

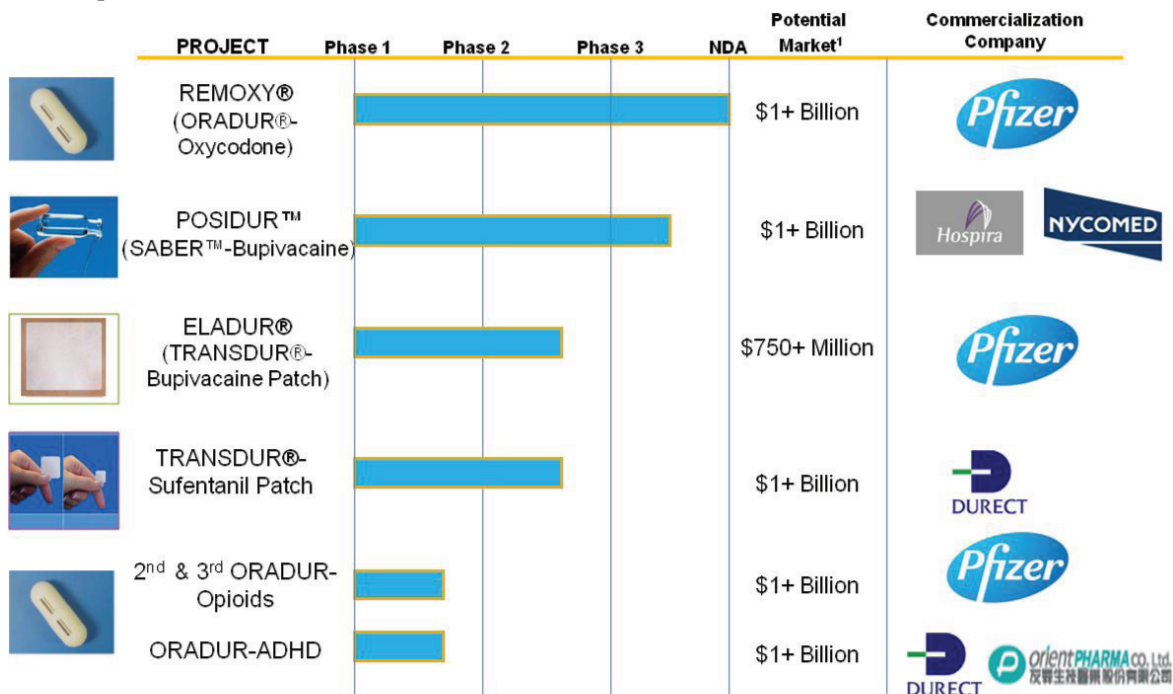


**Dear Fellow Shareholders:**

Continued progress with our late-stage pipeline has DURECT approaching two pivotal events. First, the potential approval of REMOXY® and, if approved, subsequent launch by Pfizer. Second, we expect to complete enrollment of BESST, our pivotal Phase III trial for POSIDUR™ comprising approximately 300 patients, in the third quarter of 2011 with top-line data anticipated in the fourth quarter. We have also advanced our POSIDUR, ELADUR® and ORADUR®-ADHD programs by generating relevant clinical data over the last 12 months and continued to pursue earlier stage research programs which are expected to generate the next wave of product opportunities. While advancing our pipeline, we have continued to operate in a fiscally conservative manner. Over the last six years, our average cash burn rate has been approximately \$10 million per year and we were actually cash flow positive in 2010 due to our business development activities.

We are pleased to have two major new collaborators today as compared to this time last year. In June 2010, we signed an agreement to co-develop POSIDUR with Hospira; if approved, Hospira would also be exclusive marketer of POSIDUR in the U.S. and Canada. As a leader in injectable pharmaceuticals with a major hospital-based presence and a stated desire to bolster its leadership position in acute-care proprietary pharmaceuticals, we view Hospira as an ideal partner for this market. On a worldwide basis, our total upfront payments and milestones to date from this program are \$49.5 million, with \$365 million in potential future milestones and royalties that generally start around 15% and go up from there. In February 2011, Pfizer completed its acquisition of King Pharmaceuticals (King) and thereby assumed the rights and obligations of programs covering REMOXY, three other ORADUR-based opioids, and ELADUR (TRANSDUR®-Bupivacaine). Given Pfizer's established worldwide capabilities and desire to grow its pain franchise, we view Pfizer's involvement as a significant benefit to the development and commercial prospects for these partnered programs.





**Product Pipeline**



1) Estimates for potential market opportunities are based on publicly available information, research reports and company reports

### Update of Programs:

- **REMOXY.** The U.S. Food and Drug Administration (FDA) has set a June 23, 2011 PDUFA goal date for the REMOXY New Drug Application (NDA) which was resubmitted in December 2010 by King following a Complete Response Letter received by Pain Therapeutics in December 2008. Pfizer completed its acquisition of King in February 2011. During Pfizer's first quarter earnings call on May 3, 2011, Pfizer stated that it was working to address a specific issue in the manufacturing section of the REMOXY application, as well as to understand any potential implications of FDA's recent class-wide REMS announcement for extended release opioids. Pfizer stated that these issues could delay the timing of approval or the launch of REMOXY. As a result of its acquisition of King, Pfizer has assumed the development and commercialization rights and obligations to REMOXY. Pfizer also has commercialization rights to three other licensed ORADUR-based opioid drug candidates (hydrocodone, hydromorphone and oxymorphone).

 <p>Remoxy®</p>	Crushed		<u>Tamper Resistant</u> <ul style="list-style-type: none"><li>• Snorting</li><li>• Smoking</li><li>• Injecting</li><li>• Dissolving in drinks</li></ul>
 <p>Long Acting Oxycodone Tablets</p> <p>Intact</p>	Crushed		

REMOXY, an investigational drug, is a unique long acting oral formulation of oxycodone intended to treat moderate to severe pain. Based on DURECT's ORADUR technology, which is covered by issued patents and pending patent applications owned by us, REMOXY is designed to resist common methods of prescription drug misuse and abuse.

- **POSIDUR (SABER™-Bupivacaine).** We continued enrolling patients in our U.S. pivotal Phase III clinical study known as BESST (Bupivacaine Effectiveness and Safety in SABER Trial), which comprises approximately 300 patients. We expect to complete enrollment of BESST in the third quarter of 2011 with top-line data anticipated in the fourth quarter.

In 2010 and early 2011, we announced top-line results from two Phase II studies conducted in Europe by Nycomed. These studies explored use of POSIDUR in two additional surgical models, hysterectomy and shoulder surgery, and generated data that would be included in an NDA with the U.S. FDA.



POSIDUR is our post-operative pain relief depot that utilizes our patented SABER technology to deliver bupivacaine to provide up to three days of pain relief after surgery. POSIDUR is licensed to Hospira for commercialization in the U.S. and Canada, and to Nycomed for commercialization in Europe and other defined countries. We have retained commercialization rights in Japan and all other countries not subject to the Nycomed and Hospira licenses.

- **ELADUR (TRANSDUR-Bupivacaine).** Pfizer completed its acquisition of King in February 2011 and as a result has assumed the development and commercialization rights and obligations to ELADUR. In April 2011, we announced top-line results from a Phase II clinical trial conducted by King Pharmaceuticals for the treatment of chronic low back pain. The primary efficacy endpoint for the trial was not met. Complete data analysis is on-going. We and Pfizer are continuing to analyze these data and will work together to determine next steps for ELADUR.

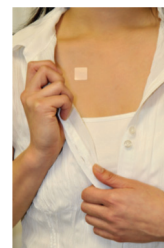
ELADUR is our proprietary transdermal patch intended to deliver bupivacaine for a period of up to three days from a single application. ELADUR demonstrated a positive efficacy trend in a Phase IIa study for post-herpetic neuralgia (PHN); a poster describing this study was presented at the 27<sup>th</sup> Annual Scientific Meeting of the American Pain Society on May 8, 2008 and is accessible on DURECT's website ([www.durect.com/wt/durect/page\\_name/Publications](http://www.durect.com/wt/durect/page_name/Publications)).

- **TRANSDUR-Sufentanil.** During 2010, we conducted new market research on this product opportunity and have been incorporating that information in developing revised potential development plans for TRANSDUR-Sufentanil. We are in discussions with potential partners regarding licensing development and commercialization rights to this program to which we hold worldwide rights.

TRANSDUR-Sufentanil is our proprietary transdermal patch intended to deliver sufentanil to chronic pain sufferers for a period of up to seven days from a single application.



ELADUR  
(left)



TRANSDUR-Sufentanil  
(right)

- **ORADUR-ADHD Program.** In July 2010, we and Orient Pharma commenced a Phase I clinical trial in this program evaluating multiple formulations, and in the second quarter of 2011 we and Orient Pharma anticipate commencing a second Phase I study to evaluate additional formulations. ORADUR-ADHD applies our proprietary ORADUR technology to leading active pharmaceutical ingredients for the treatment of attention deficit disorder (ADHD). Under the agreement with Orient Pharma, we are collaborating to perform a clinical development program through a Phase II study intended to produce a data package anticipated to support later stage development of one ADHD drug candidate and subsequent licensing by DURECT. We are responsible for formulation and study design of the pre-defined clinical program, which Orient Pharma will fund and execute.
- **Feasibility Projects.** During 2010, we signed additional feasibility agreements and continued existing projects with pharmaceutical and biotechnology companies whereby we are applying our SABER and DURIN™ technologies to both small molecule and biologic agents of interest to our collaborators. We undertake these feasibility projects as a means of demonstrating that our technologies can achieve the drug delivery objectives set forth by our collaborators and are worthy of further development.

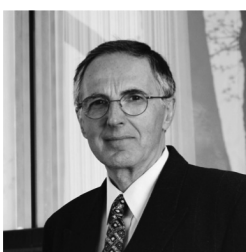
In addition to the Hospira collaboration which was established in June 2010, DURECT remains active on the business development front where we have multiple late stage programs that are the subject of partnering discussions. These include TRANSDUR-Sufentanil (worldwide), POSIDUR (Japan), ORADUR-ADHD, as well as various internal programs which we have not described publicly in detail.

For additional information on DURECT, please refer to our SEC filings including our Form 10-K, our website ([www.durect.com](http://www.durect.com)), or call us at any time.

### *Investment Highlights*

- **Multiple drug candidates in late-stage development.** The value of most pharmaceutical companies ultimately comes down to their products reaching the market and then achieving commercial success. We are fortunate to have multiple drug candidates in late-stage development, including one NDA submitted to the FDA, one product candidate in Phase III, two product candidates in Phase II and three programs in Phase I. Each of these product candidates addresses large market opportunities and has product features that represent what we believe constitute meaningful advancements over current therapies.
- **Productive R&D team.** The R&D team at DURECT is led by senior scientists that have successfully developed products in the past and that are committed to doing so in the future. In addition to the later stage programs described above, we have other pre-clinical programs underway with product candidates in attractive fields.
- **Balanced business model.** Our business model complements the diversification we possess in product candidates and technologies. Certain programs have already been licensed to strong partners on attractive terms, providing financial, development and commercialization resources beyond the means of an emerging company. Strategically, we've retained worldwide or territorial rights to other programs, which provide the basis for future partnering and financing of product development.

On behalf of everyone at DURECT, we thank you for your continued support and look forward to reporting on our progress in 2011 and beyond.



Felix Theeuwes, D.Sc.  
Chairman and Chief Scientific Officer



James E. Brown, D.V.M.  
President and Chief Executive Officer

**Forward Looking Statement:** The statements in this shareholder letter regarding the potential approval and timing of approval of REMOXY by the FDA and subsequent product launch by Pfizer, anticipated completion of enrollment of BESST and receipt of top-line data for POSIDUR, possible licensing transactions relating to TRANSDUR-Sufentanil, POSIDUR (Japan), ORADUR-ADHD or other programs, future development activities regarding ELADUR, anticipated commencement of a new Phase I trial for ORADUR-ADHD and our other drug candidates and the potential benefits and uses of our drug candidates are forward-looking statements involving risks and uncertainties that can cause actual results to differ materially from those in such forward-looking statements. Potential risks and uncertainties include, but are not limited to, the risk of adverse decisions by regulatory agencies, including product non-approval, delays and additional costs due to requirements imposed by regulatory agencies, potential adverse effects arising from the testing or use of our drug candidates, the potential failure of our clinical trials to meet their intended endpoints, our potential failure to maintain our collaborative agreements with third parties or consummate new collaborations and DURECT's (and that of its third party collaborators where applicable) difficulty or failure to obtain approvals from regulatory agencies with respect to its development activities and products, or ability to design, enroll, conduct and complete clinical trials, complete the design, development, and manufacturing process development of the referenced product candidates, manufacture and commercialize the referenced product candidates, obtain marketplace acceptance of the referenced product candidates, avoid infringing patents held by other parties and secure and defend patents of our own, and manage and obtain capital to fund its growth, operations and expenses. Further information regarding these and other risks is included in DURECT's Form 10-K on March 3, 2011 under the heading "Risk Factors."