- Clinical data to support use in procedures of interest
  - Hemorrhoidectomy, open colectomy, lap colectomy, ileostomy reversal, total knee arthroplasty, abdominoplasty, iTAP procedures
  - Phase 3 development of nerve block indication
- Quality and reimbursement environment supports replacing opioids
  - JCAHO Alerts patients at risk for opioid-related adverse events
  - HCAHPS Reimbursement pain management and patient satisfaction





### National Analysis Demonstrates Impact of Opioid-Related Adverse Events on Hospitalization Costs

 In a recent retrospective analysis of 319,898 patients in 380 U.S. hospitals, opioid-related adverse events were associated with:



### Large Integrated Delivery Network: Characteristics That Increase Risk of Opioid Related Adverse Drug Events (ORAEs)—All Patients

	ORADE Odds Ratio	95% Cl (Lower, Upper)		P value*
Risk Factor for ORADE				
Age ≥65	2.02	1.65	2.47	<0.0001
Male	2.00	1.69	2.38	<0.0001
Prior Opioid Use	1.27	1.07	1.52	0.007
COPD	2.34	1.35	4.07	0.003
Cardiac dysrhythmias	5.39	3.92	7.42	<0.0001
Regional enteritis	4.30	2.05	9.04	0.0001
Diverticulitis	2.35	1.79	3.09	<0.0001
Ulcerative colitis	3.77	1.65	8.63	0.002

CI=confidence interval.

\*Logistic regression.

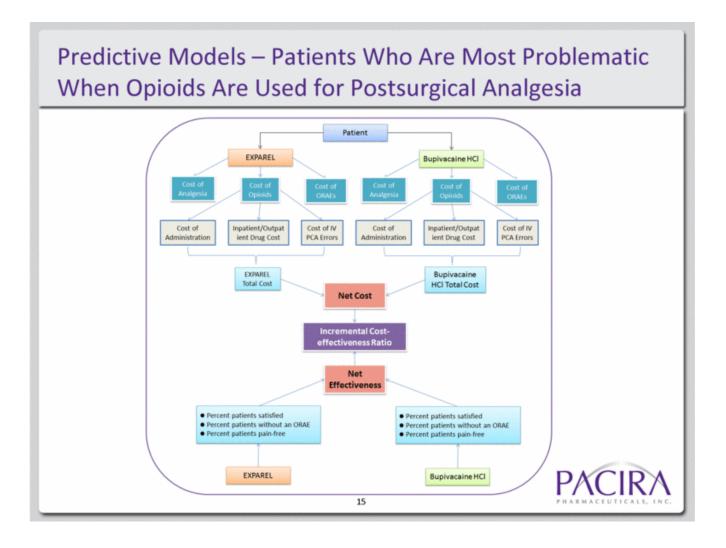
Data on file 6,274 (99.8%) who received postsurgical opioid treatment from Surgical Patient Retrospective Analysis at a single health system in Southeast United States of which 11.5% of these experienced an opioid related adverse drug event



PACIRA

### Cont. Large Integrated Delivery Network: Characteristics That Increase Risk of ORAEs by Gender

	ORADE Odds Ratio	95% CI		P value*
Risk Factor for ORADE		(Lower, Upper)		
MALE Age ≥65	1.51	1.11	2.06	0.009
Prior Opioid use	1.33	1.01	1.76	0.04
Cardiac dysrhythmias	5.99	3.70	9.69	<0.0001
COPD	2.72	1.23	5.99	0.0132
Diverticulitis	2.11	1.42	3.13	0.0002
Ulcerative colitis	6.33	2.19	18.29	0.0007
ВРН	5.18	3.24	8.31	<0.0001
Female Age ≥65	2.22	1.67	2.94	<0.0001
Cardiac dysrhythmias	4.91	3.16	7.62	<0.0001
Regional enteritis, large	8.34	3.05	22.83	<0.0001
Diverticulitis	2.48	1.67	3.69	<0.0001
Cl=confidence interval. *Logistic regression.	14		РАК	CIRA CEUTICALS, INC.



# Multimodal Strategies With EXPAREL Targeted to Reduce the Burden of Opioids

### The Joint Commission Sentinel Event

A complimentary publication of Issue 49, August 8, 2012 The Joint Commission

Safe use of opioids in hospitals

- Opioid analgesics rank among the drugs most frequently associated with adverse drug events
- A number of safety measures may reduce the risks of opioid-related adverse events
- Key patients warrant multimodal opioid sparing approaches; including non-opioid pain medications

#### Patients at the Highest Risk for Oversedation and Respiratory Depression

- Sleep apnea or sleep disorder
- Morbid obesity
- Snoring
- Older age
- · No recent opioid use
- Post-surgery, especially after upper abdominal or thoracic surgery
- · Increased opioid dose requirement
- Longer time receiving general anesthesia during surgery
- Concomitant use of other sedating drugs
- Smoker

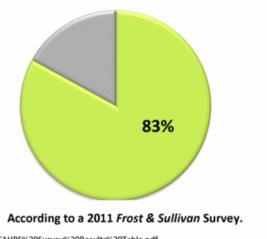
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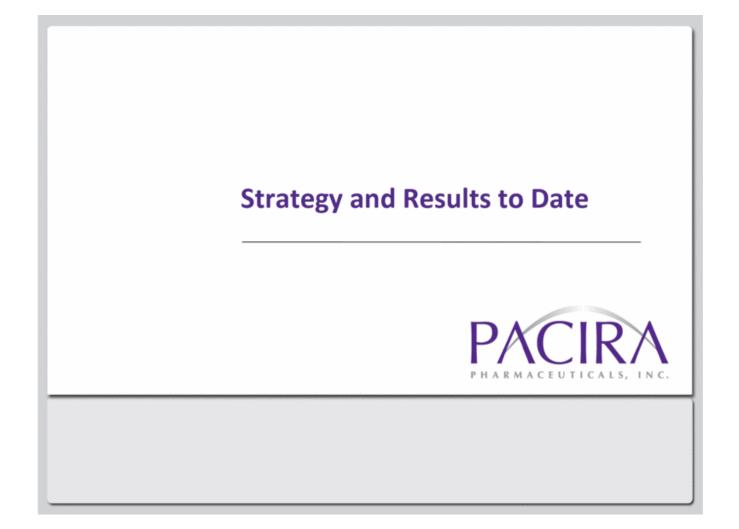
# HCAHPS - Pain Control Is an Important Metric of Patient Satisfaction With Hospital Performance

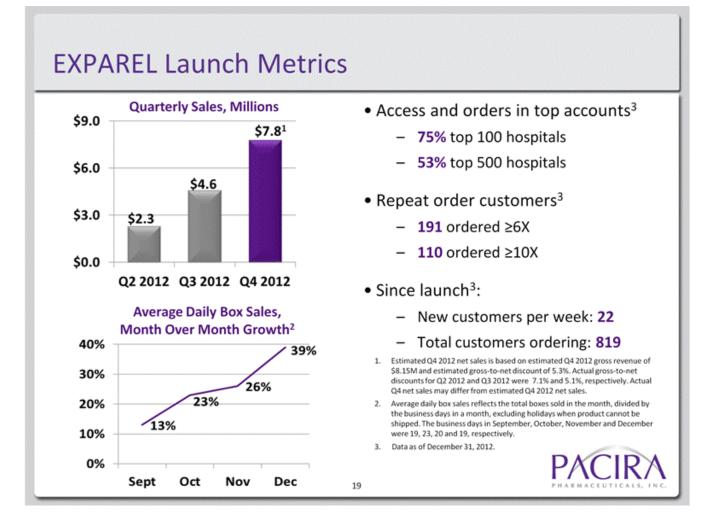
- According to the July 2012 HCAHPS report (discharges from 10/2010-9/2011), pain management received an average score of 70 (out of a possible 100)<sup>1</sup>
- Beginning with discharges in October 2012, HCAHPS performance will be used to calculate a portion of hospitals' value-based incentive payment from the Centers for Medicare & Medicaid Services (CMS)<sup>2</sup>

Medical/Surgical Nurses & CFOs Indicating That Patient Satisfaction Is Very Important to the Financial Health of Their Hospital<sup>3</sup>

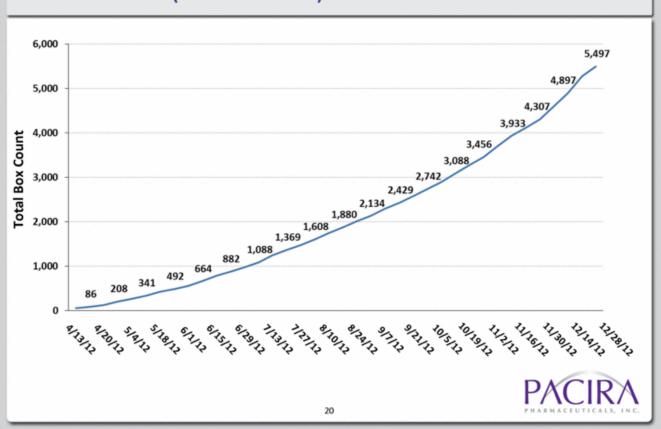


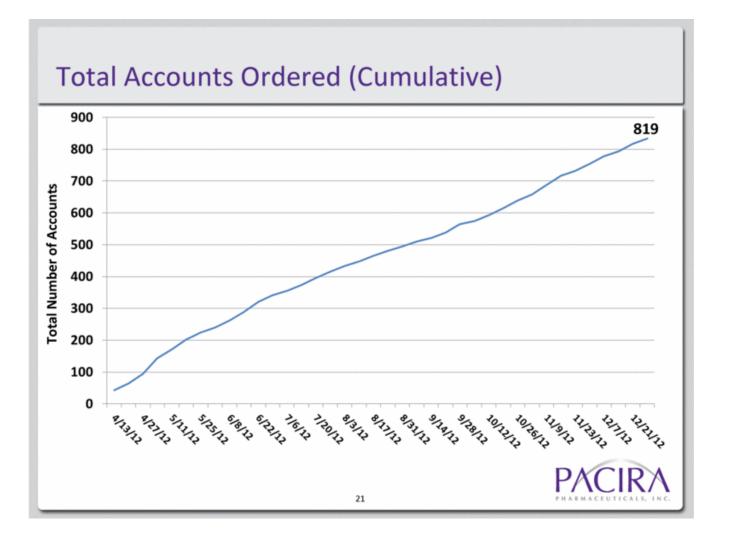
HCAHPS Website. http://www.hcahpsonline.org/files/July%202012%20Summary%20of%20HCAHPS%20Survey%20Results%20Table.pdf.
 Centers for Medicare & Medicaid Services, Baltimore, MD. December 12, 2011.
 HCAHPS fact sheet. HCAHPS Website. http://www.hcahpsonline.org. Accessed January 13, 2013.
 De Lorimier R. New Opportunities for Hospitals to Improve Economic Efficiency and Patient Outcomes: The case of EXPAREL, a long-acting, non-opioid local analgesic. Frost & Sullivan; Mountain View, CA. December 6, 2011.
 17

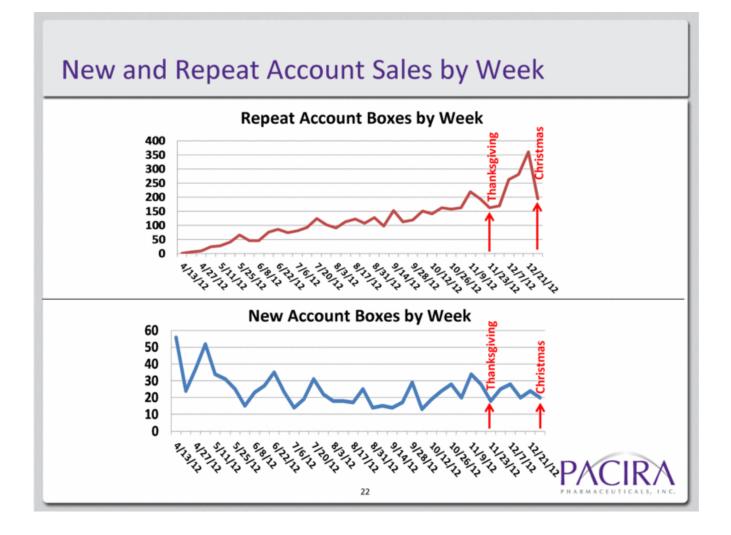




# Total Boxes (Cumulative)

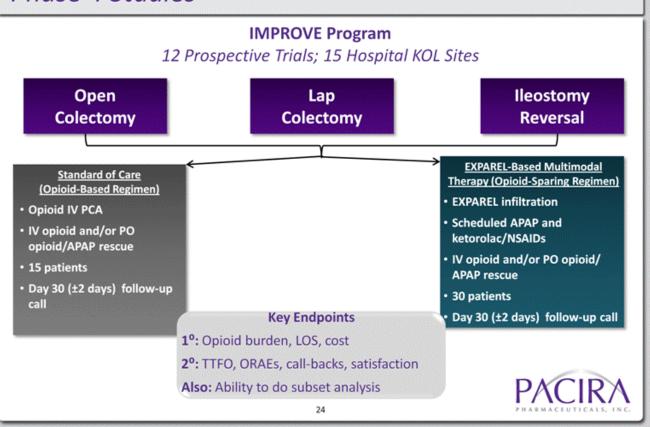








### Ongoing Clinical Development Programs Phase 4 Studies



# IMPROVE Trials: Key Opinion Leaders at Respected Sites

#### Open Colectomy

**Stephen Cohen** Southern Regional Medical Center

#### Lap Colectomy

Edward Lee Albany Medical College Eric Haas Methodist Hospital St. Luke's Episcopal Hospital Anjali Kumar Washington Cancer Institute Keith Candiotti University of Miami Jackson Memorial Hospital Sergio Bergese The Ohio State University Jorge Marcet University of South Florida

### Ileostomy Reversal

Single Center Jon Vogel Cleveland Clinic Marylise Boutros Cleveland Clinic Florida

Multicenter

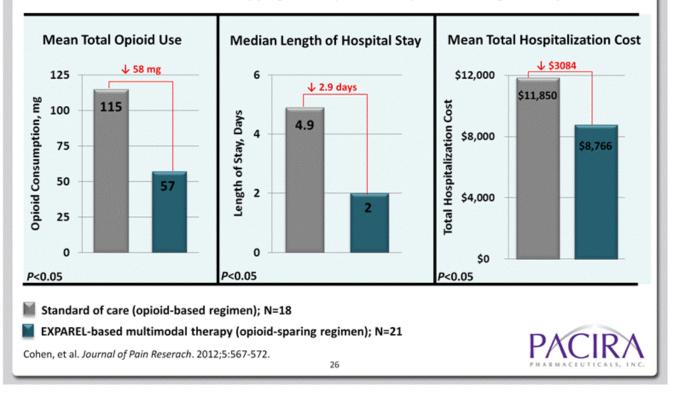
Sergio Larach Center for Colon/Rectal Surgery at the Florida Hospital Valentine Nfonsam University of Arizona Jorge Marcet University of South Florida





# Data From the Open Colectomy Study Demonstrated a 59% Reduction in LOS

EXPAREL-Based Multimodal Therapy Significantly Reduced Opioid Use, Length of Stay, and Cost



### EXPAREL Infiltration Into the Transversus Abdominis Plane (TAP) Is Safe and Effective at Flexible Volumes

- In both EXPAREL groups:
  - Patients required a mean of 0.7 oxycodone/acetaminophen tablets (5/325 mg) per day from their discharge until their Day 10 visit
  - 100% of the available subjects reported being either satisfied or extremely satisfied with their postsurgical pain control at hospital discharge, 72 hours, and Day 10
- Compared to a similar study<sup>1</sup> with bupivacaine HCl, patients had similar or better pain scores despite requiring materially fewer opioids

The volume of EXPAREL infiltrated into the TAP did not appear to influence the magnitude or duration of analgesia, supporting the contention that anesthesiologists can utilize whichever volume fits into their current practice

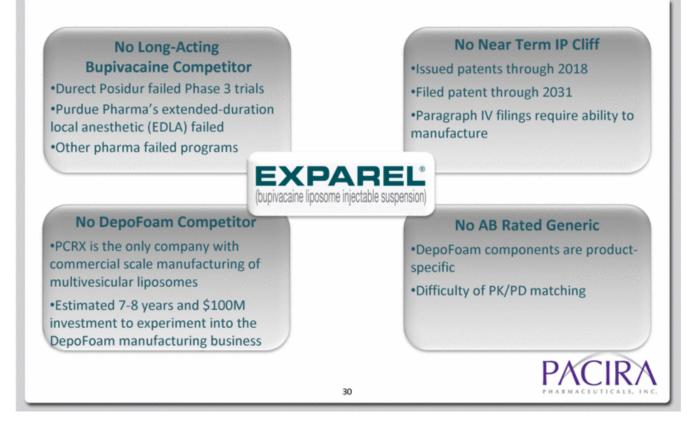
1. Chow C-H, et al. Poster presented at the American Society of Regional Anesthesia Spring Meeting, Las Vegas, NV, 2011.

### EXPAREL Launch: 1H 2013 Accelerators

- Field Force to Pacira Employees
- Continued Formulary Approvals provide access with key customer accounts hospitals, GPOs, IDNs, DoD
- Monthly Revenue growth, Repeat Customers, New Customers
- Publications and Congresses
  - Opioid Sparing data from GPO and IDN analyses
  - IMPROVE Lap Colectomy and Ileostomy reversal
  - EXCLAIM data in cosmetic dermatology procedures
  - Abstracts and Presentations at ASCRS, AORN, ASPAN, SAMBA
- First World Congress on Pain
- iTAP Phase 4 trial in abdominal soft tissue procedures
- Case Series Data Presentations
  - Orthopedics (TKA, Hip, Spine), Bariatrics, Aesthetics, iTAPS
- Collaborative training meetings with strategic partners ultrasound and device manufacturers



### EXPAREL Franchise Protection → Long-Term





Gross Margin Opportunity		Scalable Manufacturing Infrastructure
EBITDA & EPS Opportunity		Gross Margin Opportunity plus Scalable Specialty Commercial Organization
Select Financial Data	Q3 2012 (millions)	Outlook
Operating Expenses		
Cost of Revenues	\$ (9.3)	<ul> <li>For current EXPAREL manufacturing line, fixed annual expense in \$25 - \$30 million range and variable cost per unit of 10% to 15%</li> <li>DepoCyte fixed costs ~\$5 million</li> </ul>
Research and Development	(3.5)	<ul> <li>Includes ~\$12 to \$14 million to complete pivotal nerve block studies over the 6 quarters from Q3 2012 to Q4 2013</li> </ul>
Selling, General & Administrative	(11.4)	<ul> <li>Only moderate increase in selling professionals in 2013</li> <li>No expected material increase in G&amp;A</li> </ul>
Purchase of Fixed Assets	\$ (6.3)	<ul> <li>CapEx related to manufacturing expansion of ~\$5 million in Q1 2013</li> <li>Subsequent to Q1 2013, modest deferred maintenance and routine CapEx</li> </ul>
		DACIDA
		32 PHARMACEUTICALS, IN

### 2013: Year of Commitment to EXPAREL Commercialization

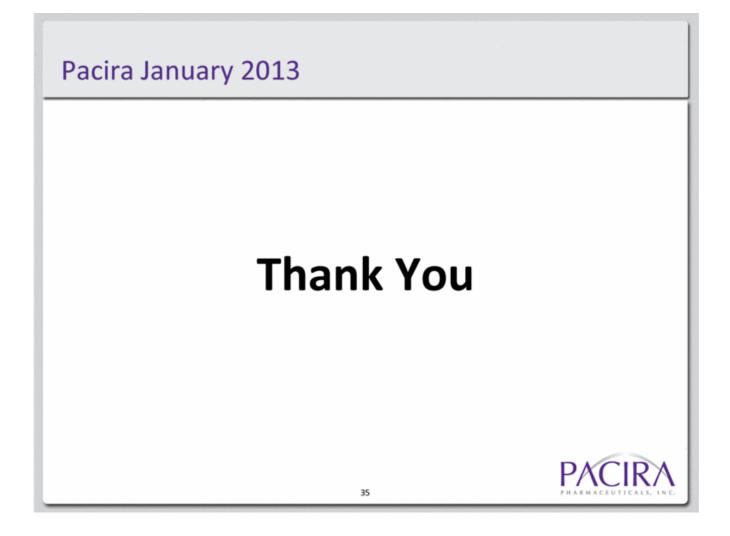
- Field Force Rolled Over to Pacira Employees 1.28.2013
  - Focus on top 500 hospitals performing >50% of US surgeries, soft tissue focus
- Scientific Affairs, Medical Affairs and Clinical Nursing Teams built out to address additional opportunities
  - Orthopedic, iTaps (anesthesia), cardiothoracic, nursing
- Commercial manufacturing build-out, fully automated manufacturing skids installed and manufacturing for sNDA approval
- Clinical development for additional indications, nerve block anesthesia audience
- Partnership opportunities
  - Partner for human EXPAREL (Ex-US)
- No competitor in clinical development for EXPAREL or DepoFoam, no generics
- EXPAREL provides the basis for Pacira as a successful investment and to continue to develop DepoFoam-based products – NSAID, Methotrexate – a multi-product specialty pain company

### Important Safety Information for EXPAREL

- EXPAREL is contraindicated in obstetrical paracervical block anesthesia
- EXPAREL has not been studied for use in patients younger than 18 years of age
- Non-bupivacaine-based local anesthetics, including lidocaine, may cause an immediate release
  of bupivacaine from EXPAREL if administered together locally. The administration of EXPAREL
  may follow the administration of lidocaine after a delay of 20 minutes or more. Other
  formulations of bupivacaine should not be administered within 96 hours following
  administration of EXPAREL
- Monitoring of cardiovascular and neurological status, as well as vital signs should be performed during and after injection of EXPAREL as with other local anesthetic products
- Because amide-type local anesthetics, such as bupivacaine, are metabolized by the liver, EXPAREL should be used cautiously in patients with hepatic disease. Patients with severe hepatic disease, because of their inability to metabolize local anesthetics normally, are at a greater risk of developing toxic plasma concentrations
- In clinical trials, the most common adverse reactions (incidence ≥10%) following EXPAREL administration were nausea, constipation, and vomiting







### **RISK FACTORS**

On January 15, 2013, Pacira Pharmaceuticals, Inc. (the "Company") announced its intention to offer \$80 million of aggregate principal amount of convertible senior notes due 2019, subject to market conditions and other factors (the "Private Placement"). We refer to these convertible senior notes due 2019 as the "notes." In connection with the Private Placement, the Company is providing the following updated 'Risk Factors,'' which are updated from the 'Risk Factors" included in the Company's Annual Report on Form 10-K for the year ended December 31, 2011 and the 'Risk Factors" included in the Company's quarterly reports on Form 10-Q for the quarters ended June 30, 2012 and September 30, 2012.

### 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 of EXPAREL. Our success depends on our ability to effectively commercialize EXPAREL, which was approved by the FDA on October 28, 2011, for administration into the surgical site to produce postsurgical analgesia.

We commercially launched EXPAREL in April of 2012, but our ability to effectively generate revenues from EXPAREL will depend on our ability to:

- create market demand for EXPAREL through our marketing and sales activities, and any other arrangements to promote this product we may later establish;
- train, deploy and support a qualified sales force which we initially developed on a contract basis with Quintiles and are in the process of hiring directly;
- 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;
- 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;
- ensure that our entire supply chain for EXPAREL 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.

As EXPAREL is a newly marketed drug, none of the members of the EXPAREL sales force have ever promoted EXPAREL. As a result, we 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,

1

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 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 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 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 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

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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 generally 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. 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 limit our ability to develop other indications for, or commercialize, EXPAREL. Our competitors may also develop drugs that are 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.

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# If we are unable to establish 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 currently building our commercial infrastructure for the marketing, sale and distribution of pharmaceutical products. In order to commercialize EXPAREL, we must build our marketing, sales and distribution capabilities. We have entered into an agreement with Quintiles for the outsourcing of our specialty sales force of approximately 60 representatives, which we are now in the process of hiring as direct employees. We may also seek to commercialize EXPAREL outside the United States, although we currently plan to do so with a marketing and sales collaborator and not with our own sales force.

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.

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.

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# 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, 2012, we had approximately 160 employees. We will 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;
- ensure that our consultants and other service providers successfully carry out their contractual obligations, provide high quality results, and meet expected deadlines;
- 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.

### We are reliant on our contract with Quintiles for the marketing and sale of EXPAREL.

We have an agreement with Quintiles for the outsourcing of a sales force to commercialize EXPAREL. The risks in outsourcing the sales function to any third party include the following:

- the third party may not apply the expected financial resources or required expertise to successfully market and sell EXPAREL;
- the third party may not invest in the development of a sales and marketing force and the related infrastructure at levels that ensure that sales of EXPAREL reach their full potential;
- the third party may not comply with applicable legal requirements, including the requirement to promote drug products only for uses for which they have been approved;

- disputes may arise between us and the third party that may adversely affect EXPAREL sales or profitability; or
- the third party may enter into agreements with other parties that have products that could compete with EXPAREL.

We are substantially dependent on the success of Quintiles in performing its responsibilities and the continued cooperation of Quintiles, including Quintiles' cooperation with our training of the sales and marketing force. Quintiles may not cooperate with us to perform its obligations under our agreement and we cannot control the amount and timing of Quintiles' resources that will be devoted to the marketing and sale of EXPAREL. The occurrence of any of these events could adversely affect the commercialization of EXPAREL and materially harm our business and stock price by slowing the pace of growth of such sales, by reducing the profitability of EXPAREL or by adversely affecting the reputation of EXPAREL in the market.

#### 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, particularly in the San Diego, California and northern New Jersey

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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 and chief executive officer. 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 chief executive officer, 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 businesss 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.

The Medicines and Healthcare products Regulatory Agency issued an inspection report noting certain critical deficiencies in our manufacturing of DepoCyt(e) and remediation of these deficiencies could result in significant costs or delays in the production and sale of DepoCyt(e).

In July 2012, the Medicines and Healthcare Regulatory Agency, or MHRA, conducted its standard inspection of our DepoCyt(e) manufacturing facility, which is located in a separate building from our EXPAREL manufacturing facility. Following its

inspection, 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. We temporarily ceased manufacturing DepoCyt(e) in order to implement a remediation plan and address the failures noted in the MHRA inspection report. In connection with the inspection report, the European Medicines Agency issued an assessment report which recommended the use of alternative treatments in countries where DepoCyt(e) is not deemed to be an essential medical product. 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." The assessment report did not recommend a recall for member countries where DepoCyt(e) is considered to have "essential medicinal product" status.

EU member states give "essential medicinal product" status to a product if there are no alternative treatments in such countries and each country made a determination of whether DepoCyt(e) was an "essential medicinal product" on a country by country basis. The extent of the recall's impact on our sales of DepoCyt(e) is difficult to predict because a number of countries that determined DepoCyt(e) was not an "essential medicinal product" also determined that it could still be used in exceptional circumstances or upon special request. The recall contributed to a reduction in product sales of DepoCyt(e) for the three and nine month ended September 30, 2012, respectively. We expect our sales of DepoCyt(e) in the EU to continue to decrease until we restart our manufacturing operations of DepoCyt(e) for the European market.

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We are close to completing the implementation of our remediation plan. In December 2012, the MHRA re-inspected our DepoCyt(e) manufacturing facility to review progress in the implementation of our remediation commitments arising from the July 2012 inspection. Following the inspection, the MHRA issued a report in which it found several major, but no critical, failures to comply with the Principles and Guidelines of Good Manufacturing Practices. On December 29, 2012, we submitted a response to this report addressing, and proposing remedies, for each of the failures identified by the MHRA. Production of DepoCyt(e) for sales in Europe remains suspended pending the MHRA's feedback on this response.

We advised the FDA of the MHRA' s inspectional findings after we received the July inspection report, and the FDA indicated it had no issue with continued distribution of DepoCyt(e) in the U.S. market pending our remediation efforts. We resumed production of DepoCyt(e) for sales in the United States in January 2013. While we will conduct additional training to address the MHRA inspection findings, we may be required to take steps to address the MHRA inspection findings that are in addition to the remediation plan we have completed and the remediation actions we have proposed to the MHRA in our December 29, 2012 response. This could result in additional costs or delays in the production and sale of DepoCyt(e), which could have a material adverse effect on our business, financial position and results of operations.

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

The use of DepoCyt(e), DepoDur, 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 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

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drugs that had unanticipated side effects. A successful product 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 current Good Manufacturing Practices, or 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, imposition of a consent decree, or withdrawal of product approval, 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.

In addition, we purchase raw materials and components from various suppliers in order to manufacture EXPAREL. If we are unable to source the required raw materials from our suppliers, we may experience delays in manufacturing EXPAREL and may not be able to meet our customers' demands for EXPAREL.

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.

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

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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.

If we are unable to achieve and maintain satisfactory production yields and quality as we expand our manufacturing capabilities, our relationships with potential customers and overall reputation may be harmed, and our revenues could decrease.

# We are the sole manufacturer of DepoCyt(e). Our inability to continue manufacturing adequate supplies of DepoCyt(e) could result in a disruption in the supply of DepoCyt(e) to our partners.

We are the sole manufacturer of DepoCyt(e). We develop and manufacture DepoCyt(e) at our facility in San Diego, California, which is the only FDA approved site for manufacturing DepoCyt(e) in the world. In connection with our response to the MHRA regarding their inspectional observations, we temporarily ceased manufacturing DepoCyt(e) in order to implement our remediation plan and address the failures noted in the MHRA inspection report. The implementation of our remediation plan is almost complete. In December 2012, the MHRA conducted a further inspection of our DepoCyt(e) manufacturing facility to review progress in the implementation of our remediation commitments arising from the MHRA's July 2012 inspection. Following the December 2012 inspection, the MHRA issued a report in which it found several major, but no critical, failures to comply with the Principles and Guidelines of Good Manufacturing Practices. On December 29, 2012, we submitted a response to this report addressing, and proposing remedies, for each of the failures identified by the MHRA. We are currently awaiting the MHRA's feedback on this response. Our ability to recommence manufacturing of DepoCyt(e) for European sales depends on the MHRA's satisfaction with the remedies proposed in our December 29, 2012, response. We advised the FDA of the MHRA's inspectional findings after we received the July inspection report, and the FDA indicated it had no issue with continued distribution of DepoCyt(e) in the U.S. market pending our remediation efforts. We resumed production of DepoCyt(e) for sales in the United States in January 2013. The temporary cessation of the manufacturing of DepoCyt(e) for sales in the United States in January 2013. The temporary cessation of the manufacturing of DepoCyt(e) for sales in the United States in January 2013. The temporary cessation of the manufacturing of DepoCyt(e) for sales in the EU could result in additional costs or delays in the production and sale of DepoCyt(e), which could have a material adverse effect on

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 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 DepoCyt(e) at our facility in San Diego, California could result in a disruption in the supply of DepoCyt(e) to our partners and breach of our contractual obligations.

### If we fail to manufacture DepoCyt(e) we will lose revenues and be in breach of our licensing obligations.

We have licensed the commercial rights in specified territories of the world to market and sell DepoCyt(e). Under those licenses we have obligations to manufacture commercial product for our commercial partners. If we are unable to timely fill the orders placed with us by our commercial partners, we will potentially lose revenue and be in breach of our licensing obligations under the agreements. In addition, we may be in breach of our obligations to comply with our supply and distribution agreements, which would in turn be a breach of our obligations under our amended and restated royalty interests assignment agreement, or the Amended and Restated Royalty Interests Assignment Agreement, with Royalty Securitization Trust I, an affiliate of Paul Capital Advisors, LLC,

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or Paul Capital. 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 cash flows, results of operations and our financial condition.

As discussed above, we have temporarily ceased manufacturing DepoCyt(e) for sales in Europe in order to implement our remediation plan to address the MHRA's inspectional observations. Our ability to recommence manufacturing of DepoCyt(e) for European sales depends on the MHRA's satisfaction with the remedies proposed in our December 29, 2012 response.

We rely on third parties for the timely supply of specified raw materials and equipment for the manufacture of DepoCyt(e). 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.

The manufacture of pharmaceutical products 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 cGMP regulations. Any failure to comply with applicable regulations, or failure of government agencies to provide necessary authorizations, may result in fines and civil penalties, suspension of production, suspension or delay in product approval for sale, product seizure or recall, or withdrawal of product approval, and would limit the availability of our product. Any manufacturing defect or error discovered after products have been produced and distributed could also result in significant consequences, including costly recall procedures, re-stocking costs, damage to our reputation, product liability claims and litigation.

# 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:

- 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 in managing multiple product development programs; and
- inability to successfully develop new products or clinical failure.

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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 other competitors in our efforts to establish new collaborations and in-licensing opportunities. These competitors likely will have access to greater financial resources than us and may have greater expertise in identifying and evaluating new opportunities. 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, unauthorized access, natural disasters, 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.

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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.

### **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.

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, 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.

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Following approval of EXPAREL or any of our product candidates, if we or others later identify undesirable side effects caused by 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 or change the labeling of the product;
- we may be subject to 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 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.

#### EXPAREL and any other products we may market, including DepoCyt(e), will remain subject to substantial regulatory scrutiny.

EXPAREL, DepoCyt(e) and any product candidates that we may develop, license or acquire will also be subject to ongoing FDA requirements with respect to the manufacturing, labeling, packaging, storage, distribution, advertising, promotion, record-keeping, post-market testing, and submission of

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safety and other post-market information on the drug. In addition, the subsequent discovery of previously unknown problems with a product, including undesirable side effects, may result in restrictions on the product, including withdrawal of the product from the market.

If EXPAREL, DepoCyt(e) or any other product that we may develop, license or acquire fails to comply with applicable regulatory requirements, such as cGMP regulations, a regulatory agency may:

- issue warning letters or untitled letters;
- require us to enter into a consent decree, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- impose fines and other civil or criminal penalties;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications filed by us;
- impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products or require a product recall.

For example, 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 have responded to the MHRA regarding the inspectional observations and were reinspected by the MHRA in December 2012. We are currently waiting for a formal response from the MHRA on the results of our remediation plan. The MHRA may require us to take additional steps to address its findings, which could result in additional costs or delays in the production and sale of DepoCyt(e) for the European market, which could have a material adverse effect on our business, financial position and results of operations.

### 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;

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- 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 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.

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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 have responded to the MHRA regarding these inspectional observations, have almost completed implementation of our proposed remediation plan and were reinspected by the MHRA in December 2012. We are currently waiting for a formal response from the MHRA. The MHRA may require us to take additional steps to address the MHRA inspection findings, which could result in additional costs or delays in the production and sale of DepoCyt(e) for the European market, which could have a material adverse effect on our business, financial position and results of operations.

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# 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, 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 our contract manufactures 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;
- 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.

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Third party payers, whether foreign or domestic, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. 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. 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:

- 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% 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% 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;
- 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% 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

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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. 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.

Recently, the President signed into law the Food and Drug Administration Safety and Innovation Act, or FDASIA. The new law and related agreements make 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;
- revises certain standards and requirements for FDA inspections of manufacturing facilities and the importation of drug products from foreign countries;

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- 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 FDA to issue a report on, among other things, ensuring the safety of prescription drugs that have the potential for abuse;
- requires FDA to hold a public meeting regarding the potential rescheduling of drug products containing hydrocodone, which was held in October 2012; and
- requires electronic submission of certain marketing applications following the issuance of final FDA regulations.

The full impact on our business of the new law 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

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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-party's generic drug product. A certification that the new product will not infringe the Orange Book-listed patents for EXPAREL, or that such patents are invalid, is called a paragraph IV certification. If the third party submits a paragraph IV certification to the FDA, a notice of the paragraph IV certification must also be sent to us once the third-party's ANDA is accepted for filing by the FDA. We may then initiate a lawsuit to defend the patents identified in the notice. The filing of a patent infringement lawsuit within 45 days of receipt of the notice automatically prevents the FDA from approving the third-party's ANDA until the earliest of 30 months or the date on which the patent expires, the lawsuit is settled, or the court reaches a decision in the infringement lawsuit in favor of the third party. If we do not file a patent infringement lawsuit within the required 45-day period, the third-party's ANDA will not be subject to the 30-month stay. Litigation or other proceedings to enforce or defend intellectual property rights are often very complex in nature, may be very expensive and time-consuming, may divert our management's attention from our core business, and may result in unfavorable results that could adversely impact our ability to prevent third parties from competing with our products.

### Because it is difficult and costly to protect our proprietary rights, we may not be able to ensure their protection and all patents will eventually expire.

Our commercial success will depend in part on obtaining and maintaining patent protection and trade secret protection for EXPAREL, DepoCyt(e), DepoFoam and for any product candidates that we may develop, license or acquire and the methods we use to manufacture them, as well as successfully defending these patents and trade secrets against third-party challenges. We will only be able to protect our technologies from unauthorized use by third parties to the extent that valid and enforceable patents or trade secrets cover them.

The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in pharmaceutical or biotechnology patents has emerged to date in the United States. Patent positions and policies outside the United States are

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even more uncertain. Changes in either the patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents.

The degree of future protection for our proprietary rights is uncertain, because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- we may not have been the first to make the inventions covered by each of our pending patent applications and issued patents;
- we may not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies or duplicate any of our product candidates or technologies;
- it is possible that none of the pending patent applications will result in issued patents;

- the issued patents covering our product candidates may not provide a basis for commercially viable active products, may not provide us with any competitive advantages, or may be challenged by third parties;
- we may not develop additional proprietary technologies that are patentable; or
- patents of others may have an adverse effect on our business; or
- competitors may infringe our patents and we may not have adequate resources to enforce our patents.

Patent applications in the United States are maintained in confidence for at least 18 months after their earliest effective filing date. Consequently, we cannot be certain we were the first to invent or the first to file patent applications on EXPAREL, our DepoFoam drug delivery technology or any product candidates that we may develop, license or acquire. In the event that a third party has also filed a U.S. patent application relating to our product candidates or a similar invention, we may have to participate in interference proceedings declared by the U.S. Patent and Trademark Office to determine priority of invention in the United States. The costs of these proceedings could be substantial and it is possible that our efforts would be unsuccessful, resulting in a material adverse effect on our U.S. patent position. Furthermore, we may not have identified all United States and foreign patents or published applications that affect our business either by blocking our ability to commercialize our drugs or by covering similar technologies that affect our drug market.

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In addition, some countries, including many in Europe, do not grant patent claims directed to methods of treating humans, and in these countries patent protection may not be available at all to protect our product candidates. Even if patents issue, we cannot guarantee that the claims of those patents will be valid and enforceable or provide us with any significant protection against competitive products, or otherwise be commercially valuable to us. Furthermore, while we generally apply for patents in those countries where we intend to make, have made, use, or sell patented products, we may not accurately predict all of the countries where patent protection will ultimately be desirable. If we fail to timely file a patent application in any such country, we may be precluded from doing so at a later date. We also cannot assure you that the patents issuing as a result of our foreign patent applications will have the same scope of coverage as our United States patents.

Some of our older patents have already expired. In the case of DepoCyt(e), key patents providing protection in Europe have expired. In the case of EXPAREL our European patent application has been granted and provides protection through November 2018. In the United States, our application is pending, and if granted, would provide protection for EXPAREL in the United States through November 2018, an existing formulation patent for EXPAREL will expire in November 2013. Once our patents covering EXPAREL have expired, we are more reliant on trade secrets to protect against generic competition.

We also rely on trade secrets to protect our technology, particularly where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. While we use reasonable efforts to protect our trade secrets, our licensors, employees, consultants, contractors, outside scientific collaborators and other advisors may unintentionally or willfully disclose our information to competitors. Enforcing a claim that a third party illegally obtained and is using our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, trade secret laws in other countries may not be as protective as they are in the United States. Thus, courts outside the United States are sometimes less willing to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

If we fail to obtain or maintain patent protection or trade secret protection for EXPAREL, DepoCyt(e), DepoFoam or any product candidate that we may develop, license or acquire, third parties could use our proprietary information, which could impair our ability to compete in the market and adversely affect our ability to generate revenues and achieve profitability.

## If we are sued for infringing intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in any litigation would harm our business.

Our ability to develop, manufacture, market and sell EXPAREL, our DepoFoam drug delivery technology or any product candidates that we may develop, license or acquire depends upon our ability to avoid infringing the proprietary rights of third parties. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the general fields of pain management and cancer treatment and cover the use of numerous compounds and formulations in our targeted markets. Because of the uncertainty inherent in any patent or other litigation involving proprietary rights, we and our licensors may not be successful in defending intellectual property claims by third parties, which could have a material adverse effect on our results of operations. Regardless of the outcome of any litigation, defending the litigation may be expensive, time-consuming and distracting to management. In addition, because patent applications can take many years to issue, there may be currently pending applications, unknown to us, which may later result in issued patents that EXPAREL or DepoCyt(e) may infringe. There could also be existing patents of which we are not aware that EXPAREL or DepoCyt(e) may infringe.

There is a substantial amount of litigation involving patent and other intellectual property rights in the biotechnology and biopharmaceutical industries generally. If a third party claims that we infringe on their products or technology, we could face a number of issues, including:

- infringement and other intellectual property claims which, with or without merit, can be expensive and time consuming to litigate and can divert management' s attention from our core business;
- substantial damages for past infringement which we may have to pay if a court decides that our product infringes on a competitor's patent;
- a court prohibiting us from selling or licensing our product unless the patent holder licenses the patent to us, which it would not be required to do;
- if a license is available from a patent holder, we may have to pay substantial royalties or grant cross licenses to our patents; and
- redesigning our processes so they do not infringe, which may not be possible or could require substantial funds and time.

### We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

As is common in the biotechnology and pharmaceutical industry, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

### **Risks Related to Our Financial Condition and Capital Requirements**

### We have incurred significant losses since our inception and anticipate that we will incur continued losses for the foreseeable future.

We are an emerging specialty pharmaceutical company with a limited operating history. We have focused primarily on developing and commercializing EXPAREL. We have incurred losses in each year since our inception in December 2006, including net

losses of \$43.3 million, \$27.1 million and \$31.7 million, for the years ended December 31, 2011, 2010, and 2009, respectively. As of September 30, 2012, we had an accumulated deficit of \$216.2 million. These losses, among other things, have had, and will continue to have, an adverse effect on our stockholders' equity and working capital. We incurred significant pre-commercialization expenses during 2010 and 2011 as we prepared for the commercial launch of EXPAREL, and we incur significant sales, marketing and manufacturing expenses, as well as continued development expenses related to the commercialization of EXPAREL. As a result, we expect to continue to incur significant losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when we will become profitable, if at all.

### We may never become profitable.

Our ability to become profitable depends upon our ability to generate revenue from EXPAREL. Our ability to generate revenue depends on a number of factors, including, but not limited to, our ability to:

- manufacture commercial quantities of EXPAREL, at acceptable cost levels; and
- continue to develop a commercial organization and the supporting infrastructure required to successfully market and sell EXPAREL.

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We anticipate incurring significant additional costs associated with the commercialization of EXPAREL. We also do not anticipate that we will achieve profitability for a period of time after generating material revenues, if ever. If we are unable to generate revenues, we will not become profitable and may be unable to continue operations without continued funding.

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.

On March 23, 2007, we entered into the Amended and Restated Royalty Interests Assignment Agreement with affiliates of Paul Capital, pursuant to which we assigned to Paul Capital the right to receive a portion of our royalty payments from DepoCyt(e) and DepoDur. To secure our obligations to Paul Capital, we granted Paul Capital a security interest in collateral, which includes the royalty payments we are entitled to receive with respect to sales of DepoCyt(e) and DepoDur, as well as to bank accounts to which such payments are deposited. Under our arrangement with Paul Capital, upon the occurrence of certain events, or the put events, including if we experience a change of control, we or PPI-CA undergo certain bankruptcy events, transfer any or substantially all of our rights in DepoCyt(e) or DepoDur, transfer all or substantially all of our assets, breach certain of the covenants, representations or warranties under the Amended and Restated Royalty Interests Assignment Agreement, or sales of DepoCyt(e) or DepoDur are suspended due to an injunction or if we elect to suspend sales of DepoCyt(e) or DepoDur as a result of a lawsuit filed by certain third parties, Paul Capital may (i) require us to repurchase the rights we assigned to it at a cash price equal to (a) 50% of all cumulative payments made by us to Paul Capital under the Amended and Restated Royalty Interests Assignment Agreement during the preceding 24 months, multiplied by (b) the number of days from the date of Paul Capital's exercise of such option until December 31, 2014, divided by 365. 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.

Our debt obligations expose us to risks that could adversely affect our business, operating results and financial condition. We may need to raise additional capital to pay our indebtedness as it comes due.

We have a substantial level of debt. As of September 30, 2012, we had \$27.5 million in aggregate principal amount of indebtedness outstanding, not including our obligation under the Amended and Restated Royalty Interests Assignment Agreement with Paul Capital.

In addition, our definitive loan and security agreement governing our \$27.5 million credit facility with Oxford Finance LLC, as lender, or the Oxford Credit Facility, contains a number of affirmative and restrictive covenants, including reporting requirements and collateral limitations, certain limitations on liens and indebtedness, dispositions, mergers and acquisitions, restricted payments and investments, corporate changes and limitations on waivers and amendments to certain agreements. Our failure to comply with the covenants in the loan and security agreement governing the Oxford Credit Facility could result in an event of default that, if not cured or waived, could result in the acceleration of all or a substantial portion of our debt and potential foreclosure on the assets pledged to secure the debt.

Although we intend to repay all amounts outstanding under, and terminate, the Oxford Credit Facility, we may enter into another credit facility or other agreement with similar or additional restrictions.

We may need to raise additional capital to pay our indebtedness as it comes due. If we are unable to obtain funds necessary to make required payments, or if we fail to comply with the various requirements of our indebtedness, we would be in default, which would permit the holders of our indebtedness to accelerate the maturity of the indebtedness and could cause defaults under any indebtedness we may incur in the future. Any default under our indebtedness would have a material

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adverse effect on our business, operating results and financial condition. If we are unable to refinance or repay our indebtedness as it becomes due, we may become insolvent and be unable to continue operations. The level and nature of our indebtedness, among other things, could:

- make it difficult for us to make payments on our outstanding debt from time to time or to refinance it;
- make it difficult for us to obtain any necessary financing in the future for working capital, capital expenditures, debt service, product and company acquisitions or general corporate purposes;
- limit our flexibility in planning for or reacting to changes in our business including life cycle management;
- reduce funds available for use in our operations;
- impair our ability to incur additional debt because of financial and other restrictive covenants;
- make us more vulnerable in the event of a downturn in our business;
- place us at a possible competitive disadvantage relative to less leveraged competitors and competitors that have better access to capital resources;
- restrict the operations of our business as a result of provisions in the Amended and Restated Royalty Interests Assignment
  Agreement with Paul Capital that restrict our ability to (i) amend, waive any rights under, or terminate any material
  agreements relating to DepoCyt(e) and DepoDur, (ii) enter into any new agreement or amend or fail to exercise any of our
  material rights under existing agreements that would materially adversely affect Paul Capital's royalty interest, and
  (iii) sell any material assets related to DepoCyt(e) or DepoDur; or

• impair our ability to merge or otherwise effect the sale of the Company due to the right of the holders of certain of our indebtedness to accelerate the maturity date of the indebtedness in the event of a change of control of the Company.

### Our short operating history makes it difficult to evaluate our business and prospects.

We were incorporated in December 2006 and have only been conducting operations with respect to EXPAREL since March 2007. Our operations to date have been limited to organizing and staffing our company, conducting product development activities, including clinical trials and manufacturing development activities, for EXPAREL and manufacturing and related activities for DepoCyt(e) and DepoDur. Further, in 2010, 2011 and 2012 we worked to establish our commercial infrastructure for EXPAREL, which we launched in the second quarter of 2012. Consequently, any predictions about our future performance may not be as accurate as they could be if we had a history of successfully developing and commercializing pharmaceutical products.

# We may need additional funding and may be unable to raise capital when needed, which would force us to delay, reduce or eliminate our product development programs or commercialization efforts.

Developing and commercializing products for use in the hospital setting, conducting clinical trials, establishing outsourced manufacturing relationships and successfully manufacturing and marketing drugs that we may develop is expensive. We may need to raise additional capital to:

- continue to fund our operations;
- continue our efforts to hire, and outsource through our relationship with Quintiles, additional personnel and build a commercial infrastructure to commercialize EXPAREL;
- qualify and outsource the commercial-scale manufacturing of our products under cGMP; and
- in-license and develop additional product candidates.

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We may not have sufficient financial resources to continue our operations or meet all of our objectives, which could require us to postpone, scale back or eliminate some, or all, of these objectives. Our future funding requirements will depend on many factors, including, but not limited to:

- the costs of maintaining a commercial organization to sell, market and distribute EXPAREL;
- the success of the commercialization of EXPAREL;
- the cost and timing of manufacturing sufficient supplies of EXPAREL to meet customer demand, including the cost of expanding our manufacturing facilities to produce EXPAREL;
- the rate of progress and costs of our efforts to prepare for the submission of an NDA for any product candidates that we may in-license or acquire in the future, and the potential that we may need to conduct additional clinical trials to support applications for regulatory approval;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights associated with our product candidates, including any such costs we may be required to expend if our licensors are unwilling or unable to do so;

- the effect of competing technological and market developments;
- the terms and timing of any collaborative, licensing, co-promotion or other arrangements that we may establish; and
- the potential that we may be required to file a lawsuit to defend our patent rights or regulatory exclusivities from challenges by companies seeking to market generic versions of extended-release liposome injection of bupivacaine.

Future capital requirements will also depend on the extent to which we acquire or invest in additional complementary businesses, products and technologies.

Until we can generate a sufficient amount of product revenue, if ever, we expect to finance future cash needs through public or private equity offerings, debt financings, product supply revenue and royalties, corporate collaboration and licensing arrangements, as well as through interest income earned on cash and investment balances. We cannot be certain that additional funding will be available on acceptable terms, or at all. If adequate funds are not available, we may be required to delay, reduce the scope of, or eliminate, one or more of our development programs or our commercialization efforts.

### Our quarterly operating results may fluctuate significantly.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- our ability to establish and maintain the necessary commercial infrastructure to sell EXPAREL without substantial delays, including engaging additional sales and marketing personnel and contracting with third parties for warehousing, distribution, cash collection and related commercial activities;
- maintaining our existing manufacturing facilities and expanding our manufacturing capacity, including installing specialized processing equipment for the manufacturing of EXPAREL;
- our execution of other collaborative, licensing or similar arrangements and the timing of payments we may make or receive under these arrangements;
- variations in the level of expenses related to our future development programs;
- any product liability or intellectual property infringement lawsuit in which we may become involved;
- regulatory developments affecting EXPAREL or the product candidates of our competitors; and
- the level of underlying hospital demand for EXPAREL and wholesaler buying patterns.

If our quarterly or annual operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly or annual fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

## Raising additional funds by issuing securities may cause dilution to existing stockholders and raising funds through lending and licensing arrangements may restrict our operations or require us to relinquish proprietary rights.

To the extent that we raise additional capital by issuing equity securities, our existing stockholders' ownership will be diluted. If we raise additional funds through licensing arrangements, it may be necessary to relinquish potentially valuable rights to our potential products or proprietary technologies, or grant licenses on terms that are not favorable to us. Any debt financing we enter into may involve covenants that restrict our operations. These restrictive covenants may include limitations on additional borrowing and specific restrictions on the use of our assets as well as prohibitions on our ability to create liens, pay dividends, redeem our stock or make investments.

### We incur significant costs as a result of operating as a public company.

As a public company, we incur significant legal, accounting, insurance and other expenses that we did not incur as a private company, including costs associated with public company reporting requirements. We also have incurred and will incur costs associated with complying with the requirements of the Sarbanes-Oxley Act of 2002 and related rules implemented by the Securities and Exchange Commission and The NASDAQ Global Select Market. The expenses incurred by public companies generally for reporting and corporate governance purposes have been increasing. We expect these rules and regulations to increase our legal and financial compliance costs and to make some activities more time-consuming and costly, although we are currently unable to estimate these costs with any degree of certainty. These laws and regulations could also make it more difficult or costly for us to obtain or maintain certain types of insurance, including director and officer liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. These laws and regulations could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as our executive officers. Furthermore, if we are unable to satisfy our obligations as a public company, we could be subject to delisting of our common stock, fines, sanctions and other regulatory action and potentially civil litigation.

# Compliance with Section 404 of the Sarbanes-Oxley Act of 2002 requires our management to devote substantial time to compliance initiatives, and if our independent registered public accounting firm is unable to provide an unqualified attestation report on our internal controls, our stock price could be adversely affected.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish a report by our management on the effectiveness of our internal control over financial reporting. The internal control report must contain (i) a statement of management's responsibility for establishing and maintaining adequate internal control over financial reporting, (ii) a statement identifying the framework used by management to conduct the required evaluation of the effectiveness of our internal control over financial reporting and (iii) management's assessment of the effectiveness of our internal control over financial reporting as of the end of our most recent fiscal year, including a statement as to whether or not internal control over financial reporting is effective.

To achieve compliance with Section 404 within the prescribed period, we are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we dedicate internal resources, hire additional employees for our finance

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and audit functions, potentially engage outside consultants and adopted a detailed work plan to (i) assess and document the adequacy of internal control over financial reporting, (ii) continue steps to improve control processes where appropriate, (iii) validate through testing that controls are functioning as documented, and (iv) implement a continuous reporting and improvement process for internal control over financial reporting. In addition, in connection with the attestation process by our independent registered public accounting firm, we may encounter problems or delays in completing the implementation of any requested improvements and receiving a favorable attestation. If we cannot favorably assess the effectiveness of our internal control over financial reporting, or if our independent

registered public accounting firm is unable to provide an unqualified attestation report on our internal controls, investors could lose confidence in our financial information and our stock price could decline.

#### The use of our net operating loss carryforwards and research tax credits may be limited.

We have significant federal and state net operating loss carryforwards and federal and state research and development tax credit carryforwards. Our net operating loss carryforwards and research and development tax credits may expire and not be used. Our net operating loss carryforwards will begin expiring in 2026 for federal purposes and 2018 for state purposes if we have not used them prior to that time, and our federal tax credits will begin expiring in 2028 unless previously used. Our state tax credits carryforward indefinitely. Additionally, our ability to use any net operating loss and credit carryforwards to offset taxable income or tax, respectively, in the future will be limited under Internal Revenue Code Sections 382 and 383 if we have a cumulative change in ownership of more than 50% within a three-year period. Such an ownership change may be triggered by the completion of our initial public offering. private placements and other transactions that have occurred, coupled with any future offering that we may undertake to fulfill our need to raise substantial additional funding to finance our operations. In the event such an ownership change occurs, we will be limited regarding the amount of net operating loss carryforwards and research tax credits that could be utilized annually in the future to offset taxable income or tax, respectively. Any such annual limitation may significantly reduce the utilization of the net operating loss carryforwards and research tax credits before they expire. In addition, California and certain states have suspended use of net operating loss carryforwards for certain taxable years, and other states are considering similar measures. As a result, we may incur higher state income tax expense in the future. Depending on our future tax position, continued suspension of our ability to use net operating loss carryforwards in states in which we are subject to income tax could have an adverse impact on our results of operations and financial condition.

# Our results of operations and liquidity needs could be materially negatively affected by market fluctuations and economic downturns.

Our results of operations could be materially negatively affected by economic conditions generally, both in the United States and elsewhere around the world. Continuing concerns over inflation, energy costs, geopolitical issues, the availability and cost of credit, the U.S. mortgage market and a declining residential real estate market in the United States have contributed to increased volatility and diminished expectations for the economy and the markets going forward. These factors, combined with volatile oil prices, declining business and consumer confidence and increased unemployment, have precipitated an economic recession and fears of a possible depression. Domestic and international equity markets continue to experience heightened volatility and turmoil. These events and the continuing market upheavals may have an adverse effect on us. In the event of a continuing market downturn, our results of operations could be adversely affected by those factors in many ways, including making it more difficult for us to raise funds if necessary, and our stock price may further decline.

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### Risks Related to Our Indebtedness and Our Common Stock

### The notes are effectively subordinated to our secured indebtedness and any liabilities of our subsidiaries.

The notes will rank senior in right of payment to our future indebtedness that is expressly subordinated in right of payment to the notes; equal in right of payment to our existing and future liabilities that are not so subordinated; effectively junior in right of payment to any of our secured indebtedness to the extent of the value of the assets securing such indebtedness; and structurally junior to all existing and future liabilities (including trade payables) of our subsidiaries. In the event of our bankruptcy, liquidation, reorganization or other winding up, our assets that secure indebtedness ranking senior in right of payment to the notes will be available to pay obligations on the notes only after the secured indebtedness has been repaid in full from these assets. There may not be sufficient assets remaining to pay amounts due on any or all of the notes then outstanding. The indenture governing the notes does not prohibit us

from incurring additional senior indebtedness or secured indebtedness, nor does it prohibit any of our subsidiaries from incurring additional liabilities.

As of September 30, 2012, our total consolidated indebtedness was \$29.2 million, all of which was secured indebtedness, and our subsidiaries had no indebtedness (in each case, excluding trade payables, intercompany liabilities and income tax-related liabilities). After giving effect to the issuance of the notes (assuming no exercise of the initial purchasers' option to purchase additional notes) and the application thereof as described under "Use of Proceeds," as of September 30, 2012, our total consolidated indebtedness would have been \$81.7 million, of which \$1.7 million would have been secured indebtedness.

# The notes are our obligations only and a portion of our operations are conducted through, and a substantial portion of our consolidated assets are held by, our subsidiaries.

The notes are our obligations exclusively and are not guaranteed by any of our operating subsidiaries. A substantial portion of our consolidated assets is held by our subsidiaries. Accordingly, our ability to service our debt, including the notes, depends on the results of operations of our subsidiaries and upon the ability of such subsidiaries to provide us with cash, whether in the form of dividends, loans or otherwise, to pay amounts due on our obligations, including the notes. Our subsidiaries are separate and distinct legal entities and have no obligation, contingent or otherwise, to make payments on the notes or to make any funds available for that purpose. In addition, dividends, loans or other distributions to us from such subsidiaries may be subject to contractual and other restrictions and are subject to other business considerations. Transferring cash from our foreign subsidiaries may result in adverse tax consequences to us and, therefore, we do not intend to repatriate funds from our foreign subsidiaries to repay the notes.

# Servicing our indebtedness requires a significant amount of cash, and we may not have sufficient cash flow from our business to pay our substantial indebtedness.

Our ability to make scheduled payments of the principal of, to pay interest on or to refinance our indebtedness, including the notes, or to make cash payments in connection with any conversion of notes depends on our future performance, which is subject to economic, financial, competitive and other factors beyond our control. Our business may not continue to generate cash flow from operations in the future sufficient to service our indebtedness and make necessary capital expenditures. If we are unable to generate such cash flow, we may be required to adopt one or more alternatives, such as selling assets, restructuring indebtedness or obtaining additional equity capital on terms that may be onerous or highly dilutive. Our ability to refinance our indebtedness will depend on the capital markets and our financial condition at such time. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations.

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### Recent regulatory actions may adversely affect the trading price and liquidity of the notes.

We expect that many investors in, and potential purchasers of, the notes will employ, or seek to employ, a convertible arbitrage strategy either by selling short our common stock underlying the notes and dynamically adjusting their short position while holding the notes, or by entering into swaps on our common stock in lieu of or in addition to short selling our common stock. Accordingly, any rules regulating short selling of securities or equity swaps or other governmental action that interferes with the ability of market participants to establish and maintain a convertible arbitrage strategy with respect to the notes could adversely affect the trading price and liquidity of the notes.

The SEC and other authorities have implemented rules and may adopt additional rules that may impact those engaging in short selling activity involving equity securities. In particular, Rule 201 of SEC Regulation SHO generally restricts short selling when the price of a "covered security" (including our common stock) triggers a "circuit breaker" by falling 10% or more from the security's closing price as of the end of regular trading hours on the prior day. If this circuit breaker is triggered, short sale orders can be displayed

or executed only if the order price is above the current national best bid, subject to certain limited exceptions. Additionally, the SEC approved a pilot program (which has been extended to February 4, 2013) allowing securities exchanges and the Financial Industry Regulatory Authority, Inc., or "FINRA", with respect to securities included in the S&P 500 Index, Russell 1000 Index and over 300 exchange traded funds, to halt trading in the securities if the price of any such security moves 10% or more from a sale price in a five-minute period; or with respect to National Market System stocks, to halt trading in the event of any price movement of 30% or more or 50% or more depending upon the trading price of the stock in a five-minute period. The pilot program excludes all rights and warrants from the trading halt. The SEC has also approved two proposals submitted by FINRA and the exchanges to establish a "Limit Up-Limit Down" plan. The proposal, which will go into effect on February 4, 2013, establishes procedures, including trading pauses, to prevent trading in particular stocks outside of specified price bands during trading hours.

The enactment of the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act. also introduced regulatory uncertainty that may impact trading activities relevant to the notes. This new legislation, when fully implemented through regulatory rulemaking, will require many over-the-counter swaps and security-based swaps to be centrally cleared through regulated clearinghouses and traded on exchanges or comparable trading facilities. In addition, swap dealers, security-based swap dealers, major swap participants and major security-based swap participants will be required to register with the SEC or the Commodity Futures Trading Commission and comply with margin and capital requirements as well as public reporting requirements.

Although the direction and magnitude of the effect that the amendments to Regulation SHO, FINRA and exchange rule changes and implementation of the Dodd-Frank Act may have on the trading price and the liquidity of the notes will depend on a variety of factors, many of which cannot be determined at this time, past regulatory actions (such as the emergency orders issued by the SEC in 2008 prohibiting short sales of stock of certain financial services companies) have had a significant impact on the trading prices and liquidity of convertible debt instruments. Any governmental action that similarly restricts the ability of investors in, or potential purchasers of, the notes to establish and maintain a convertible arbitrage strategy with respect to the notes (including any increasing costs incurred by investors in implementing such strategy) could adversely affect the trading price and the liquidity of the notes.

# Our common stock price may be subject to significant fluctuations and volatility, which could adversely impact the trading price of the notes and our shares issuable upon conversion of the notes.

Our stock price is volatile, and from February 3, 2011, the first day of trading of our common stock, to January 14, 2013, the trading prices of our stock have ranged from \$6.16 to \$19.42 per

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share. Our stock could be subject to wide fluctuations in price in response to various factors, including the following:

- the commercial success of EXPAREL;
- results of clinical trials of our product candidates or those of our competitors;
- changes or developments in laws or regulations applicable to our product candidates;
- introduction of competitive products or technologies;
- failure to meet or exceed financial projections we provide to the public;
- actual or anticipated variations in quarterly operating results;
- failure to meet or exceed the estimates and projections of the investment community;

- the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;
- general economic and market conditions and overall fluctuations in U.S. equity markets;
- developments concerning our sources of manufacturing supply;
- disputes or other developments relating to patents or other proprietary rights;
- additions or departures of key scientific or management personnel;
- issuances of debt, equity or convertible securities;
- · changes in the market valuations of similar companies; and
- the other factors described in this "Risk Factors" section.

In addition, the stock market in general, and the market for small pharmaceutical and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

### Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

As of December 31, 2012, our executive officers, directors and 5% stockholders and their affiliates beneficially own approximately 60% of our outstanding voting stock. As a result, these stockholders have significant influence and may be able to determine matters requiring stockholder approval. For example, these stockholders may be able to materially affect elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transactions. This concentration of ownership could delay or prevent any acquisition of our company on terms that other stockholders may desire.

Future sales in the public market or issuances of our common stock could lower the market price for our common stock and adversely impact the trading price of the notes.

In the future, we may sell additional shares of our common stock to raise capital. Except in certain limited instances, we are not restricted from issuing additional common stock, including securities that are convertible into or exchangeable for, or that represent the right to receive, common stock. The issuance of additional shares of our common stock or convertible securities, including our outstanding options and restricted shares, or otherwise, will dilute the ownership interest of our common stockholders.

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In addition, our existing stockholders may sell a substantial number of shares in the public market. Furthermore, a substantial number of shares of our common stock is reserved for issuance upon the exercise of stock options and upon conversion of the notes. We cannot predict the size of future sales or issuances of our common stock or the effect, if any, that they may have on the market price for our common stock. The liquidity and trading volume of our common stock is limited. For the three months ended December 31, 2012, the average per day trading volume of our common stock was 275,771 shares. The issuance and/or sale of substantial amounts of common stock, or the perception that such issuances and/or sales may occur, could adversely affect the trading price of the notes and the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities.

### Despite our current indebtedness levels, we may still incur substantially more indebtedness or take other actions which would intensify the risks discussed above.

Despite our current consolidated indebtedness levels, we and our subsidiaries may be able to incur substantial additional indebtedness in the future, subject to any restrictions contained in our then-existing debt instruments, some of which may be secured indebtedness. We will not be restricted under the terms of the indenture governing the notes from incurring additional indebtedness, securing existing or future indebtedness, recapitalizing our indebtedness or taking a number of other actions that are not limited by the terms of the indenture governing the notes that could have the effect of diminishing our ability to make payments on the notes.

### Our management will have broad discretion over the use of the proceeds we receive in this offering and might not apply the proceeds in ways that increase the value of your investment.

We intend to use a portion of the net proceeds from this offering for general corporate purposes, which may include the acquisition of companies, businesses or assets, or working capital. Our management will have broad discretion to use the net proceeds from this offering, and you will be relying on their judgment regarding the application of these proceeds. Our management might not apply our net proceeds from this offering in ways that increase the value of your investment. Our management might not be able to yield a significant return, if any, on any investment of these net proceeds. You will have no opportunity to influence our decisions on how to use our net proceeds from this offering.

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### The conditional conversion feature of the notes, if triggered, may adversely affect our financial condition and operating results.

In the event the conditional conversion feature of the notes is triggered, holders of the notes will be entitled to convert the notes at any time during specified periods at their option. If one or more holders elect to convert their notes, we would be required to settle any converted principal through the payment of cash, which could adversely affect our liquidity. In addition, even if holders do not elect to convert their notes, we could be required under applicable accounting rules to reclassify all or a portion of the outstanding principal of the notes as a current rather than long-term liability, which would result in a material reduction of our net working capital.

## The accounting method for convertible debt securities that may be settled in cash, such as the notes, could have a material effect on our reported financial results.

In May 2008, the Financial Accounting Standards Board, which we refer to as FASB, issued FASB Staff Position No. APB 14-1, Accounting for Convertible Debt Instruments That May Be Settled in Cash upon Conversion (Including Partial Cash Settlement), which has subsequently been codified as Accounting Standards Codification 470-20, Debt with Conversion and Other Options, which we refer to as ASC 470-20. Under ASC 470-20, an entity must separately account for the liability and equity components of the convertible debt instruments (such as the notes) that may be settled entirely or partially in cash upon conversion in a manner that reflects the issuer's economic interest cost. The effect of ASC 470-20 on the accounting for the notes is that the equity component is required to be included in the additional paid-in capital section of stockholders' equity on our consolidated balance sheet at the issuance date and the value of the equity component would be treated as debt discount for purposes of accounting for the debt component of the notes. As a result, we will be required to record a greater amount of non-cash interest expense in current periods presented as a result of the amortization of the discounted carrying value of the notes to their face amount over the term of the notes. We will report larger net losses in our financial results because ASC 470-20 will require interest to include both the current period's amortization of the debt discount and the instrument's coupon interest, which could adversely affect our reported or future financial results, the trading price of our common stock and the trading price of the notes. In addition, under certain circumstances, convertible debt instruments (such as the notes) that may be settled entirely or partly in cash are currently accounted for utilizing the treasury stock method, the effect of which is that the shares issuable upon conversion of the notes are not included in the calculation of diluted earnings per share except to the extent that the conversion value of the notes exceeds their principal amount. Under the treasury stock method, for diluted earnings per share purposes, the transaction is accounted for as if the number of shares of common stock that would be necessary to settle such excess, if we elected to settle such excess in shares, are issued. We cannot be

sure that the accounting standards in the future will continue to permit the use of the treasury stock method. If we are unable to use the treasury stock method in accounting for the shares issuable upon conversion of the notes, then our net losses per share would be increased.

Some provisions of our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our restated certificate of incorporation and our bylaws, as well as provisions of the Delaware General Corporation Law, or DGCL, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders, including transactions in which stockholders might otherwise receive a premium for their shares. These provisions include:

- authorizing the issuance of "blank check" preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;
- prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;
- eliminating the ability of stockholders to call a special meeting of stockholders; and
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings.

These provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management. In addition, we are subject to Section 203 of the DGCL, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with an interested stockholder for a period of three years following the date on which the stockholder became an interested stockholder, unless such transactions are approved by our board of directors. This provision could have the effect of delaying or preventing a change of control, whether or not it is desired by or beneficial to our stockholders.

### We do not intend to pay dividends on our common stock for the foreseeable future.

We have never declared or paid cash dividends on our common stock. In addition, we must comply with the covenants in our credit facilities if we want to pay cash dividends. We currently intend to retain our future earnings, if any, to finance the further

development and expansion of our business and do not intend to pay cash dividends in the foreseeable future. Any future determination to pay dividends will be at the discretion of our board of directors and will depend upon our financial condition, results of operations, capital requirements, restrictions contained in current or future financing instruments and such other factors as our board of directors deems relevant.