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Reason for Report:
Initiating Coverage

Changes	Previous	Current
Rating	--	Overweight
Price Tgt	--	$14.00
FY11E Rev (mil)	--	$18.9
FY12E Rev (mil)	--	$50.8
FY11E EPS	--	($3.20)
FY12E EPS	--	($1.12)

Price:	$6.87
52 Week High:	$7.25
52 Week Low:	$6.16
12-Month Price Target:	$14.00
9x our 2014 EPS est. of $2.38, disc. at 25%	
Shares Out (mil):	17.2
Market Cap. (mil):	$118.2
Avg Daily Vol (000):	95
Book Value/Share:	$0.11
Net Cash Per Share:	$1.81
Debt to Total Capital:	36%
Est LT EPS Growth:	NA
P/E to LT EPS Growth (FY11):	NA
Est Next Rep Date:	06/01/2011
Fiscal Year End:	Dec

Rev (mil)	2010E	2011E	2012E
Mar	NA	$4.6E	NA
Jun	NA	$3.1E	NA
Sep	NA	$3.3E	NA
Dec	NA	$7.9E	NA
FY	$16.5E	$18.9E	$50.8E
CY	$16.5E	$18.9E	$50.8E
FY RM	7.2x	6.3x	2.3x
CY RM	7.2x	6.3x	2.3x

EPS	2010E	2011E	2012E
Mar	NA	($0.61)E	NA
Jun	NA	($0.42)E	NA
Sep	NA	($0.49)E	NA
Dec	NA	($1.68)E	NA
FY	($2.52)E	($3.20)E	($1.12)E
CY	($2.52)E	($3.20)E	($1.12)E
FY P/E	NM	NM	NM
CY P/E	NM	NM	NM

For 2010, our estimate reflects PCRX's audited actual for the nine months ending 9/30/10

Pacira Pharmaceuticals (PCRX - $6.87)

Overweight

Comfortably Numb: Bullish on Exparel; Initiating with an Overweight and $14 PT

CONCLUSION:

We are initiating coverage of Pacira Pharmaceuticals with an Overweight rating and a $14 price target. We believe that PCRX's Exparel, a long-acting formulation of the anesthetic bupivacaine for post-operative pain, has the potential to provide more optimal pain relief as well as reduce the risk of complications associated with opioid use. With the product nearing commercialization (the FDA action date on the NDA is 7/28/11), we believe PCRX has good visibility to cash generation (we believe profitability by 2013 is realistic). We believe Exparel sales of over $200M by 2015 are achievable. We further believe that the complexities surrounding this liposome-based formulation translates into a remote risk of generic competition.

- **Exparel: potential to be a valuable post-surgery pain management resource.** Exparel can provide pain relief for as long as 72 hours post-dose, compared to around 7-10 hours post-dose for conventional immediate-release (IR) bupivacaine, which is a widely used local/regional analgesic in post-operative pain management. Exparel was shown to be statistically superior to placebo in two Phase III studies (a soft-tissue surgery and an orthopedic surgery) in reducing pain, as well as reducing the need for opioid rescue medication and total opioid consumption (bearing in mind that opioid-related adverse events are a common pitfall seen in post-operative pain management). Exparel's superiority to placebo in reducing pain clears the main regulatory hurdle for Exparel in our view (placebo-controlled studies are generally required by the FDA for registration).

- **We see differentiation versus other pain management modalities.** In an earlier head-to-head study, use of Exparel has resulted in reduced reliance on opioids (e.g., morphine) relative to IR bupivacaine. Further, we believe Exparel can take significant share from elastomeric infusion pumps, which are expensive, labor-intensive catheter-based systems that can deliver bupivacaine over a long period (i.e. 0.5 days to 5 days post-operation) directly to the surgical site. These pumps alone constitute of up anywhere from $150M-$300M U.S. market, and Exparel can accomplish what these pumps do with a single, convenient and potentially less expensive injection.

- **DepoFoam delivery technology provides platform for additional products.** PCRX's DepoFoam technology, upon which Exparel is based, has already yielded two FDA-approved niche products (DepoDur and DepoCyt). As PCRX transitions to a hospital-focused company with its own sales infrastructure, we envision the advancement of additional products based on the technology.

INVESTMENT RECOMMENDATION:

We believe the risk/reward profile for PCRX shares is favorable given the value proposition associated with Exparel. We base our $14.00 price target on our 2014 EPS estimate of $2.38, times a P/E of 9x (a discount to the group but reflective of PCRX currently being a single product story), discounted at 25%.

RISKS TO ACHIEVEMENT OF TARGET PRICE:

Risks include regulatory and commercial risks associated with Exparel.

COMPANY DESCRIPTION:

Pacira is focused on hospital-based products for pain management.

INVESTMENT HIGHLIGHTS

We are initiating coverage of Pacira with an Overweight rating and a 12-month price target of $14.00 per share, representing upside of 104% over Pacira's current share price. Pacira Pharmaceuticals is an emerging specialty pharmaceutical company focused on pain management in the hospital setting. We believe that PCRX's key value driver Exparel, a long-acting formulation of the local/regional anesthetic bupivacaine for the management of post-operative pain, has the potential to provide longer, more optimal pain relief versus conventional bupivacaine. A bigger value proposition associated with Exparel in our view is the potential for reduced opioid use, resulting in reduced potential for post-operative complications associated with common opioid-related adverse effects including impaired gastrointestinal motility, excessive sedation, and respiratory depression. With Exparel nearing commercialization (the FDA action date on the pending NDA is 7/28/11), we believe PCRX has good visibility to cash flow generation (we believe profitability by 2013 is realistic). We believe Exparel sales of $216 million by 2015 are achievable, with peak sales potential considerably higher particularly given that we could see label expansions for Exparel longer-term in other injection modalities (namely epidural injection and nerve block). Further, other products that incorporate PCRX's long-acting delivery technology DepoFoam, upon which Exparel is based, have the potential to drive additional value creation. With a clear value proposition in the post-operative pain management setting, as well as limited regulatory risk in our view, we believe that PCRX shares are trading at an attractive risk/reward profile, particularly in the context of a market capitalization of only $119 million. Our $14.00 price target is based on our 2014 EPS estimate of $2.38, times a P/E of 9x, discounted at 25%, and is supported by our sum of the parts analysis.

Key value driver Exparel has the potential to be a valuable post-surgery pain management resource with good visibility to commercialization. A single injection of Exparel (via a commonly used technique known as wound infiltration, in which the anesthetic is injected directly into the surgical site prior to the completion of the procedure) can provide pain relief for as long as 72 hours post-dose, compared to around 7-10 hours post-dose for conventional immediate-release (IR) bupivacaine, one of a number of sodium channel blockers that have been commercially available for decades (all of which are short-acting) and widely used by anesthesiologists. Exparel was shown to be statistically superior to a placebo in two Phase III studies, one in patients undergoing hemorrhoidectomy and another in patients undergoing bunionectomy (this follows the standard approach to registration-quality studies in this setting in which the manufacturer runs a study in soft tissue and orthopedic surgery models). Further, treatment with Exparel was statistically superior in reducing the need for opioid rescue medication (for instance, p-value of less than 0.0007 on the endpoint of the percentage of patients who were opioid-free in hemorrhoidectomy study), and total opioid consumption ($p=0.0006$ in the hemorrhoidectomy study and $p<0.05$ in the bunionectomy study) bearing in mind that despite the significant potency of opioids, they are nonetheless fraught with pitfalls. Exparel's superiority to placebo in reducing pain clears the main regulatory hurdle for Exparel in our view (placebo-controlled studies are generally required by the FDA for registration). We note that the FDA has recently approved a number of analgesic medications for acute use on placebo-controlled studies, including Cadence's intravenous formulation of acetaminophen Ofirmev in November 2010, Cumberland's intravenous formulation of ibuprofen Caldolor in June 2009, and Xanodyne's oral capsule formulation of diclofenac Zipsor in June 2009. Given that approaches to post-surgical pain management generally incorporate multiple agents, particularly in more highly invasive surgeries, we do not view these agents as direct competitors to Exparel, and if anything, given that they are from different drug classes, we could see these agents as complementary to Exparel. The key takeaway is that there is clear evidence that placebo-controlled trials, not active comparator studies, are acceptable for FDA approval. Additionally, with a strong safety profile for Exparel (most notably no evidence of cardiotoxicity or QT prolongation; this is a concern with the sodium channel blocker class mainly at very high doses), we do not see significant regulatory risk for the product.

Potential for significant share gains at expense of other bupivacaine-based treatments. In an earlier head-to-head Phase II study, use of Exparel has resulted in reduced reliance on opioids (e.g., morphine) relative to IR bupivacaine. In this trial in 100 patients, total consumption of opioids was reduced by 66% for patients on Exparel at 300 mg compared to patients on IR bupivacaine at 75 mg ($p<0.05$). A major part of PCRX's commercialization efforts will be Phase IIIb/IV studies as well as patient registries to further elucidate this opioid-reducing benefit. That said, there is an even faster way to meaningful adoption of Exparel, and we believe this can come from Exparel taking significant share from elastomeric infusion pumps. These products, which constitute a market of at least $150 million and possibly as high as $300 million, are expensive, labor-intensive catheter-based systems that can deliver bupivacaine over a long period (i.e. 0.5 days to up to 5 days post-operation) directly to the surgical site. A key limitation of these systems is the risk of infection, since the patient is tethered to a catheter that runs right to the surgical site. The market leader in this space, the ON-Q pump (marketed by Kimberly Clark subsidiary I-Flow), has roughly $150 million to $200 million in U.S. sales. We believe that Exparel can essentially accomplish what these pumps do with a single, convenient and potentially less expensive injection. It is noteworthy that the Exparel wound infiltration injection is exactly how conventional bupivacaine is currently administered by anesthesiologists in most cases (in other words,

there is virtually no learning curve for anesthesiologists for this product). We note that the ON-Q pump costs roughly $275 per patient procedure, whereas Pacira has suggested that it would price Exparel closer to $200 per patient procedure.

Competitive landscape favorable: hard to envision any generic competition, and competition from other brands should also not be a concern. In terms of generic competition for Exparel, we see the threat as minimal at worst given the complexities associated with Pacira's DepoFoam technology. DepoFoam incorporates multi-vesicular liposomes that surround the therapeutic and erode/reorganize over time, allowing for the release of active drug over an extended period. The company has a facility in San Diego where it will manufacture the product. As we outline in our report, the manufacturing process associated with Exparel is complex, and it would take a generics company at least several years to develop the capability to make liposome-based products. Further, PCRX has several patents issued related to multi-vesicular liposomes, as well as a number of patent applications pending on more efficient manufacturing processes associated with Exparel, which could confer protection out to 2031. As such, the only new competition that we would expect would come from other brands. We note that DURECT/Hospira are developing their own long-acting bupivacaine product known as Posidur, but the product is still enrolling patients in a Phase III study and we would not expect to see it on the market until 2013 at the earliest. Based on our read of Phase II data for Posidur, we see the product as at best having a similar efficacy and safety profile relative to Exparel. In any case, with an estimated 24 million surgical procedures using a local/regional anesthetic (i.e., a sodium channel blocker like bupivacaine or lidocaine), we believe the market is certainly large enough to accommodate multiple brand entrants.

DepoFoam delivery technology provides platform for additional products. DepoFoam has already yielded two FDA-approved niche products for the hospital setting: DepoDur, a long-acting formulation of morphine for use as an epidural injection, and DepoCyt, a long acting formulation of cytarabine for treatment of lymphomatous meningitis. These products are sold by third parties and should generate around $13 million in revenue to PCRX in 2011. As PCRX transitions to a fully-integrated hospital-focused company specializing in pain management, we envision the advancement of additional products based on DepoFoam, with PCRX leveraging its hospital-based sales infrastructure that it will deploy to support Exparel. The company already has long-acting injectible versions of methotrexate, one of the most commonly used agents for the treatment of rheumatoid arthritis, and a non-steroidal anti-inflammatory drug (NSAID), in early development. We note that the advancement of both products is dependent on additional funding. We note that payments from potential partnerships (such as an ex-U.S. partner on Exparel or PCRX partnering with other companies looking to use DepoFoam for their own products) could very well provide non-dilutive sources of capital. That said, we would not expect to see PCRX start meaningful clinical work on these additional opportunities until Exparel reaches critical mass (read: is self-funding). The key takeaway here is that DepoFoam provides a platform that over time will allow the company to expand its reach in the acute care setting and potentially drive further value creation.

RISKS TO OUR THESIS

The biggest near-term risk to our thesis is regulatory risk (the PDUFA date for Exparel is 7/28/11). Though Exparel was successful in two placebo-controlled Phase III studies and was shown to have a strong tolerability profile (with a safety database consisting of over 1,300 patient exposures), there were earlier active comparator Phase III studies that did not meet their primary endpoint, so from an efficacy perspective, the development program for Exparel did not yield squeaky clean results. That said, the fact that the drug was superior to placebo (generally that is the regulatory hurdle that needs to be met in pain studies) in two different surgical models gives us a high degree of confidence in a timely approval.

Other risks to our thesis include the following: (1) commercial risks, namely related to the ability of Pacira to make the case to hospitals that Exparel has meaningful advantages over conventional bupivacaine; (2) reimbursement risks, namely the risk that hospitals balk at the higher price point of Exparel versus conventional bupivacaine particularly considering that generic versions of conventional bupivacaine have been available for a number of years; (3) competitor risks, namely the risk of brand competition over the long-term given that DURECT/Hospira's own long-acting bupivacaine product is around 1.5 to 2 years away from commercialization in the U.S., and (4) liquidity risks, with the company likely needing to access additional capital in 2012 in order to continue to build out its commercial organization as well as move Exparel into market expanding studies (namely studies testing the drug as an epidural and as a nerve block).

UPCOMING CATALYSTS AND MILESTONES

Figure 1: Pacira Calendar of Upcoming Events

Product/Program	Event	Expected Date
Exparel - wound infiltration	FDA action on filing for the management of post-surgical pain	7/28/2011
Exparel	U.S. commercial launch	4Q11
Exparel - nerve block	Advancement into Phase II/III studies	2H12/2013
Exparel - epidural injection	Advancement into mid-stage clinical studies	2H12/2013
DepoMethotrexate	Possible advancement into trials in rheumatoid arthritis	2013
DepoNSAID	Possible advancement into trials for for pain	2013

Abbreviations: NSAID non-steroidal anti-inflammatory drug

Source: Company reports and PJC estimates

Figure 2: Pacira Product Pipeline

Product candidates	Indication	Preclinical	Ph I	Ph II	Ph III	NDA Filed	Marketed
Exparel	Postsurgical analgesia by infiltration						
	Postsurgical analgesia by nerve block						
	Postsurgical analgesia by epidural administration						
DepoCyt(e)	Lymphomatous meningitis						
DepoDur	Post-operative pain						
DepoNSAID	Acute pain						
DepoMethotrexate	Rheumatoid arthritis						
	Oncology						

Source: Company reports, industry reports, and PJC estimates

FINANCIAL OVERVIEW

Expectations for Exparel commercialization and timeline to Pacira profitability. Our model reflects an Exparel U.S. launch in late 2011, with 2012 sales of $35.4 million, the drug's first full year on the market. Our 2011 net loss per share estimate is ($3.20), with a net loss per share estimate of ($1.12) in 2012 (this assumes the impact from another equity offering with net proceeds of $48 million). We also note that our 2011 net loss per share estimate reflects a $10 million approval milestone payment to Skye Pharma (where the DepoFoam technology comes from). We estimate that Pacira will achieve full year profitability in 2013, with an EPS estimate of $0.41, based on Exparel sales of $86.6 million.

Longer-term, we expect Exparel U.S. sales to grow to $143 million by 2014 and $216 million by 2015. Our model reflects a price per patient procedure of $200 upon launch, and conservatively does not assume any price increase in later periods. For 2014, our estimate of $143 million reflects nearly 712,000 patient procedures using Exparel (we model near 386,000 in-patient and near 326,000 out-patient procedures) . According to Pacira, there are nearly 24 million surgeries in the U.S. that use a local/regional anesthetic like bupivacaine (or its "cousin" compounds such as lidocaine or ropivacaine), so our 2014 estimate implies only a 3% penetration.

Margins and expenses. Pacira's gross margin on Exparel is dependent to a large extent on the build-out of additional manufacturing capabilities at its San Diego, CA facilities. The additional capabilities should result in lower manufacturing costs, and assuming no pricing pressure over the next several years, significantly higher gross margins relative to the margins that Pacira would get on Exparel supply made at its older manufacturing suite, known as suite A. We estimate that Pacira will have its more efficient manufacturing suite, known as suite C, fully on line in 2013. We are conservatively estimating a 2012 gross margin of 35%, growing to 60% in 2013 and 73% in 2014, reflecting the efficiencies from production of Exparel in this manufacturing suite (we say conservative since management has suggested that greater margins are possible from the new suite).

With Pacira preparing to launch Exparel on its own in the U.S., SG&A expenses will be considerable, though we note that the headcount required to support a hospital-based product portfolio is similar to the headcount required to support non-hospital products sold into concentrated physician audiences, such as neurology and gastroenterology. Pacira envisions launching Exparel with about 40 reps, growing the sales force to roughly 100 reps by the third year Exparel is on the market. Assuming an annual all-in cost per rep of roughly $200,000 to $225,000, the annual cost of a sales force of 100 reps would be around $20 million to $23 million. We are modeling 2011 SG&A costs of $24.1 million, growing to $35.6 million in 2012 and $42.3 million in 2013. We note that SG&A expenses also include costs associated with Phase IIIb/IV studies, as post-approval studies to support the labeled indication are generally considered to be sales and marketing costs. We are modeling relatively light R&D expenses of $5.4 million and $3.0 million in 2011 and 2012, respectively. The extent to which Pacira can access additional capital will go a long way in determining if and when the company advances additional programs, including label expansion programs for Exparel and early-stage pipeline programs.

Figure 3: Summary of PJC Estimates for Pacira

$ in millions, except per share	2010E	2011E	2012E	2013E	2014E	2015E
Revenue						
Exparel sales (U.S.)	$0.0	$2.5	$35.4	$86.6	$142.5	$215.5
Total revenue	**$16.5**	**$18.9**	**$50.8**	**$100.7**	**$157.3**	**$231.1**
Expenses						
COGS	$13.6	$40.7	$33.0	$40.3	$42.5	$53.1
R&D	$19.9	$5.4	$3.0	$6.0	$6.3	$6.9
SG&A	$5.3	$24.1	$35.6	$42.3	$48.7	$53.1
Operating income	($22.3)	($51.4)	($20.8)	$12.1	$59.7	$117.8
Net Income	($26.8)	($55.6)	($24.2)	$10.4	$61.1	$113.7
EPS, diluted	**($2.52)**	**($3.20)**	**($1.12)**	**$0.41**	**$2.38**	**$4.35**
Shares outstanding, diluted	10.7	17.4	21.7	25.2	25.7	26.2

Source: Company reports and PJC estimates

Balance sheet and cash flow: cash on hand sufficient to fund operations into 1H12, assuming no partnerships that bring in additional capital. Following Pacira's IPO, we estimate that the company had nearly $65 million in cash on hand and near $30 million in total debt outstanding. The use of the approximately $38 million in proceeds from the IPO will be to fund the commercialization of Exparel in the U.S., inclusive of the build-out of a hospital-based sales force of 40 reps, initial launch costs, Phase IIIb/IV studies and patient registries that assess overall health and pharmacoeconomic outcomes, and the completion of the build-out of a new manufacturing suite at the company's San Diego facility (known as suite C). Management estimates that the proceeds will be sufficient to fund operations into 1H12. The company has suggested that it is engaged in a number of discussions with third parties regarding Exparel (specifically the potential for a partnership in markets outside of the U.S.), its early-stage products and the use of DepoFoam in compounds controlled by other companies. As such, it is possible that partnerships could materialize that provides a source (or sources) of non-dilutive financing.

Based on our estimated trajectory for Exparel, we believe that Pacira will generate cash from operations of $16 million in 2013, growing to $66 million in 2014. We also estimate that the company will have paid down most if not all of its outstanding debt by the end of 2013.

VALUATION

We base our $14 price target on our 2014 EPS estimate of $2.38, times a P/E of 9x, discounted at 25%. Our P/E is based on an analysis of profitable (i.e., well-established) and emerging branded specialty pharma companies (refer to Figure 4 below). We believe a P/E for Pacira of 9x is appropriate and generally in keeping with the average P/E multiple for specialty pharma companies driven largely by a single product. That said, the broader brand specialty pharma group generally trades at a P/E of around 12x 2012 EPS, so in this context, we are valuing PCRX at a discount to the broader group, reflecting the regulatory and commercial risks associated with Exparel and the reality that the product is currently the only meaningful value driver for the company for the next 1-2 years. Successful commercialization of Exparel would drive multiple expansion in our view, particularly given our view that this is not a product that will be threatened by generics for the foreseeable future (mainly due to complexity and expense associated with manufacturing, in addition to an established and growing patent estate). We believe

a 25% discount rate appropriately reflects the risks associated with Pacira, namely regulatory risk and commercial risk surrounding Exparel.

We note that our valuation conclusion is supported by our sum-of-the-parts analysis (refer to Figure 5 below). For our price target of $14, Exparel U.S. net cash flows account for just over $13 per share (97% of Pacira's net present value). We do not ascribe value to the other pipeline products given that they are relatively early and advancement is dependent on additional funding (via another public offering or a partnership). We also do not ascribe value to Exparel outside the U.S. since commercialization in ex-U.S. markets will be dependent on Pacira securing partnerships with third parties.

Figure 4: Pacira Peer Group Valuation Analysis

($M except per share and multiples)			Market	Ent.	EPS		P/E		Revenue		EV/Revenue	
Ticker	**Company**	**Price [1]**	**Cap**	**Value**	**2011E**	**2012E**	**2011E**	**2012E**	**2011E**	**2012E**	**2011E**	**2012E**
HSP	Hospira	$54.23	$9,037	$10,181	$4.47	$5.13	12.1x	10.6x	$4,480	$4,857	2.3x	2.1x
ALKS	Alkermes	$12.34	$1,176	$999	($0.33)	($0.09)	NM	NM	$210	$252	4.8x	4.0x
JAZZ	Jazz Pharma	$28.71	$1,157	$1,160	$3.85	$3.94	7.5x	7.3x	$309	$345	3.8x	3.4x
QCOR	Questcor Pharma	$13.14	$821	$706	$1.04	$1.28	12.7x	10.3x	$194	$221	3.6x	3.2x
CADX	Cadence	$8.76	$553	$448	($0.30)	$0.51	NM	17.1x	$116	$214	3.9x	2.1x
DPMD	Depomed	$8.84	$468	$400	$0.41	$1.19	21.6x	7.4x	$137	$215	2.9x	1.9x
MAPP	MAP Pharma	$15.34	$463	$395	($0.53)	($0.38)	NM	NM	$75	$155	5.3x	2.5x
SPPI	Spectrum	$7.97	$414	$319	($0.42)	$0.77	NM	10.4x	$100	$169	3.2x	1.9x
DRRX	Durect	$3.39	$296	$239	($0.28)	($0.06)	NM	NM	$39	$60	6.1x	4.0x
ZGNX	Zogenix	$5.12	$174	$152	($0.65)	($0.61)	NM	NM	$49	$86	3.1x	1.8x
POZN	Pozen	$4.67	$140	$76	($0.47)	$0.09	NM	NM	$40	$65	1.9x	1.2x
PATH	NuPathe	$7.76	$113	$71	($1.87)	($2.19)	NM	NM	$0	$22	NM	3.2x
CPIX	Cumberland	$5.15	$105	$46	$0.41	$0.55	12.6x	9.4x	$65	$77	0.7x	0.6x
NGSX	Neurogesx	$3.57	$64	$8	($2.34)	($0.86)	NM	NM	$17	$48	0.4x	0.2x
Average - Pacira Peer Group							**13.3x**	**10.4x**			**3.2x**	**2.3x**
PCRX	**Pacira**	**$6.88**	**$119**	**$81**	**($3.20)**	**($1.12)**	**NM**	**NM**	**$19**	**$51**	**4.3x**	**1.6x**

Prices as of March 14, 2011

Source: PJC estimates, First Call, and company reports

Figure 5: Sum of Parts Analysis for Pacira

$M, except per share	Peak Potential	Peak Year	Discount Rate	NPV of Net Cash Flows	NPV per Share	% of Value
Exparel U.S. Sales - Wound infiltration [1]	$514	2022	25%	$226	$13.12	97%
Other product revenue	$16	2015	10%	$8	$0.47	3%
Total				**$234**	**$13.59**	

(1) Reflects peak gross margins of 80% by 2016, SG&A as a percentage of sales of 93% in 2012, declining to 23% by 2015 and falling into a steady-state 15%-20% range after 2015, and assumes PCRX is fully-taxed starting in 2017.

Source: PJC Research

DEPOFOAM: A VALIDATED DRUG DELIVERY PLATFORM

Pacira's drug delivery technology is known as DepoFoam, which is based on liposomes, or vesicles that consist of a lipid (i.e., fatty) bilayer. A vesicle is essentially a bubble of liquid within a chamber of liquid. Liposomes have long been known as useful for the delivery of a variety of active drugs over a sustained or extended period. The DepoFoam technology specifically consists of multi-vesicular liposomes (MVLs), which are composed of numerous drug-containing aqueous chambers that take on a honeycomb-like formation. The chambers are separated by lipid membranes, and following administration, these lipid layers erode/reorganize over time, resulting in the release of active drug over an extended period. MVL's are ideal for local (i.e., non-systemic) delivery, since the large particle sizes generally prevents entry into the systemic circulation (a key consideration for bupivacaine; more on this below). Further, the particles are theoretically safe since lipids are a tissue component of the body (i.e., should not be any concern over immunogenicity) and since the chambers are aqueous, residual lipids are minimal once the active drug has been release (less than 3% of the DepoFoam liposomes consist of lipids). The types and amount of lipids in the MVL determines the rate of delivery of active drug.

Potential to leverage DepoFoam beyond Exparel. Though Pacira's main focus for the foreseeable future is on Exparel, the company has been exploring ways to further leverage its platform technology, both via internal development of additional products as well as via potential licensing of the technology to third parties for use with other compounds. Pacira has begun exploratory, pre-clinical work on two additional products, one being a non-steroidal anti-inflammatory drug (NSAID) incorporating DepoFoam, and the other being a formulation of the chemotherapeutic agent methotrexate that incorporates DepoFoam. Both products have yet to enter clinical trials (see below for more details).

Two FDA-approved products are based on the DepoFoam technology. There are two products commercially available in the U.S. that incorporate the DepoFoam technology: DepoCyt(e) (cytarabine), which was approved in 1999, and DepoDur (morphine), which was approved in 2004. We estimate that combined 2010 revenue for both products (consisting of royalties and manufacturing revenue), will be $13.1 million, noting that revenue for the nine months ending September 30, 2010 for both products totaled $9.9 million. Below we provide additional details on these two products:

- **DepoCyt(e).** DepoCyt(e) is indicated for the treatment of lymphomatous meningitis, a severe complication of lymphoma. While the conventional form of cytarabine must be injected into the spinal cord twice a week, DepoCyt(e) needs to be dosed only once every two weeks in an outpatient setting. Pacira manufactures DepoCyt(e) and supplies Sigma-Tau Pharmaceuticals and Mundipharma, who have commercial rights to market the drug in North America and Europe, respectively.

- **DepoDur.** DepoDur is indicated for the treatment of post-operative pain. DepoDur is a long-acting injectible formulation of morphine that is specifically indicated for epidural administration following major surgery. The drug has been shown to effectively provide pain relief for 48 hours, without the need for either an IV or catheter. Revenues in 2009 from DepoDur have totaled $0.8 million. Pacira manufactures DepoCyt(e) and supplies EKR and Flynn, who have commercial rights to market the drug in the Americas and Europe, South Africa, and the Middle East, respectively.

EXPAREL: PACIRA'S KEY VALUE DRIVER AND A PROMISING SHOT-ON-GOAL IN THE HOSPITAL SETTING

Pacira's evolution from a company focused on the manufacturing of pharmaceuticals for third parties using DepoFoam to a fully integrated specialty pharmaceutical company focused on products for the hospital setting is centered around Exparel (previously known as SKY0402; the DepoFoam technology and therefore Exparel came from Skye Pharma), a long-acting formulation of the anesthetic bupivacaine for the management of post-operative pain. An NDA filing for Exparel at 300 mg for use via wound infiltration is now pending at the FDA, with a PDUFA date of 7/28/11. Given that bupivacaine is a well-established and widely used agent in the hospital setting, Pacira submitted its filing via the 505(b)(2) pathway, allowing the company to reference data for the predecessor compound. That said, the safety and efficacy database for Exparel is extensive (both from Phase III and earlier studies; more on this below).

The Exparel Value Proposition, In Brief

Below we provide a brief overview of what we believe are the key points of differentiation for Exparel versus conventional, short-acting bupivacaine (we discuss these features in greater detail starting on page 14):

- **Exparel has a longer duration of action versus conventional bupivacaine.** Pharmacokinetic studies comparing conventional bupivacaine to Exparel showed a half-life that was nearly twice as long for Exparel (conventional bupivacaine has a half-life of closer to 7 hours). As such, Exparel offers the potential to provide local anesthesia at the surgical site for a longer period, thereby improving the patient post-operative recovery experience.

- **Potential for less reliance on other modalities, particularly opioids.** Opioids remain the most widely used agents for the management of patients' pain post-surgery. Though they are and will continue to play a central role in pain management, we believe there is a need to optimize the use of these agents since they are fraught with a number of pitfalls, including excessive sedation, significant impairment of gastrointestinal motility (constipation being a major problem). We believe that a longer-acting local anesthetic could reduce the reliance on opioids to an extent that reduces the risk of opioid-related complications.

- **Exparel is more convenient and potentially cheaper than other modalities that look to deliver bupivacaine over an extended period.** The use of elastomeric infusion pumps, or bags, that allow for continuous delivery of bupivacaine into the surgical site for an extended period (up to 5 days post-surgery) has become more commonplace in recent years. The good news for Exparel is that the commercial acceptance of this modality, which has sales in the U.S. market potentially as high as $300 million, represents clear evidence that at least a portion of the anesthesiology community sees value in the delivery of bupivacaine over an extended period, with the goal of reducing reliance on opioids. There is further good news for Exparel in that this modality can be complicated, and therefore labor intensive for the hospital staff, can inhibit patient ambulation, and has been associated with infections at the surgical site. Exparel can essentially accomplish pharmacologically with a single injection what these complicated devices are doing and at a potentially lower cost.

Figure 6: Summary of Commercial Opportunities for Exparel

	Wound Infiltration	Nerve Block	Epidural
Exparel Status	NDA filed	Phase II	Phase I trial completed
Number of procedures in each potential market (1)	24 million	8 million	6 million
Types of procedures	Ambulatory surgery; Major surgery incl. hip surgery, hemorroidectomy	Chronic pain relief, breakthrough cancer pain relief, ambulatory surgery	labor/delivery; in addition to general anesthesia, i.e. orthopedic surgery, general surgery, vascular surgery
Anesthetics currently in use	bupivacaine, lidocaine, prilocaine	IR bupivacaine, lidocaine	bupivacaine, lidocaine, chloroprocaine, morphine

Source: Company reports, industry reports, PJC research

Figure 7: Wound Infiltration Procedures

Local Anesthetic	# of Procedures
Lidocaine	15 million
Bupivacaine	7 million
Ropivacaine	600,000

Source: Company reports, PJC research

How Does Bupivacaine Work and How is it Used?

A well-established local/regional anesthetic; key part of multi-drug approach to pain management in the surgical setting. The conventional formulation of bupivacaine (i.e., immediate-release) was originally approved in the U.S. in decades ago under the trade name Marcaine. The drug is now available as a generic, with a number of manufacturers distributing the product in the U.S. (generic manufacturers of bupivacaine include Hospira, which distributes branded and generic versions and APP Pharma, which distributes the branded generic Sensorcaine). Bupivacaine is approved for use in a number of settings, including local or regional anesthesia or analgesia for surgery, dental and oral surgery procedures, diagnostic and therapeutic procedures, and for obstetrical spinal anesthesia. In the hospital setting, the product is generally administered as a local anesthetic (i.e., not a systemic treatment), often directly into the surgical wound before the completion of the surgical procedure. As the patient recovery proceeds, it is generally impractical to administer additional treatment directly to the surgical site (though this is tried; more on this below), and as a result, systemic therapies such as opioids and NSAIDs are introduced to manage the patients' pain. As such, local anesthetics such as bupivacaine are almost always part of a multi-modal approach to post-operative pain management.

Figure 8: Summary of Available Local/Regional Anesthetics

Drug	Half-life	Uses
Bupivacaine	3 hrs	Local anesthesia including infiltration, nerve block, epidural administration
Prilocaine	>2.5 hrs	Often combined with lidocaine for dermal anesthesia; often used for intravenous regional anesthesia
Ropivacaine	2 hrs	Local anesthesia including infiltration, nerve block, epidural, intrathecal administration
Mepivacaine	1.75 hrs	Infiltration and regional anesthesia
Lidocaine	1.5-2 hrs	Local anesthetia for minor surgery, dental anesthetic; topical administration for outpatient use

Source: PJC research and industry reports

Bupivacaine belongs to a class of agents that inhibit sodium channels, and as a result, prevent the entry of sodium ions into neurons, in turn preventing nerve cell depolarization. There are a number of FDA-approved agents from this class, including

lidocaine, prilocaine, and ropivacaine. Communication between neurons is dependent on membrane depolarization (which in turn results in action potential, or known more colloquially as a nerve impulse), so inhibiting depolarization essentially slows down the transmission of nerve impulses. Nerve fibers that transmit pain signals tend to be more lightly myelinated (myelin insulates nerves and is essential to proper nerve functioning) than nerve fibers that transmit other signals, so bupivacaine can more easily penetrate these nerve fibers. As such, according to the Marcaine label, "the order of loss of nerve function is as follows: (1) pain, (2) temperature, (3) touch, (4) proprioception [(position-movement sensation)], and (5) skeletal muscle tone." In short, the higher the dose, the greater the sensory block, but the given the wide experience with the drug, there is a clear dosing range at which bupivacaine is especially effective at slowing down perception of painful stimuli without affecting perception of other stimuli (and it is no coincidence that bupivacaine and agents like it are also referring to as numbing agents). The drug has over the years become a widely used product by anesthesiologists for the management of acute pain following surgery. As a local analgesic in the surgical setting, the drug is more widely used than other sodium channel blockers in invasive surgeries since bupivacaine has a relatively longer duration of activity (bearing in mind that all of these agents in the class are short-acting, though conventional bupivacaine can provide analgesia for up to roughly 7-10 hours). Lidocaine is actually the most commonly used sodium channel blocker; the drug has a shorter half-life versus bupivacaine and is therefore is perceived as being suitable for minor procedures as well as dental procedures.

Below we provide a few examples of the ways in which bupivacaine is currently used:

- **Anesthesia for longer surgeries requiring local or regional anesthesia.** Bupivacaine is often used in lengthier surgeries requiring local or regional anesthesia since it tends to be longer acting than other sodium channel blockers, though to be clear, longer acting is a relative term given that the agents in the class tend to have very short durations of activity. Local or regional anesthesia can last for 7-8 hours when bupivacaine is administered with epinephrine, which prolongs the effect of sodium channel blockers.

- **Bupivacaine is used for obstetric anesthesia.** The drug is known to have limited ability to transfer to the placenta and is often used in Caesarian sections.

- **Wound infiltration for the management of patient recovery.** This is the most common way in which bupivacaine is used, and involves injection of the drug directly into the surgical site.

Bupivacaine has a well-established track record of safety. Given that bupivacaine and agents in the class are generally locally acting when dosed appropriately, the incidence of systemic toxicity is exceedingly rare. Though central nervous system (CNS) and cardiotoxicity are theoretical risks, appropriate dosing and administration generally confers almost no risk to the patient. Further, therapeutic window of agents like bupivacaine is fairly wide, meaning that the difference between a therapeutic dose and a toxic dose is wide. Below we provide a bit of color on the toxicity risks and why this is not problematic:

- **Cardiotoxicity: minimal risk; Exparel did not show any red flags in thorough QT studies.** Systemic exposure to bupivacaine and other sodium channel blockers at very high doses can be cardiotoxic, and bupivacaine can be even more cardiotoxic than other in the class since the drug enters the sodium channels more quickly and exits more slowly than other agents in the class. Generally speaking, the rare cases of cardiotoxicity events are generally due to inappropriately high doses or accidental intravascular injection. Toxicity can encompass decreased cardiac output and hypotension, as well as bradycardia, heartblock, ventricular arrhythmias, and cardiac arrest. In the context of wound infiltration, when bupivacaine is administered to directly to the site appropriately and the correct dosing, the risk to the patient is almost negligible.

  Though the risk of cardiac adverse events is minimal if bupivacaine is used properly, Pacira nonetheless conducted thorough studies assessing the potential for QT prolongation. The company ran two trials, known as SKY0402-C-105 and SKY0402-C-107. Study 105 was a single center, randomized, double-blind, placebo- and active-controlled, five-way crossover study in 49 healthy volunteers looking at two doses of Exparel, 300 mg and 450 mg. Exparel was administered by subcutaneous injection for all doses. The 107 study was an extension of the 105 study with 16 of the same subjects in 105 receiving two additional higher doses of Exparel at 600 mg and 750 mg. The 750 dose was considered the highest volume feasible for injection, and was administered by multiple injections, while all other doses were given as a single dose. ECG values were recorded at baseline, and mean and median QT/QTc values were calculated for each timepoint. No QTc prolongation was seen with the 300 mg, 450 mg, 600 mg, or 750 mg doses. In

the 107 study, a small number of patients showed minor ECG abnormalities outside the normal range, but none were considered to have clinical significance.

- **Central nervous system (CNS) toxicity: risks also minimal.** CNS toxicity can encompass CNS excitation or depression. Though the incidence of CNS toxicity is also exceedingly low, the threshold for CNS toxicity is lower than the threshold for cardiotoxicity. As is the case with cardiotoxicity, the risk of CNS effects is minimal if the drug is given appropriately at standard therapeutic doses.

Background on Post-Surgical Pain and Current Treatment Paradigms

When we use the term post-surgical pain, we are generally referring to acute pain, which is essentially characterized by severe pain for a defined (i.e., limited) period. Management of pain post-surgery is a key consideration in the overall management of the patient in virtually any surgical context. During surgery, trauma to tissues and peripheral nerves stimulates hypersensitivity of the central nervous system, resulting in intense pain. The severity and duration of pain depends in part on the type and duration of surgery, as well as the underlying health of the patient and individual (and subjective factors) such as overall tolerance for pain. The trauma that surgery entails makes it no surprise that the most extreme pain generally occurs during the first few days following surgery. There are an estimated 45 million surgical procedures performed annually in the U.S. (according to data from Thomson Reuters for October 2006-October 2007).

Post-surgical pain management has no gold standard and often involves multiple agents. The management of pain following surgery, particularly more invasive procedures, often involves the use of several analgesics/local anesthetics. According to the World Federation of Societies of Anesthesiologists (WFSA) guidelines for managing acute pain such as that experienced in the postsurgical setting, the recommended treatment is a strong injected opioid plus a local anesthetic. Pain management often begins before the end of the surgical procedure with local anesthetics administered directly to the wound (this is known as wound infiltration). After surgery, patients then are often given systemic opioids to manage basal (i.e., an acceptable baseline level) pain levels, with the option of receiving systemic short-acting opioids for breakthrough pain, which is defined as intense pain that comes on rapidly and is not managed by a patient's normal pain medication. Patients may also be prescribed non-steroid anti-inflammatory drugs (NSAIDs).

Brief Overview of Pain Medications Commonly Used Post-Surgery

Below we provide a brief overview of the various agents that are used to manage pain in post-operative patients. We note that there are numerous cases where an agent from each class is used, with the main takeaway here that the management of acute pain often requires :

- **Opioids: potent, widely used, but fraught with pitfalls.** Opioid agents are a class of pharmaceuticals that bind to opioid receptors, which play a central role in mediating pain perception and are widely found in the central and peripheral nervous system, as well as the gastrointestinal (GI) tract. Opioids are among the oldest known drugs in the world and are the most commonly administered drugs for the management of post-surgical pain. There are a number of opioid receptors and sub-receptors, with nearly all involved in some way in mediating analgesia.

  Opioids that are commonly used for the management of post-surgical pain include morphine, hydromorphone, oxycodone, fentanyl, and meperidine. The most commonly used opioid for managing acute pain following surgery is the mu-opioid receptor agonist morphine. As we mention above, excessive sedation, GI side effects, particularly constipation but also nausea and vomiting, respiratory depression, and mood changes, are all pitfalls associated with opioid use. Further, morphine is excreted renally, and therefore altered drug clearance and potential accumulation of the drug could pose (actually in the case of morphine, its metabolites can accumulate) additional toxicity risks in patients with renal impairment (a population in which opioids are heavily used for the obvious reason that these are patients who are generally in poor health with significant co-morbid illness). For instance, the morphine metabolite morphine-6-glucuronide (M6G), which accumulates in the presence of renal impairment, is an even more potent analgesic than morphine itself. M6G crosses the blood-brain-barrier more slowly than morphine, so it is possible that in patients with renal impairment, central nervous system (CNS) effects such as sedation and dizziness can not only be more severe than in patients with normal renal functions, but can also be present after morphine treatment has been completed. Regarding opioid use, anesthesiologists generally need to exercise extra caution in patients with renal or hepatic impairment.

Though opioids can vary widely in terms of pharmacokinetic profile and therapeutic window (i.e., the difference between a therapeutic dose and a toxic dose), the various drugs in the class all are hampered to some extent or another by the same limitations. That said, opioids are the most potent analgesics available in the pain management arsenal and are therefore going to continue to have a role in post-operative pain management in our view. That said, there are various subgroups of patients, such as those with renal and/or liver impairment as mentioned above, elderly patients (many of whom are more likely to have some renal or liver impairment), and patients in whom respiratory depression may be more dangerous (such as obese individuals or those with sleep apnea), where significant opioid use, or opioid use at all, would be ill-advised. These are examples of patients in whom non-opioids like bupivacaine and/or NSAIDs can play a major role (and certainly populations that Pacira will target in its launch of Exparel).

- **NSAIDs: widely considered effective, though not as potent as opioids, have their own toxicity pitfalls.** Non-steroidal anti-inflammatory drugs (NSAIDs) act in part by inhibiting the enzyme cyclooxygenase (COX), specifically cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2). COX is involved in the formation of prostaglandins, which play a key role in inflammation. Many NSAIDs such as ketorolac, naproxen and ibuprofen are non-selective for COX-1 and COX-2 (i.e., they inhibit both). Although NSAIDs certainly do not have the risks that are associated with opioids (such as respiratory depression or sedation), they are associated with GI toxicity and renal complications.

  NSAIDs are considered useful in the post-operative pain management setting since they also have antipyretic activity (fever reducing properties). That said, there is meaningful risk of GI toxicity, particularly GI bleeding, as well as renal impairment. NSAIDs can cause fluid retention, particularly in patients with renal impairment, and can exacerbate hypertension. One of the most commonly used NSAIDs in the post-operative setting is ketorolac, which can be given via IV and directly to tissue, meaning that it can be used in wound infiltration as well as in the early post-operative setting in patients who are unable to hold down oral solids. Ketorolac is one of the most potent NSAIDs available. However, the drug primarily inhibits COX-1, which happens to be the pathway involved in GI protection. Despite this, the drug, as is the case for many NSAIDs, is nonetheless considered to be safer than opioids, and has played a role in reducing opioid requirements.

- **Local anesthetics (sodium channel blockers): non-systemic activity a key advantage here.** This is the class to which bupivacaine belongs. Local and regional anesthetics are widely used, including use pre-operatively in order to facilitate the surgery, during surgery as would infiltration in order to make the patient recovery time more comfortable, and post-operatively in order to manage pain. The numerous sodium channel blockers available are short-acting agents that have an effect last several hours. The obvious advantage of these agents is the lack of systemic exposure. When considering that plus the different mechanism of analgesic effect relative to other drug classes, is it relatively easy to see how these agents can be readily combinable with other drugs.

Figure 9: Summary of Drug Classes Used for the Management of Post-Operative Pain

	Acetaminophen (APAP)	NSAIDs	Opioids	Sodium Channel Blockers
Description	Centrally acting analgesic and antipyretic (i.e., fever-reducing agent)	Inhibitors of COX-1 and COX-2 enzymes associated with inflammation	Bind opioid receptors; most commonly administered drug class for treating acute postsurgical pain	Prevent depolarization of nerve cells by binding to and blocking sodium channels
Commonly Used Agents	NA	ketorolac, ibuprofen, aspirin	morphine, fentanyl, oxycodone	bupivacaine, lidocaine
Use in Practice	May be used in combination with NSAIDs and/or opioids for baseline post-surgical pain control	For baseline level of post-surgical pain control; often combined with opioids	Most commonly administered by IV PCA; used most often to manage acute breakthrough pain episodes	As a local anasthetic in administered directly to the wound; also used as epidural and nerve block
Advantages	-Antipyretic properties; orally available	Respiratory depression and sedation not risks as is case with opioids; some agents like ketorolac more potent than APAP	Considered most efficacious class of drugs available for managing pain	Limited systemic activity (local) activity; easily combinable with other agents
Limitations	-Does not have anti-inflammatory properies; less potent as analgesic versus opioids and a number of NSAIDs	Used with caution in postsurgical setting due to increased bleeding risk plus GI and renal complications	Numerous side effects (respiratory depression, sedation, impaired GI motility); not ideal in patients already opioid tolerant	-Relatively short duration of action (only approximately 7 hours or less with traditional formulations)

Source: PJC research and industry reports

Administration Modalities a Key Consideration; Exparel Has an Advantage in This Respect

There are obviously a number of ways to deliver analgesics to patients undergoing surgery, and mode of administration can vary considerably based on the underlying surgery type, the patient's ability to hold down oral agents, and the need (or lack of a need) for rescue medication to manage breakthrough pain in the recovery period. Given that hospitals are continually exploring ways to cut down on the risk of medication errors, minimizing post-operative complications and ultimately reducing recovery times (all with an eye towards holding down costs), mode and ease of administration is an important consideration, and in this respect, we believe Exparel will resonate with anesthesiologists and other key stakeholders involved in the patient recovery post-surgery. Below we provide additional detail on common administration modalities and how Exparel may have an advantage.

Elastomeric infusion pumps: complex, labor intensive way to deliver bupivacaine for an extended period; Exparel can accomplish this with a single injection. Elastomeric infusion pumps are used to deliver analgesics over an extended period directly to the surgical incision site via an elastic balloon connected to a catheter. These systems generally are used to deliver locally acting analgesics, bupivacaine in most cases. The most widely used elastomeric infusion system is the I-Flow's ON-Q, which has been commercially available in the U.S. since 2004. I-Flow was acquired by Kimberly Clark in November 2009 for a net transaction value of $276 million. The goal of using the device is to deliver potent analgesia while reducing the reliance on opioids. We estimate that annual sales of the ON-Q system are in the $150 million to $200 million range (we further estimate that I-Flow has a market share of over 50% of the elastomeric infusion pump market in the U.S.). I-Flow reported that over 700 hospitals using ON-Q for post-surgical pain management in 2008, with over 500,000 units placed. The device is fairly labor intensive, with placement required intra-operatively. Lastly, the system is not cheap, with a cost that runs at roughly $275 per patient (we note that Pacira has alluded to Exparel pricing being closer to $200). Below we highlight the limitations associated with elastomeric infusion pumps:

- **Patient is catheterized, and therefore tethered to the device.** The patient is tethered to the device during the recovery period, potentially limiting patient ambulation. The device must be removed by the surgeon once it is no longer needed.
- **Potential for catheter-related infections.** The use of the device is not without risk given that the catheter placement directly to the surgical site can result in infection, potentially resulting in lengthier hospital stays.
- **Inaccurate delivery of active drug on occasion, and technical problems associated with the device.** Inaccurate delivery of active drug is can be a pitfall. Further, other problems such as the pump failing to deflate, and the catheter may become dislodged or disconnected, can also occur.

Figure 10: Examples of Elastomeric Infusion Pumps

Source: I-FLOW, Symbios

We believe that the elastomeric infusion pump portion of the market constitutes fertile ground for Exparel adoption. The goal of Exparel and elastomeric infusion pumps is generally the same: provide non-opioid-based pain relief for an extended period. Exparel essentially accomplished pharmacologically what the elastomeric infusion pumps can do but in a far less labor intensive, complicated and potentially costly manner (inclusive of the costs associated with catheter-related infections). Exparel essentially constitutes a single injection to the wound site (i.e., wound infiltration) and is free of the management and monitoring requirements associated with elastomeric infusion systems.

IV patient-controlled analgesia (PCA): standard mode of administering rescue medication, but fraught with limitations. Patients recovering from surgery often need treatment with IV-based agents such as antibiotics and fluids to prevent or treat dehydration. Opioids are also commonly used via IV administration, commonly in a patient-controlled manner, to manage breakthrough pain episodes and keep pain levels at bay. Morphine and fentanyl are the two most commonly administered agents used in IV PCA. We outlined the pitfalls of opioids above. According to one study published in the *Journal of Pain and Symptom Management*, opioid-related adverse events accounted for 59% of all adverse events at LDS Hospital in Utah over a 10 year period (Oderda, 2003), and the cost of these adverse events added $499 to the cost of the surgical procedure. In addition to these pitfalls, IV PCA systems can also be complex and labor intensive in terms of setting up and monitoring. According to an FDA database of IV PCA-related medical events, 79% of these events were possibly related to device errors, with pump programming errors responsible for 5% of documented events. Further, the cost of using IV PCA over a three day period can run to near $600, according to available literature (and the cost of opioid-related adverse events obviously imposes additional costs, not to mention conferring risk to patient well-being).

Figure 11: Examples of Intravenous (IV) Patient-Controlled Analgesia (PCA) Devices

Source: Hospira, Monet Medical

We do not see Exparel obviating the need for patient-controlled analgesia. Breakthrough pain will continue to be a reality for patients, and there will continue to be a wide need for safe and effective breakthrough pain medications and safe/simple delivery modalities. That said, we believe an agent like Exparel can reduce the reliance on opioids to some extent in certain surgical settings.

Figure 12: Modalities for Drug Administration for Surgical Patients

	PCA (Patient Controlled Analgesia)	Elastomeric Bags	Oral Administration	Wound Infiltration	Epidural Administration	Nerve Block
Description	IV administration of analgesics for "rescue" therapy; controlled by a patient-controlled pump	Catheter-based system to administer non-opioid such as bupivacaine directly to surgical site over extended period	Includes NSAIDs, opioids, and acetaminophen	Injection of a non-opioid into the wound space during surgery to provide baseline pain control	Medication is injected via a catheter into epidural space outside of the spinal fluid	Injection of local anesthesia near or on nerve sites
Number of procedures in U.S. using this modality	16 million	1 million	NA	24 million	6 million	8 million
Drugs used	opioids (mainly morphine, fentanyl)	mostly bupivacaine	acetaminophen, oxycodone, aspirin	bupivacaine	bupivacaine, opioids (morphine, fentanyl)	bupivacaine, lidocaine
Advantages	patient-controlled (vs nurse-controlled) pain relief	Provides longer-lasting non-opioid (e.g., bupivacaine)	Ease of use	Ability to begin pain control during surgical procedure	Allows for sustained drug delivery when catheter is used	Complications from peripheral nerve blocks are rare
Limitations	Potential for programming and medication errors; costly	Requires surgical procedure to remove; potential for catheter infections; system is costly	Oral pain relief medication not typically as effective as IV; longer time to onset	Pain relief does not last typically for greater than 7 hours for conventional local/regional anesthetics	Potential for catheter complications	Limited duration of effect

Source: PJC research and industry reports

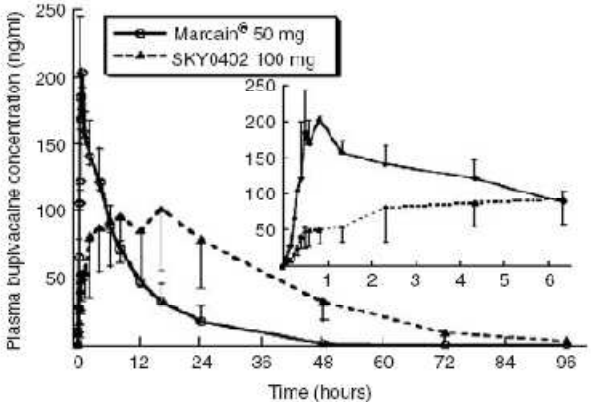
Pharmacokinetic Profile of Exparel Underscores Advantages Over Conventional Bupivacaine

Pacira has run numerous studies looking at the pharmacokinetic (PK) profile of Exparel versus conventional immediate-release bupivacaine. In a randomized, double-blind, Phase I study, healthy patients received either Exparel at 100 mg or Marcaine at 50 mg as a single epidural injection. The mean plasma concentration of Exparel peaked later than the mean peak in the Marcaine group. Further, the peak for the Exparel group never exceeded a concentration of 113 ng/mL, compared to the peak concentration of 214 ng/mL in the Marcaine group. Further, the half-life of Exparel was 15 hours, compared to 6.5 hours for Marcaine. The key takeaway here is that Exparel produces a smoother PK profile relative to conventional bupivacaine, with less of a spike (but still achieving highly therapeutic levels) and a longer duration of activity.

Figure 13: Pharmacokinetic Profile of Exparel Versus IR Bupivacaine

	CB (Marcain) 50 mg N = 2	SKY0402 100 mg N = 8
C_{max} (ng/mL)[1]	214 (0)	113 (40)
T_{max} (hr)[2]	0.7 (0.5–0.9)	7.3 (0.5–16.3)
AUC_{0-last} (hr*ng/mL)[1]	1764 (26)	3854 (33)
$T_{1/2}$ (hr)[2]	6.5 (6.1–6.9)	14.9 (9.8–29.6)

[1]Geometric Mean (CV%); [2]Median (min-max).



Source: Company reports

Background on Clinical Studies for Exparel

Pacira successfully completed two placebo-controlled pivotal studies evaluating Exparel in post-operative pain. Not surprisingly, the FDA wanted studies in both an orthopedic surgical model and a soft tissue surgical model. The soft tissue model was hemorrhoidectomy and the orthopedic model was bunionectomy. These studies formed the basis of the September 2010 NDA submission.

Figure 14: Summary of Exparel Pivotal Randomized Phase III Clinical Trials

Indication	Trial Description	Number of Patients	Primary Endpoint	Secondary Endpoints
Hemorrhoidectomy	Exparel at 300 mg versus placebo	189 (14 sites in Central and Eastern Europe)	-30% reduction in NRS pain scores at 72 hours as measured by AUC (p<0.0001) -Statistically significant difference in pain scores through every tested timepoint (p<0.0001)	-28% of patients on Exparel were opioid-free through 72 hours vs 10% of patients on placebo (p<0.0007) -Total opioid consumption was 45% less for Exparel patients versus placebo patients through 72 hrs (p=0.0006) -Median time to first opioid rescue placebo patients 1 hr 10 mins, Exparel patients 14 hrs 20 mins (p<0.0001) -Patients were satisfied with Exparel compared to placebo at both 24 and 72 hours post-dose (p=0.007)
Bunionectomy	Exparel at 120 mg versus placebo	193 patients (4 sites in the U.S.)	-Statistically significant reduction in NRS pain scores as measured by AUC at 24 hours (p=0.0005) -Statistically significant reduction in pain scores out to 36 hours	-Significant decrease in percentage of patients pain-free favoring Exparel group through 8 hours (p=0.0078) -Significant decrease in percentage of patients not needing opioid rescue through 24 hours (p=0.05) -Significant decrease in total opioid consumption (p<0.05)

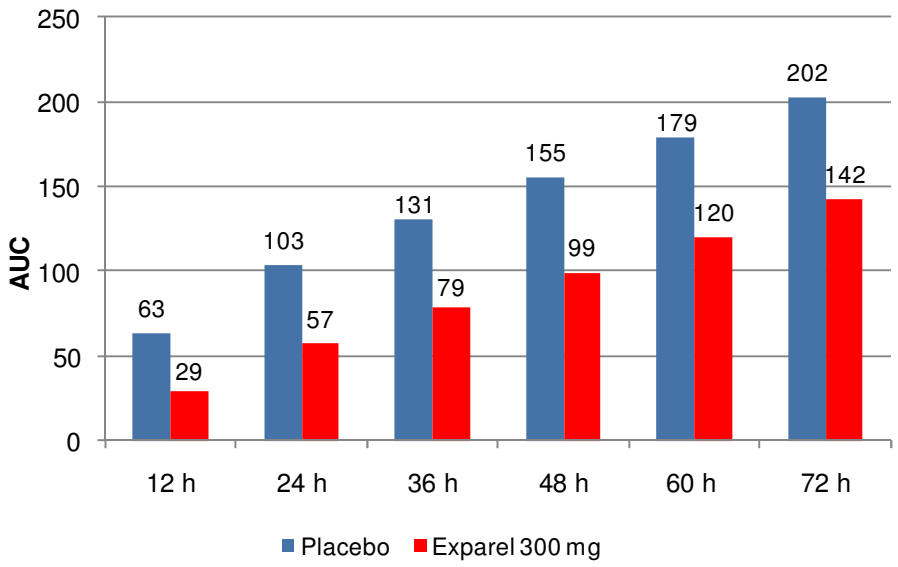
NRS-R=numeric rating score at rest measured on a scale from 0 to 10, with 10 representing the worst possible pain;
AUC=area under curve: represents a sum of the patient's pain at several time points
Source: Company reports, PJC research

Phase III hemorrhoidectomy study. This was a randomized, double-blind, multicenter, placebo-controlled trial that evaluated 189 patients treated with either Exparel or placebo. The trial was conducted in 14 sites in Central and Eastern Europe (the sites were in Poland, Georgia, and Serbia) in patients 18 years of age and older. Exparel at 300 mg was tested. The trial's primary endpoint was pain control at 72 hours post-surgery measured by the area under the curve (AUC) of the NRS-R (numeric rating scale at rest) scale, a pain scale that scores pain from 0 to 10 with 10 being the most extreme level of pain experienced. The measurement of AUC of the NRS-R denotes the total amount of pain experienced by a patient over a given time period. Patients had the option of receiving morphine rescue, but did not receive any other pain medications (other than active drug if they were randomized to Exparel). Secondary endpoints included the percentage of patients requiring opioid rescue medication, the percentage of pain-free patients, time to first opioid rescue medication usage, total opioid usage, and patient satisfaction.

Patients treated with Exparel experienced a 30% improvement in pain scores relative to placebo at the 72-hour time point, with a p-value of less than 0.0001. The Exparel arm was also statistically superior to placebo on the NRS-R AUC measure at 12, 24, 36, and 60 hours following surgery. Exparel was also statistically superior to placebo on the following secondary endpoints:

- **Avoidance of opioid rescue medication.** 28% of patients on Exparel received no opioid rescue medication through 72 hours, compared to 10% of placebo patients (p=0.0007)
- **Consumption of opioids.** The mean total amount of opioids consumed through 72 hours was 45% less in patients on Exparel relative to placebo patients (p=0.0006)
- **Portion of patients who were pain-free at specific time points.** Increased number of pain free patients at all times (p=0.0448)
- **Patient satisfaction.** Improved patient satisfaction at 24 and 72 hours (p=0.0007)

Figure 15: Phase III Hemorrhoidectomy Trial: Primary Endpoint of AUC of NRS-R Pain Intensity Scores



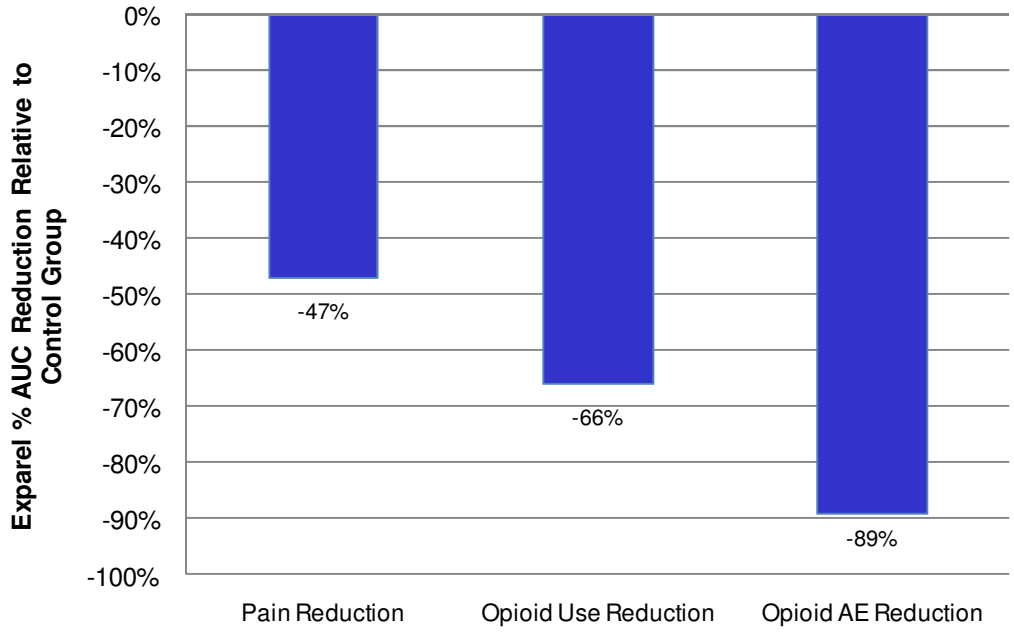
Abbreviations: AUC=area under the curve, NRS-R=numeric rating scale at rest
Source: Company reports

Phase III bunionectomy study. This was a randomized, double-blind, multicenter, placebo-controlled trial in which 193 patients were treated with either Exparel or placebo. We note that in this study, Exparel at 120 mg was tested and pain control was assessed out to 24 hours post-surgery. The difference in dosing and duration of evaluation versus the hemorrhoidectomy study was that this surgical model is not nearly as invasive (the surgical incision is far smaller) and therefore the extent of pain several days after surgery is far lower than the extent of the pain experienced by hemorrhoidectomy patients (particularly in the context of the Milligan-Morgan technique for hemorrhoid removal). This study enrolled patients at four sites in the United States. As was the case with the hemorrhoidectomy study, the primary endpoint of the trial was pain control as measured by AUC of the NRS-R. Patients also had the option of receiving opioid rescue medication.

Patients treated with Exparel experienced a statistically significant reduction in pain at the 24-hour timepoint, with a p-value of 0.0005. Exparel was also statistically superior to placebo on a number of secondary endpoints, including avoidance of opioid rescue medication through 12 hours (p=0.0003) and 24 hours (p=0.0404), percentage of patients who were pain-free at 2 hours (p=0.0019), 4 hours (p=0.0002), 8 hours (p=0.0078), and 48 hours (p=0.0153) post-surgery (though the difference was not statistically significant at 24 hours). As was the case in the hemorrhoidectomy trial, there were no serious safety issues.

Prior Phase II study versus conventional bupivacaine showed advantage for Exparel in terms of opioid use. In this study, Exparel at a dose of 300 mg was tested head-to-head versus immediate-release bupivacaine at 75 mg in 100 patients undergoing hemorrhoidectomy. The primary endpoint of the study was AUC (area under the curve) of the numeric rating scale at rest (NRS-R) of pain intensity at 72 hours, with Exparel showing a statistically significant 46% decrease in pain scores compared to immediate-release bupivacaine . The most important positive takeaway from the trial in our view was that total consumption of opioids in patients on Exparel was reduced by 66% versus the active comparator arm. Further, there was an 89% decrease in the incidence of opioid-related adverse events versus the active control arm.

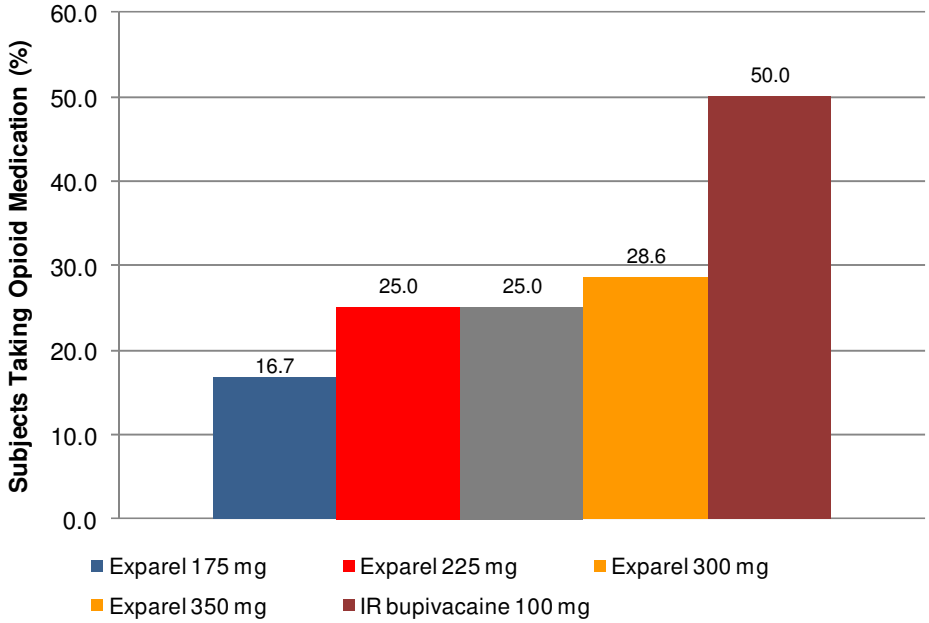
Figure 16: Phase II Hemmoroidectomy Study: Exparel at 300 mg Versus IR Bupivacaine at 75 mg Through 72 Hours



Source: Company reports

Additional Phase II studies also showed reduced opioid consumption relative to conventional bupivacaine. Pacira ran a number of other studies testing Exparel versus conventional bupivacaine, looking at endpoints such as total opioid consumption as well as opioid-related adverse events. Figure 17 below highlights results from a Phase II multi-dose study (Exparel at doses of 175, 225, 300 and 350 mg versus IR bupivacaine at 100 mg) in 76 patients undergoing hernia repair. In this study, 50% of patients on IR bupivacaine used opioids in the study. In contrast, 29% of patients treated with Exparel at 300 mg (a dose that Pacira is planning to commercialize) used opioid medications.

Figure 17: Phase II Hernia Repair Study: Percentage of Subjects Taking Supplemental Opioid Pain Medication



Source: Company reports

Setbacks from Prior Phase III Studies Not a Red Flag

Pacira did not get the pivotal studies right on the first go-around. Under the prior management team, the company designed and ran three pivotal studies testing Exparel via wound infiltration. Pacira completed two of these studies in 2009. The trials evaluated patients undergoing total knee arthroplasty (TKA; i.e., knee replacement surgery) and hemorrhoidectomy. These trials enrolled a total of 223 patients who received Exparel along with additional concomitant analgesics. Both of these studies did not meet their primary endpoints, though Exparel was shown to be safe and well-tolerated in both trials. Following the setbacks, Pacira stopped enrollment of a third study testing Exparel in patients undergoing breast augmentation (the design of which was similar to the other two studies).

We believe that the main reasons these studies failed were due to flaws in trial design that made it exceedingly difficult for Exparel to show superiority versus control. Below we provide additional color explaining why these studies failed, and why we do not believe the prior setbacks will meaningfully impact regulatory risk.

- **Both the hemorrhoidectomy and TKA studies were superiority studies that used conventional bupivacaine as an active control, and use of background concomitant medications were allowed.** The hemorrhoidectomy study tested Exparel at 300 mg versus immediate-release bupivacaine at 100 mg. The TKA study tested Exparel at 600 mg versus immediate-release bupivacaine at 200 mg (the dosing in the TKA was higher since TKA involves a very long incision of around 8-9 inches with a longer and more painful recovery time than most other surgeries). Both studies were powered for superiority, a difficult hurdle in itself. To make matters worse, patients received an injection of the NSAID ketorolac and all patients also received acetaminophen. These additional background medications in the context of a superiority design made it exceedingly difficult to tease out a benefit for Exparel versus immediate-release bupivacaine. In the TKA study, patients were also allowed opioid rescue medication, making it even harder to tease out a benefit.

- **Hemorrhoidectomy study was not particularly invasive.** The failed study tested patients undergoing the Ferguson surgical method, which involves a partial excision of the hemorrhoid. This type of procedure is not as invasive as the virtually curative Milligan-Morgan technique, which involves a deep incision that is around 2-3 inches in order to remove the hemorrhoid, and as a result, the recovery period is far more painful. The failed trial was performed in the U.S., where the Ferguson method is fairly typical. In addition to the design flaws discussed above, this procedure is simply not that painful, making it especially difficult to tease out a benefit for Exparel. The successful hemorrhoidectomy study was performed in Central and Eastern Europe, where the Milligan-

Morgan technique is more common. That study did not incorporate background NSAIDs or APAP, and was a painful enough procedure where a high placebo response that could prevent a statistical separation was unlikely (bearing in mind that placebo responses in pain studies are usually strong).

- **Flaws with data collection.** In both of the failed Phase III studies, patients were given paper diaries (questionnaires) to fill out. Pacira noted that monitoring of patients was non-consistent, specifically noting that monitoring to ensure that patients were filling out their diaries at specified time intervals was not well organized.

Placebo-controlled studies should be adequate for FDA approval, particularly if recent FDA activity is any indication. We note that placebo-controlled trials are generally the hurdle required for approval of pain medications, both in an inpatient and outpatient setting. Further, our combing of the available literature did not come across any active comparator studies of bupivacaine or products related to bupivacaine (such as ropivacaine and levobupivacaine, both of which are FDA-approved) that showed superiority to the conventional product. In the context of active controls, a non-inferiority design would likely have been successful. In terms of opioid consumption, one would think that despite the failure on the primary endpoints, we would have at least seen a difference favoring Exparel. That was not the case here, and the flaws in patient monitoring and especially the liberal use of background medications in both arms (the TKA study incorporated background ketorolac and acetaminophen) made for an exceedingly difficult bar for showing a difference on this front. Ultimately, we believe that Pacira will have to make the case that there is an opioid-reducing impact and opioid adverse event impact via Phase IIIb and Phase IV studies, which are a major part of the early commercialization phase of the product's life.

Figure 18:Recent FDA Approvals on Non-Opioid Analgesics on Placebo-Controlled Studies

Company	Drug Name	Description	Indication	FDA Approval	Summary of Pivotal Studies
Cadence Pharmaceuticals	Ofirmev	IV acetaminophen (APAP)	Mild to moderate pain; moderate to severe pain as an adjunct to opioids	Nov-10	Two placebo-controlled Phase III studies: -total hip or knee replacement -abdominal laparoscopic surgery
Roxro Pharma	Sprix	keterolac nasal spray	Moderate to moderately severe acute pain	May-10	Two placebo-controlled Phase III studies: -elective abdominal or orthopedic surgery -elective abdominal surgery
Cumberland Pharmaceuticals	Caldolor	IV ibuprofen	Mild to moderate pain; moderate to severe pain as an adjunct to opioids	Jun-09	Two placebo-controlled Phase III studies: -elective abdominal hysterectomy -elective abdominal or orthopedic surgery
Xanodyne Pharmaceuticals	Zipsor	diclofenac oral capsules	Mild to moderate acute pain	Jun-09	Two placebo-controlled Phase III studies in bunionectomy patients with osteotomy

Source: PJC research and industry reports

Minimal Learning Curve Related to Exparel Administration and Storage In Our View

Exparel administration via wound infiltration the same as how conventional bupivacaine is administered. One of the more favorable aspects of Exparel in our view is that the product is administered in the same manner as conventional bupivacaine. The product is given via wound infiltration, and is dosed to volume with saline solution. There is no mixing of solution required prior to injection. In this sense, the learning curve for anesthesiologists is minimal.

Refrigeration requirement should not be an issue. Due to the temperature sensitivity of the drug-containing liposomes, Exparel must be refrigerated. The product has a shelf-life of approximately 2 years, but if the product is stored at room temperature, the shelf-life is closer to 30 days. When the liposome particle is stored between 4° and 8° C (approximately 39° to 46° F) in saline, its structure is maintained and the drug remains inside the lipid chambers. While hospitals are well equipped for cold storage, there is always the possibility of human error (in other words, freezing the product instead of refrigerating it, or leaving the product in a warm temperature environment). When a vial of Exparel freezes, about 50% of the liposomes fall off the active drug, but there is no visible difference seen in the look and feel of the vial. The result is that if a vial is used after it was frozen and then unfrozen, patients essentially would be receiving free bupivacaine. However, Pacira has noted that even if half of the liposomes fall off, the amount of free bupivacaine released would still be at a safe amount (i.e., 150 mg of free bupivacaine if the 300 mg vial is frozen, then unfrozen, and then used). For a total knee replacement surgery, the average dose of bupivacaine is about 150-200 mg, so the key takeaway here is that the amount of free bupivacaine released from the 300 mg vial that had previously been frozen would not pose a risk to the patient. Vials also should not be shaken because this may cause some of the liposomes to fall off. When the vial is overheated, the appearance of the vial will

change with the liposomes taking on a "stringy" shape. So in this context, it is easier for a nurse or surgeon to discern that something is amiss with the vial.

Pacira has taken a number of steps to ensure that the risk of mistakes related to storage and handling is minimized. Below we highlight these steps:

- **Temperature indicator on the box containing the vial.** Pacira is incorporating a temperature indicator on the box containing the vial in order to ensure that box is properly stored.

- **Temperature indicator also on each vial.** The vials themselves will also include an indicator. Specifically, a light indicator will denoted if the vials are too hot or too cold.

- **No headspace in vials as a precaution against freezing and shaking.** Pacira has developed vials without any additional headspace (i.e., empty space between the fluid and the stopper). The idea here is that the solution will expand if frozen, but the appearance of the vial may still look the same. Incorporating a design that does not include headspace means that as the solid expands, the stopper on the vial will pop off without any headspace, rendering it unusable. This ensures that a previously frozen vial will not be used. The lack of headspace also means that even if the vial is somehow shaken (this runs the risk of the liposomes falling off), the liquid will not more around as much which reduces the risk of the liposomes falling off, resulting in free bupivacaine being released.

- **Risk evaluation and management strategy (REMS) to be implemented around storage and handling.** Pacira has proposed a REMS around minimizing the risks of improper storage and handling. As we mention above, if a vial is overheated, the solution develops a stringy appearance. The labeling language would guide users on what to look for in this case, as well as cautionary language regarding not freezing the vial.

Our Thinking on Exparel Sales and Margin Potential

Commercial plan encompasses both inpatient and outpatient surgical procedures. Pacira is proposing a label for Exparel that encompasses post-surgical pain broadly speaking, with the drug used by local wound infiltration. The company's sales force will focus on major hospitals and ambulatory surgery centers in the U.S., targeting anesthesiologists, surgeons, nurses, and pharmacists. The goal here is to address physicians and surgeons performing both inpatient and outpatient surgeries. Pacira also plans to target hospital purchasing decision makers with the goal of making the case that the use of Exparel can result in cost savings to the hospital. We note that Pacira is in discussion with potential partners for markets outside of the U.S.

We estimate that Exparel will become commercially available in 4Q11, with 2012 sales totaling $35 million, growing to $216 million by 2015. Below we provide additional color on our assumptions underlying our sales estimates:

- **Addressable market and estimates for penetration.** According to available literature, estimates for the total number of surgical procedures performed in the U.S. range from around 32 million to over 45 million. These encompass the following settings: general surgery, orthopedics, obstetrics/gynecology, cardiothoracic, and plastic surgeries. Pacira has estimated that there are a total of approximately 24 million surgeries where a long-acting analgesic would be appropriate (in other words, surgeries that require at least several days of recovery time and where IR sodium channel blockers are already used). We estimate that this market is split roughly evenly between inpatient and outpatient procedures. By 2014, we estimate that 11% of inpatient procedures would actually be considered for a long-acting analgesic, and 10% of outpatient procedures would be considered for a long-acting analgesic, translating into eligible procedures of 1.5 million and 1.3 million for the inpatient and outpatient settings, respectively. We assume an Exparel penetration of 65% for both inpatient and outpatient settings in 2014, translating into a total combined procedure volume for Exparel of around 712,000. Our estimates in 2014 reflect the presence of Hospira/DURECT's Posidur (we estimate a 2013 launch of the product).

- **Pricing.** Our model assumes a cost per patient procedure of $200. The price is based on a 300 mg dose of Exparel and a cost per milligram of $0.67. Further, our estimates do not reflect any price increases over time.

- **Sales force.** Pacira plans to deploy a sales force of approximately 40 sales representatives upon launch, with the goal of expanding the sales force to 100 representatives by year 3. The company is planning to target the top 1,000

hospitals in terms of annual volume of surgical procedures. These 1,000 hospitals represent 70% of the target audience for Exparel.

Figure 19: Exparel Sales Projections

(Sales $ in millions)	2010E	2011E	2012E	2013E	2014E	2015E
U.S. Sales - Postsurgical Analgesia						
In-patient procedures eligible for long-acting analgesic	12,600,000	12,820,500	13,044,859	13,273,144	13,505,424	13,741,769
% of procedures where long-acting analgesic is considered		*0.5%*	*4.0%*	*8.0%*	*11.0%*	*15.0%*
Procedures where long-acting analgesic is considered		64,103	521,794	1,061,852	1,485,597	2,061,265
Long-acting bupivacaine share of long-acting analgesic market		*10.0%*	*20.0%*	*30.0%*	*40.0%*	*50.0%*
Procedures where long-acting bupivacaine is used		6,410	104,359	318,555	594,239	1,030,633
Exparel share of long-acting bupivacaine market (1)		*100.0%*	*100.0%*	*75.0%*	*65.0%*	*60.0%*
Procedures using Exparel		6,410	104,359	238,917	386,255	618,380
Price per mg Exparel		$0.67	$0.67	$0.67	$0.67	$0.67
Avg dose Exparel per procedure (mg)		300	300	300	300	300
Price per procedure		$200	$200	$200	$200	$200
Exparel Sales in in-patient Surgeries		**$1.3**	**$20.9**	**$47.8**	**$77.3**	**$123.7**
Out-patient procedures eligible for long-acting analgesic	11,700,000	11,904,750	12,113,083	12,325,062	12,540,751	12,760,214
% of procedures where long-acting analgesic is considered		*0.5%*	*3.0%*	*7.0%*	*10.0%*	*12.0%*
Procedures where long-acting analgesic is considered		59,524	363,392	862,754	1,254,075	1,531,226
Long-acting bupivacaine share of long-acting analgesic market		*10.0%*	*20.0%*	*30.0%*	*40.0%*	*50.0%*
Procedures where long-acting bupivacaine is used		5,952	72,678	258,826	501,630	765,613
Exparel share of long-acting bupivacaine market (1)		*100.0%*	*100.0%*	*75.0%*	*65.0%*	*60.0%*
Procedures using Exparel		5,952	72,678	194,120	326,060	459,368
Price per mg Exparel		$0.67	$0.67	$0.67	$0.67	$0.67
Avg dose Exparel per procedure (mg)		300	300	300	300	300
Price per procedure		$200	$200	$200	$200	$200
Exparel Sales in out-patient Surgeries		**$1.2**	**$14.5**	**$38.8**	**$65.2**	**$91.9**
Total Exparel U.S. Sales		**$2.5**	**$35.4**	**$86.6**	**$142.5**	**$215.5**

(1) Assumes FDA approval of DRRX/Hospira's Posidur in late 2012/early 2013

Source: Company reports and PJC estimates

A word on margins: manufacturing efficiencies to drive expansion longer-term. Exparel will be manufactured out of Pacira's San Diego facility. The product is currently made out of a 2,500 square foot manufacturing suite, referred to by management as suite A. The company has noted that this suite is semi-automated, and as a result, carries higher production costs relative to the current suite, known as suite C, that is being built out. With the current IPO funding and cash position, management expects to move forward with the completion of the more automated (and therefore more efficient) suite C following the FDA approval of Exparel. As such, production of Exparel for the launch will come out of suite A. Management has noted that suite A has enough capacity to produce roughly $50 million worth of Exparel in a given year (assuming a cost per patient procedure of $200), with the ability to make another $15M-$20M worth of product in the pre-launch period (for a total of up to $70 million in capacity out of suite A).

According to management, the gross margin on product made out of suite A would be around 50% (again assuming a cost per patient procedure of $200). The build-out of suite C could be complete in 2013, with Exparel produced primarily out of that suite that year (though this is dependent of course on approval and an eventual capital raise post-approval, likely in the late 2011 or 2012 timeframe). The gross margins out of suite C would be about 80% according to management (inclusive of royalties to third parties that amount to about 5% of sales; the biggest royalty obligation would be to Skye Pharma at 3% of sales). We note that suite C would have significantly more capacity than suite A, with Pacira having the ability to make roughly $150 million worth of drug in a given year.

Beyond suite C, Pacira is developing an even more efficient and in some respects novel manufacturing process that beyond 2013 offers the potential to drive gross margins even higher. The new processes are part of the patent application # 61/322,814, which has claims related to a process to make multi-vesicular liposomes. The build-out of these new capabilities

is dependent on additional funding. That said, assuming that Pacira can leverage these new capabilities, gross margins potentially could approach 90%.

Phase IIIb/IV program will accompany the rollout; designed to provide hospitals with data pointing to positive health economic outcomes. A major part of the Exparel rollout will be centered around what Pacira refers to as health economic outcome studies. There is no question that hospitals operate under significant cost constraints, and in the context of surgery, reimbursement is in a capitated paradigm, meaning that the hospital receives a fixed, per capita amount for a defined period from managed care for the surgery itself and all elements associated with the surgery, from the cost of medications, surgical equipment, to the cost of the operating room time and costs related to the recovery time. In the capitation payment method, the volume of procedures does not have any effect on the payment.

Part of the health economics analyses will include patient registries looking at outcomes in specific surgical settings. The Phase IIIb/IV program, which Pacira has already initiated, will include retrospective and as well as prospective analyses.

- **Retrospective analyses.** A series of retrospective analyses through hospital networks will analyze outcomes of patients where treatment with opioids is most problematic. These patients will include the elderly, obese individuals, patients with Type II diabetes, patients with sleep apnea, and patients undergoing orthopedic surgeries who are opioid tolerant (in other words, patients treating osteoarthritis and rheumatoid arthritis with opioids on a chronic use basis). The idea here is to assess these groups of patients who have been on Exparel, and tease out the pharmacoeconomic benefits (i.e., in terms of less opioid consumption and therefore opioid-related adverse events, as well as length of hospital stays).

- **Prospective studies.** For these studies, the initial focus will be in abdominal and soft tissue surgeries including colectomy, total hysterectomy, and colisystectomy (gall bladder removal). Pacira will also assess bariatric surgery patients. These are highly invasive procedures commonly in patients who are obese or elderly (or both). One analysis will look at hospital data, to be reported in the spring of 2011. This will be an observational single center study looking at 16-20 abdominal surgery patients treated with Exparel. Data will be collected on the following endpoints: 1) cost of various adverse events, and 2) time to discharge readiness.

Additional Opportunities for Exparel: Epidural Administration and Nerve Block

Pacira is also exploring the development of Exparel for both epidural administration and as a nerve block. We note that our model does not reflect contribution from these additional indications. The advancement of the product in these two indications is dependent on additional funding. Below we provide additional color on these expansion opportunities.

- **Epidural administration.** The epidural route of analgesia administration involves placing a catheter within the epidural space of the spinal canal, outside of the spinal fluid. The drug is then administered continuously by a pump. The catheter placement allows prolonged drug delivery than occurs with a single epidural injection. This route of administration can be used during major surgeries such as lung surgery. Both opioids, such as morphine and fentanyl, and non-opioids including bupivacaine, are routinely delivered by epidural analgesia. According to Pacira, there are approximately 6 million procedures in the U.S. that incorporate epidural analgesic, with near 600,000 of these involving bupivacaine.

  The advantage of using Exparel in epidural administration is that since the drug is long-acting, a single injection can accomplish the same thing as the catheter that allows for continuous drug delivery. Pacira completed a Phase I trial of 24 patients receiving Exparel via epidural administration, with the drug demonstrating strong safety and tolerability. Assuming additional funding, Pacira would be in a position to move Exparel via epidural administration into additional Phase II and Phase III trials once additional capital becomes available.

- **Nerve block.** Nerve block refers to the injection of local anesthesia near or onto nerves. Post-surgery, nerve block can be used for pain relief. Anesthetics injected for nerve block include bupivacaine, lidocaine, mepivacaine, and prilocaine. According to Pacira, there are an estimated 8 million procedures in the U.S. that incorporate analgesia via nerve block, with nearly half of these involving bupivacaine.

  Pacira completed two Phase II trials in which a total of 40 patients received Exparel via nerve block. One Phase II trial tested Exparel administered via ankle nerve block in patients undergoing bunionectomy. The primary endpoint

of the trial was time to first use of supplemental pain medication. Patients were randomized to receive either Exparel at three different doses, or 125 mg of conventional bupivacaine. Assuming additional funding, Pacira would be in a position to move Exparel via nerve block into additional Phase II and Phase III trials in the second half of 2011.

Competitive Landscape: High Barriers for Generics; Not Worried About Potential Brand Competitors

Manufacturing Complexities and Patent Estate Make Generic Competition Unlikely

Complicated manufacturing process related to DepoFoam provide significant barrier for generics. The manufacturing of products incorporating the DepoFoam technology is highly complex, and as a result, we would be surprised to see a generic manufacturer try to replicate Exparel. The manufacturing of products using DepoFoam takes place using an aseptic process, meaning that the process is free of contact with microorganisms (not just microorganisms that can cause disease). In manufacturing circles within the pharmaceutical industry, aseptic product is considered to be difficult, with difficult hurdles for validation and regulatory approvals. Further, a number of steps involved in the process of manufacturing bulk product for an agent that uses DepoFoam incorporates the creation of emulsions, processes that generics companies in general have limited experience with. Lastly, other complexities including particle size distribution and the handling of one of the emulsions, plus the specific equipment involved in product add to the barriers for potential generic entrants. We note that Pacira's DepoCyte was approved by the FDA in 1999, and there are no generic competitors despite the fact that U.S. patents on the product expired in 2006. Pacira has noted that it believes that a generic manufacturer would need at least several years to build out and validate such a site as well as obtain regulatory approval. Pacira also noted that the expense associated with the build-out of such manufacturing capabilities would likely be cost prohibitive for generic manufacturers (up to $100 million in total build-out costs).

Several issued patents in the U.S., with a number of applications on additional patents pending. Pacira has a number of issued U.S. patents with claims surrounding the composition of Exparel (active ingredient bupivacaine using DepoFoam) as well as claims surrounding the product's release profile. The patents on these claims expire in November 2013 and January 2017, respectively. Additional U.S. patent applications are related to the composition of Exparel and manufacturing processes and these patents, if issued, would expire in September 2018 and November 2018. Lastly, Pacira filed a provisional patent related to a new manufacturing process associated with Exparel and other products using DepoFoam. This is the process that would be used rather than the process used in suite C if Pacira is able to secure additional funding down the road to complete the build-out of these capabilities. The patent, if issued, would expire in 2031. This application, US 61/322,814, is related to a new process to make MVLs. Though Pacira has not discussed the application in great detail, it noted that the process allows for manufacturing at a larger scale and involves lower costs relative to the processes used in its currently functional manufacturing suites as well as suite C. We note that at a minimum, Exparel will have three years of exclusivity under Hatch-Waxman. That said, given the manufacturing complexities and patent estate, we do not see generic competition as a realistic possibility. We believe the main source of competition will come from other brands.

Figure 20. Summary of Issued Patents and Pending Patent Applications in the U.S. for Exparel

Patent/ Application #	Status	Description	Summary of Claims	Expiry
6,132,766	Issued	MVLs for CR	Manufacturing process	11/16/2013
5,766,627	Issued	MVLs for CR	Manufacturing process	11/16/2013
5,891,467	Issued	Neutral lipids	Manufacturing process	1/31/2017
5,931,809	Issued	Epidural administration	Method of use	7/14/2015
6,428,529	Issued	Epidural administration	Method of use	7/14/2015
11/097756	Pending	Anesthetic compositions	Composition/method	NA
11/678,615	Pending	Production of MVLs	Process	NA
61/322,814	Provisional	Improved process	Apparatus, method, PbP	NA

Abbreviations MVL multivesiscular liposomes

Source: PJC research and industry reports

Overview of Branded Competition: Posidur One to Two Years Behind Exparel; Market Can Easily Accommodate Multiple Players

Durect's Posidur is 1-2 years behind Exparel in clinical development. A potential competitor to Exparel is DURECT's Posidur, also a long-acting form of bupivacaine in development for post-operative pain. We note that Hospira has rights to the product in North America, and Nycomed has rights to the product in Europe. Posidur incorporates DURECT's SABER gel delivery technology, which is an injectible, biodegradable drug delivery technology. The technology allows for a long-acting product delivered in a 12% bupivacaine solution. DURECT is currently running a pivotal study known as The Bupivacaine Effectiveness and Safety in SABER Trial (BESST), which is nearing completion of patient enrollment. The study is comparing Posidur to both placebo and an active comparator (i.e., conventional bupivacaine) in approximately 300 patients undergoing abdominal surgeries. The primary endpoint of the trial is pain intensity on movement. Supplemental opioid use for 3 days post-dose will also be assessed. We are likely to see results in 2H11, with an NDA possible in 1H12.

Differentiation of Exparel and Posidur likely to come down to perceptions of safety and ease of use/handling. One of the interesting aspects of Posidur in our view is that it is a gel consisting of 12% bupivacaine. The potential pitfall for Posidur is that it may be a more viscous product relative to Exparel. Further, though Posidur is also administered at the surgical site (i.e., wound infiltration), the volumes administered are either 2.5 mL or 5 mL, equivalent to doses of 330 or 660 mg bupivacaine respectively. These volumes are larger than those used for Exparel. Lastly, the 5 mL volume delivers a particularly high dose, bearing in mind that that highest dose of Exparel is 300 mg. We're not sure that surgeons and anesthesiologists will be comfortable with the higher volume dose of Posidur.

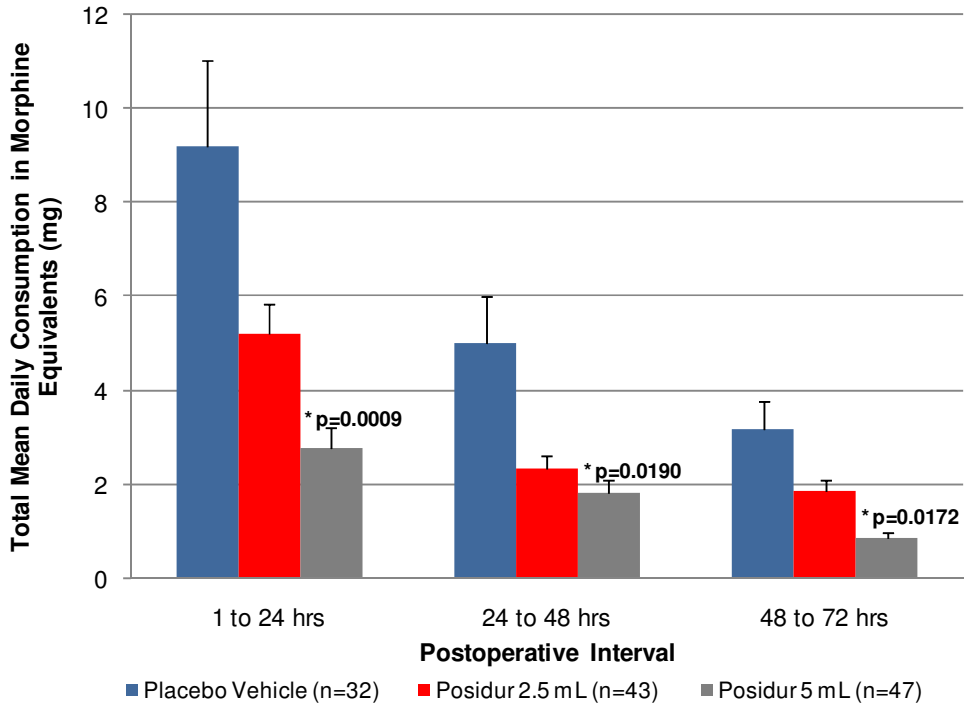
Figure 21: Comparison of Exparel vs Posidur: Method of Use

Product	Delivery/Potential Indications	Dosing	Reconstitution	Storage
Exparel	Wound infiltration, nerve block, epidural	Exparel can be used in large or small wounds: dosed to volume with normal saline	No mixing required prior to use	Requires cold storage
Posidur	Wound infiltration	Larger injection volume compared to Exparel (2.5 and 5 ml volumes)	No mixing required but potentially more viscous than Exparel	Does not require cold storage

Source: Company reports, PJC research

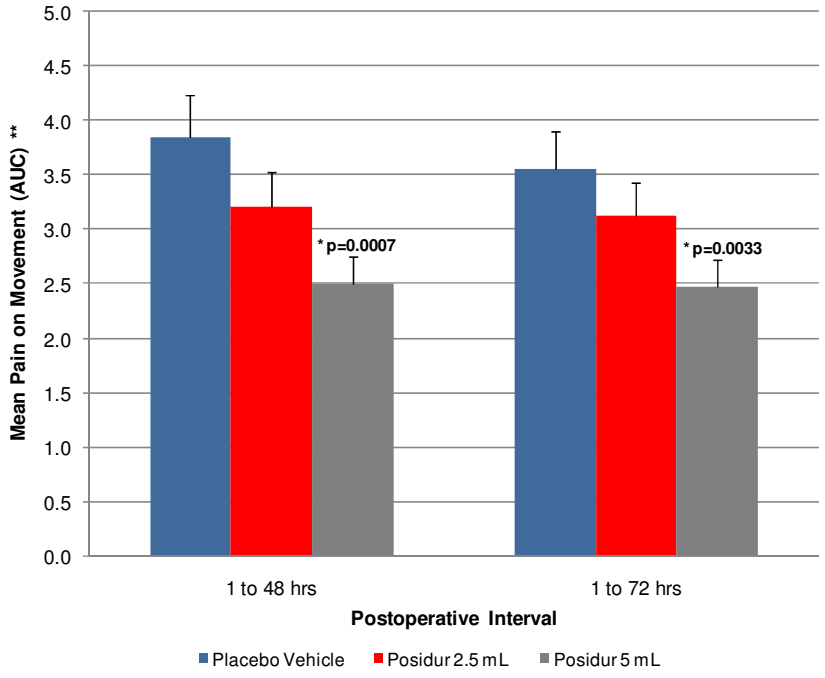
Ultimately, the main current advantage for Exparel, particularly in the absence of Phase III data for Posidur, is its potential head-start. That said, we would expect that Posidur will be able to show superiority to a placebo in terms of pain reduction, and would also expect evidence of an opioid-reducing effect (along the lines of what Pacira reported in its successful Phase II head-to-head study). DURECT has run a number of Phase II studies in various surgical models. The company recently announced top-line results from a Phase IIb conducted in Europe evaluating Posidur in patients undergoing shoulder surgery. Patients were assigned to receive either Posidur, placebo, or immediate-release bupivacaine. In this study of 107 patients, the primary endpoint of reduction in pain intensity was positive. On the second primary endpoint of total opioid use, there was a trend of decreased total opioid use (statistically significant under an alternative pre-specified statistical method). Results from earlier studies also suggested an opioid-reducing effect, if only versus a placebo. Figures 24 and 25 below highlight data on opioid consumption and pain intensity for Posidur at two doses versus placebo.

Figure 22: Posidur Placebo-Controlled Phase II Data on Opioid Consumption



Source: Nicholson poster, American Hernia Society, 2008

Figure 23: Posidur Placebo-Controlled Phase II Data on Pain Intensity



Source: Nicholson poster, American Hernia Society, 2008

Recently launched injectible acetaminophen (Ofirmev) not a competitor to Exparel in our view... Cadence Pharmaceuticals' Ofirmev is the first intravenous formulation of acetaminophen (APAP) to become available in the U.S. The product was approved by the FDA in November 2010 for the management of mild to moderate pain, in combination with

adjunctive opioids for the management of moderate to severe pain, and for fever reduction. Cadence recently launched the product in the U.S., with the product priced at $10.75 for a 100 mL vial at 10 mg/mL concentration (bearing in mind that the dose used for pain, which depends on body weight and age, ranges from 75 mg per day to 4000 mg per day, so the daily cost can be as high as $43). Cadence management recently noted on its 4Q10 call that the product has gained acceptance on 203 hospital formularies, and the company believes that between 800 to 1,000 hospitals could have the drug on their formularies by December 31, 2011. Though Cadence has positioned Ofirmev as a product that can reduce the consumption of opioids, there are a few considerations that we would keep in mind in explaining the product's strong initial acceptance. First, acetaminophen is widely considered to be a milder analgesic compared to certain NSAID's like ketorolac and sodium channel blockers like bupivacaine, but given that it is the first IV formulation of APAP to become available, and given that many patients recovering from invasive surgeries cannot take oral medications, we are not surprised that the product is seeing a receptive audience. Second, Ofirmev is just as likely to be used as a fever-reducing agent, and APAP indeed is the most widely used agent for the reduction of fever. In this context, it is not surprising that Cadence has a hospital sales force of nearly 150 reps, which is larger than the 100 rep sales force envisioned by Pacira. With APAP having a broader range of uses (i.e., mild analgesia and fever reducer), Cadence has to cast a wider net. In contrast, there is a more concentrated audience for Exparel, with around 1,000 hospitals accounting for nearly 70% of all bupivacaine use in the U.S.

In terms of the competitor dynamics, we could see Ofirmev as complementary to other non-opioid pain management modalities, bearing in mind that the drug is used strictly on a post-operative basis (i.e., not intra-operatively via wound infiltration). We see the product as having a role in patients who have developed a fever (not uncommon post-surgery; a common cause is urinary tract infections due to catheterization), since the medication can serve the twin purposes of reducing fever and helping to manage pain. In this context, we hardly see a zero-sum game between a product like Ofirmev and Exparel.

…and neither is an injectible version of ibuprofen (Caldolor). Cumberland Pharmaceuticals' Caldolor became the first intravenous formulation of ibuprofen to gain FDA approval. The drug was launched in the U.S. in September 2009. For the 9 months ending September 30, 2010, sales of Caldolor were only $79,000. We note that revenue for the product was $3 million for 3Q09, its first quarter on the market. That said, sales have languished since then, and with the availability of Ofirmev, which we believe is seen as a better option for fever reduction, we would be surprised to see a major ramp in sales of the product.

Isomers of bupivacaine see limited use; not a competitive concern. Ropivacaine and levobupivacaine, two stereoisomers of bupivacaine, were approved by the FDA in 1996 and 1999, respectively. The idea here was to develop products that would confer less toxicity risk than bupivacaine. That said, efficacy compared to conventional bupivacaine was questionable. Levobupivacaine is not currently marketed in the U.S. Ropivacaine is marketed by APP Pharmaceuticals and sees relatively limited use (Pacira estimates that only 0.9 million infiltration procedures in the U.S. use ropivacaine).

ADDITIONAL PRODUCTS THAT INCORPORATE DEPOFOAM

Pacira has two products in early stage development: DepoMethotrexate (DepoMTX), and DepoNSAID (Pacira has yet to specify which NSAID it is developing that incorporates DepoFoam). Both products represent intriguing opportunities in our view. Pacira has noted that it is further along in its development of DepoMTX, meaning that it is closer to moving the product into human trials. That said, advancement of either or both of these products is dependent on additional funding.

DepoNSAID. Pacira has DepoFoam formulations of several different NSAIDs, and hopes to select a lead product candidate in 2011. The company is currently examining intra-articular delivery of NSAIDs for arthritis pain or acute joint pain in preclinical studies. The currently available injectible NSAIDs provide pain relief from between 4-6 hours, and it is the goal of the DepoNSAID program to allow for pain relief over a longer period.

DepoMethotrexate. A second product incorporating DepoFoam is an extended-release form of methotrexate, which is an agent used widely for rheumatoid arthritis. Methotrexate is the most commonly used treatment for rheumatoid arthritis with over 500,000 patients prescribed the drug annually. The advantage of the DepoFoam product candidate is that this drug would allow for a smoother PK profile, which may decrease common side effects including nausea and vomiting, which are associated with peak blood levels of the drug. The current product formulation has one year of stability data, and is further advanced relative to the NSAID program.

COMPANY MANAGEMENT

We believe that Pacira's management team is uniquely equipped to manage a commercial product launch in the hospital setting. CEO David Stack is the former CEO of The Medicines Company, where he successfully managed the launch of acute cardiac care product Angiomax. A number of commercial and reimbursement professionals from his team are part of the Pacira team, and the group as a whole has significant experience with hospital channels. Below we provide further details on Pacira's senior management team:

David Stack, CEO. David Stack has been Pacira's President and CEO since December 2007. He has had over 25 years of experience in the pharmaceutical industry. Mr. Stack was President and CEO of The Medicines Company from September 2001 to August 2004 and was previously the President and General Manager of Innovex Inc. At The Medicines Company, Mr. Stack successfully launched Angiomax in 2001 and helped grow the drug to nearly $150 million in annual sales by 2004 (the product now has annual sales over $400 million).

Gary Patou, MD, Chief Medical Officer. Gary Patou has held the role of Chief Medical Officer at Pacira since 2009, with over 20 years of experience in clinical and regulatory affairs. Prior to joining Pacira, Dr. Patou was CMO of Oscient Pharmaceuticals, Inc. after Oscient merged with GeneSoft Pharmaceuticals, where he oversaw the successful FDA submission and approval of the company's main product, Factive. Dr. Patou has also been responsible for product development at SmithKline Beechham, now part of GlaxoSmithKline.

James Scibetta, CFO. James Scibetta has served as Chief Financial Officer at Pacira since August 2008. Mr. Scibetta previously served as CFO of Bioenvision Inc., a biotechnology company which focused on commercializing oncology products and which was sold to Genzyme in 2007 under Mr. Scibetta's leadership. Mr. Scibetta has over ten years of experience in investment banking experience for private and public life science and healthcare companies.

William Lambert, PhD, Senior Vice President, Pharmaceutical Development. William Lambert has served as the SVP of Pharmaceutical Development at Pacira since the company's creation and has over 20 years of experience in drug development. At Pacira, Mr. Lambert manages the company's R&D and intellectual property. Mr. Lambert has held director positions at Eisai, as well as investigator roles at Pfizer and The Upjohn Company.

Mark Walters, Senior Vice President, Technical Operations and Business Development. Mark Walters has served as Senior Vice President, Technical Operations and Business Development for Pacira since the company was created. Mr. Walters has over 30 years of pharmaceutical experience, with executive positions in operations, business development, sales and marketing. Prior to Pacira, Mr. Walters was Vice President of Commercial Development for seven years at SkyePharma.

INVESTMENT RISKS

Regulatory risks. Though bupivacaine is a well-known drug, and Exparel was successful in two placebo-controlled Phase III studies (with a strong tolerability profile), there is always the possibility that the FDA will want additional data to support approval of Exparel, particularly in light of the earlier unsuccessful Phase III studies.

Commercial risks. As noted above, Pacira is planning commercialize Exparel in the U.S. without the assistance of a partner, and will start with a hospital-based sales force of roughly 40 reps. Pacira will be competing against larger hospital-focused companies such as Hospira and Baxter, as well as companies that distribute generic versions of bupivacaine (including Hospira and APP Pharmaceuticals). Pacira will have to convince anesthesiologists and hospital administrators of the benefits of Exparel despite its higher price point relative to conventional immediate-release versions of bupivacaine. If Pacira has a difficult time selling anesthesiologists and hospital administrators on the Exparel value proposition, the company may not be able to achieve profitability in the timeline that is reflected in our estimates (full-year profitability in 2013).

Reimbursement risks. There is always the possibility that reimbursement for Exparel will be limited given that short-acting bupivacaine has been available for many years and is inexpensive. Limited managed care access would limit the sales potential of Exparel and potentially delay Pacira's timeline to profitability.

Competitor risks. Though there is no near-term competitive threat to Exparel from a brand perspective, DURECT/Hospira's Posidur is in late-stage development and is one to two years away from commercialization at the earliest. Though we do not

see Posidur as having any obvious advantages over Exparel, there is the possibility that DURECT/Hospira prices the product lower than the price of Exparel, potentially pressuring Exparel sales.

Pacira - Quarterly and Annual Income Statement

Fiscal Year Ends December 31 *($ In millions, except for EPS)*	2009A	2010E	2011E 1QE	2011E 2QE	2011E 3QE	2011E 4QE	2011E	2012E	2013E	2014E	2015E
Revenues											
Exparel U.S. sales						$2.5	$2.5	$35.4	$86.6	$142.5	$215.5
Exparel ex-U.S. revenue								0.0	0.0	0.0	0.0
(DepoCyte/DepoDur) [1]	10.4	13.1	3.1	3.1	3.3	3.4	12.9	13.4	14.1	14.8	15.5
Milestone revenue/other [2]	4.6	3.4	1.5	0.0	0.0	2.0	3.5	2.0	0.0	0.0	0.0
Total revenue	**$15.0**	**$16.5**	**$4.6**	**$3.1**	**$3.3**	**$7.9**	**$18.9**	**$50.8**	**$100.7**	**$157.3**	**$231.1**
Cost of sales [3]	12.3	13.6	6.8	5.5	4.8	23.6	40.7	33.0	40.3	42.5	53.1
Gross Profit	**$2.7**	**$3.0**	**($2.2)**	**($2.4)**	**($1.5)**	**($15.7)**	**($21.9)**	**$17.8**	**$60.4**	**$114.8**	**$177.9**
Research & development	26.2	19.9	0.3	0.2	1.0	3.9	5.4	3.0	6.0	6.3	6.9
Selling, general, and administrative	5.0	5.3	6.9	3.6	5.0	8.7	24.1	35.6	42.3	48.7	53.1
Total expenses	**$43.6**	**$38.8**	**$14.0**	**$9.3**	**$10.7**	**$36.2**	**$70.3**	**$71.7**	**$88.6**	**$97.5**	**$113.2**
Operating Income	**($28.5)**	**($22.3)**	**($9.4)**	**($6.2)**	**($7.4)**	**($28.4)**	**($51.4)**	**($20.8)**	**$12.1**	**$59.7**	**$117.8**
Interest income	0.1	0.1	0.2	0.2	0.2	0.2	0.6	1.0	1.3	1.6	1.8
Interest expense	(3.6)	(4.8)	(1.2)	(1.2)	(1.2)	(1.2)	(4.8)	(4.3)	(3.0)	(0.2)	0.0
Other income (expense)	0.4	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Other income (expense), net	(3.2)	(4.6)	(1.1)	(1.1)	(1.1)	(1.1)	(4.2)	(3.3)	(1.7)	1.4	1.8
Income (loss) before taxes	**($31.7)**	**($26.8)**	**($10.5)**	**($7.3)**	**($8.5)**	**($29.4)**	**($55.6)**	**($24.2)**	**$10.4**	**$61.1**	**$119.6**
Income tax provision	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	(6.0)
Net income (loss)	**($31.7)**	**($26.8)**	**($10.5)**	**($7.3)**	**($8.5)**	**($29.4)**	**($55.6)**	**($24.2)**	**$10.4**	**$61.1**	**$113.7**
EPS, basic	**($3.60)**	**($2.52)**	**($0.61)**	**($0.42)**	**($0.49)**	**($1.68)**	**($3.20)**	**($1.12)**	**$0.47**	**$2.70**	**$4.91**
EPS, diluted	**($3.60)**	**($2.52)**	**($0.61)**	**($0.42)**	**($0.49)**	**($1.68)**	**($3.20)**	**($1.12)**	**$0.41**	**$2.38**	**$4.35**
Shares outstanding, basic [4]	8.5	10.7	17.2	17.3	17.4	17.5	17.4	21.7	22.2	22.7	23.2
Shares outstanding, diluted [4]	8.5	10.7	17.2	17.3	17.4	17.5	17.4	21.7	25.2	25.7	26.2
Expenses as % of sales:											
COGS	155.0%	82.1%	148.0%	179.0%	144.0%	300.0%	215.8%	65.0%	40.0%	27.0%	23.0%
R&D		120.7%	7.0%	6.0%	30.0%	50.0%	28.8%	6.0%	6.0%	4.0%	3.0%
SG&A		31.8%	150.0%	115.0%	150.0%	110.0%	127.6%	70.0%	42.0%	31.0%	23.0%
Margins:											
Gross margin								35.0%	60.0%	73.0%	77.0%
Operating margin									12.0%	38.0%	51.0%
Net income									10.3%	38.9%	49.2%
Income Tax									0.0%	0.0%	5.0%
Y-O-Y Growth rates:											
Exparel U.S. sales									*144.6%*	*64.5%*	*51.3%*
Total revenue			**11.6%**	**-24.8%**	**-20.0%**	**89.7%**	**14.2%**	**169.3%**	**98.1%**	**56.2%**	**46.9%**
R&D			-93.5%	-96.3%	-80.1%	-21.0%	-72.7%	-43.9%	98.1%	4.1%	10.2%
Selling, general, and administrative			425.2%	171.4%	276.8%	559.2%	358.2%	47.8%	18.9%	15.3%	9.0%
Operating profit										394.9%	97.2%
Net income										489.5%	85.9%

(1) Reflects manufacturing revenue and royalties from third parties on DepoCyte and DepoDur
(2) 2011 and beyond reflects milestone payments from NovoNordisk related to DepoFoam partnership
(3) Includes $10M milestone payment in 4Q11 to Skye Pharma related to the approval and launch of Exparel
(4) Assumes additional common share offering in 2012

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Pacira - Annual Cash Flow Statement

($ in millions)

	2008A	2009A	2010E	2011E	2012E	2013E	2014E
Beginning Cash & Equivalents	**$7.2**	**$12.4**	**$7.1**	**$27.6**	**$6.3**	**$16.0**	**$22.9**
Operating Activities							
Net Income (Loss)	($41.9)	($31.7)	($26.8)	($55.6)	($24.2)	$10.4	$61.1
Depreciation & Amortization	$3.8	$4.4	$4.2	$5.2	$5.7	$6.3	$6.9
Other	($4.8)	$1.9	$0.5	$0.5	$0.5	$0.5	$0.5
Stock-based Compensation	$0.2	$0.5	$0.4	$0.6	$0.8	$1.1	$1.2
Net Change in Assets and Liabilities	$13.4	$4.0	$0.3	($2.1)	($6.1)	($2.6)	($4.2)
Cash From Operations	**($29.2)**	**($20.8)**	**($21.4)**	**($51.4)**	**($23.3)**	**$15.6**	**$65.6**
Investing Activities							
Capital Expenditures	($5.8)	($5.5)	($12.0)	($8.0)	($5.0)	($3.0)	($3.0)
Short-Term Investments	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Acquisition of Tangible Assets	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Acquisition of Intangibles	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Other Investment [1]	($0.0)	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Cash From Investing Activities	**($5.9)**	**($5.5)**	**($12.0)**	**($8.0)**	**($5.0)**	**($3.0)**	**($3.0)**
Financing Activities							
Debt Issuance [1]	$0.0	$21.3	$67.0	$0.0	$5.0	$0.0	$0.0
Debt Repayments [1]	$0.0	$0.0	($15.0)	$0.0	($15.0)	($8.7)	($7.0)
Dividends	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Share Repurchases	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Stock and Option Issuances [2]	$40.2	$0.0	$2.0	$38.0	$48.0	$3.0	$3.0
Other, Net	($0.0)	($0.2)	$0.0	$0.0	$0.0	$0.0	$0.0
Cash From Financing Activities	**$40.1**	**$21.0**	**$54.0**	**$38.0**	**$38.0**	**($5.7)**	**($4.0)**
Net Change In Cash	$5.1	($5.3)	$20.6	($21.4)	$9.7	$6.9	$58.6
Year End Cash & Equivalents	**$12.4**	**$7.1**	**$27.6**	**$6.3**	**$16.0**	**$22.9**	**$81.5**

(1) Reflects the impact of $26.25M of long-term debt borrowed under the Hercules Credit Facility, plus issuance of $7.5M convertible note. Also includes repayment of $11.25M under the GECC Credit Facility in 2010

(2) Reflects net proceeds of $38M from February 2011 IPO. Also assumes additional share offering in 2012.

Proprietary to Piper Jaffray & Co. March 14, 2011

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Pacira - Annual Balance Sheet

($ in millions)

	2008A	2009A	2010E	2011E	2012E	2013E	2014E
Current Assets							
Cash & Equivalents	$12.4	$7.1	$27.6	$6.3	$16.0	$22.9	$81.5
Short-term invsetments	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Accounts Receivable, net	$2.6	$1.5	$2.5	$3.1	$9.7	$12.4	$17.2
Inventories	$2.0	$1.7	$1.1	$3.3	$3.6	$4.4	$4.7
Other Current Assets	$2.4	$2.3	$2.4	$2.5	$2.6	$2.8	$2.9
Total Current Assets	**$19.4**	**$12.5**	**$33.6**	**$15.2**	**$32.0**	**$42.5**	**$106.3**
Property, Plant & Equipment, Net	$18.0	$19.6	$27.4	$30.2	$29.5	$26.2	$22.3
Intangible Assets, Net	$13.1	$11.2	$11.2	$11.2	$11.2	$11.2	$11.2
Other Assets	$0.1	$0.7	$0.7	$0.7	$0.7	$0.7	$0.7
Total Assets	**$50.5**	**$44.0**	**$72.9**	**$57.3**	**$73.3**	**$80.5**	**$140.4**
Liabilities & Equity							
Current Liabilities	$17.0	$14.4	$15.1	$15.9	$16.7	$17.5	$18.4
Total Debt	$0.0	$22.2	$26.7	$26.7	$16.7	$8.0	$1.0
Other Liabilities	$26.0	$30.3	$31.2	$32.2	$33.1	$34.1	$35.1
Equity (deficit)	$7.5	($22.9)	($0.1)	($17.5)	$6.8	$20.9	$85.9
Total Liabilities & Equity	**$50.5**	**$44.0**	**$72.9**	**$57.3**	**$73.3**	**$80.5**	**$140.4**

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Important Research Disclosures

Notes: The boxes on the Rating and Price Target History chart above indicate the date of the Research Note, the rating, and the price target. Each box represents a date on which an analyst made a change to a rating or price target, except for the first box, which may only represent the first Note written during the past three years.

Legend:

I: Initiating Coverage

R: Resuming Coverage

T: Transferring Coverage

D: Discontinuing Coverage

S: Suspending Coverage

OW: Overweight

N: Neutral

UW: Underweight

B: Buy (Piper Jaffray discontinued use of the B, N, and S ratings on June 30, 2009)

N: Neutral

S: Sell

AL On/AL Off: Placed on/removed from the Alpha List maintained by Piper Jaffray (AL use discontinued March 2010)

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UR: Under Review

Distribution of Ratings/IB Services
Piper Jaffray

			IB Serv./Past 12 Mos.	
Rating	Count	Percent	Count	Percent
BUY [OW]	313	49.80	66	21.09
HOLD [N]	266	42.40	26	9.77
SELL [UW]	49	7.80	3	6.12

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Important Research Disclosures

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— Michael Dinerman, M.D., Research Analyst

The views expressed in this report accurately reflect my personal views about the subject company and the subject security. In addition, no part of my compensation was, is, or will be directly or indirectly related to the specific recommendations or views contained in this report.

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