2009 Annual Report

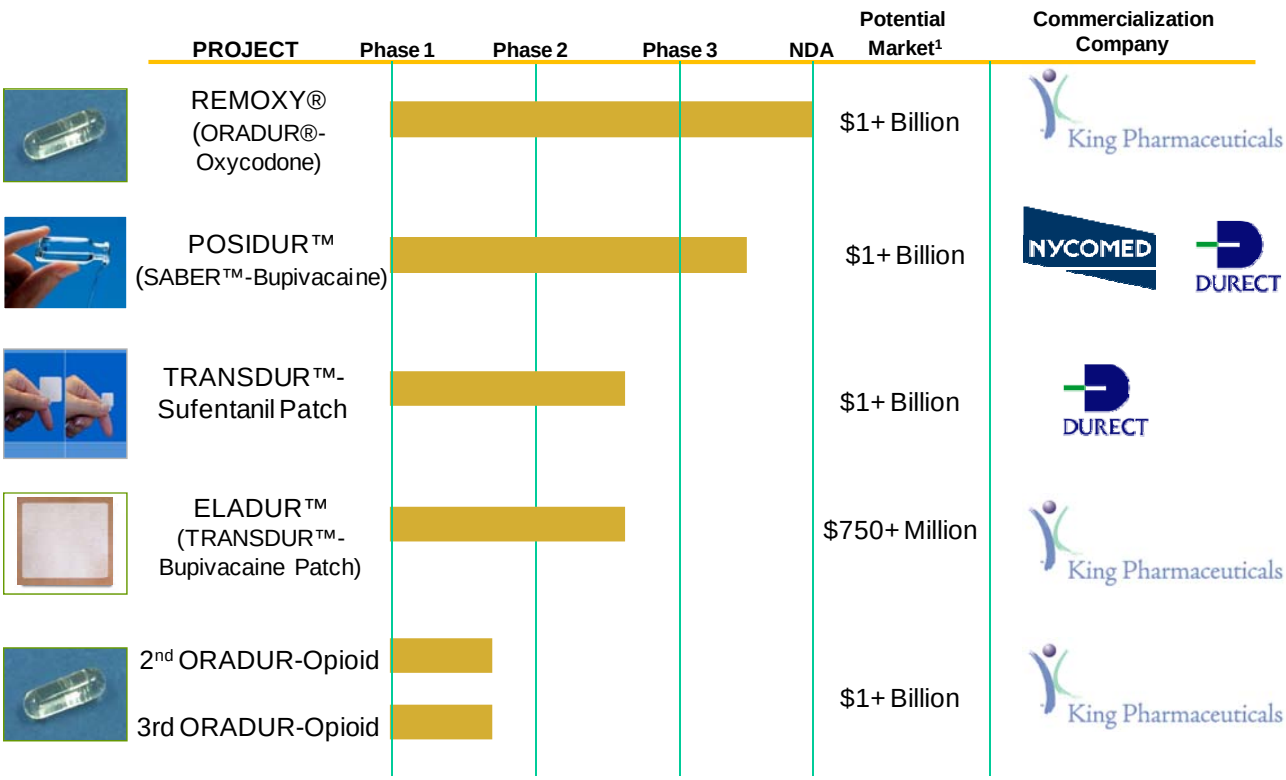
Letter to the Shareholders

Dear Fellow Shareholders:

One of the hallmarks of our Company has been operating the business in a fiscally conservative manner. Over the last five years, while investing in building a pipeline of late stage product candidates, our average cash burn rate has been approximately $14 million per year. In that spirit, we've decided once again to communicate via this internally produced shareholders letter. For additional information on DURECT, please refer to our SEC filings including our 10-K, our website (www.durect.com), or call us at anytime.

DURECT continued to advance our late stage pipeline in 2009 and early 2010. Of note, BESST, our pivotal U.S. Phase III clinical study for POSIDUR™, is well underway. With respect to our partnered programs, King Pharmaceuticals is preparing the NDA resubmission for REMOXY® by year-end 2010 and has initiated a Phase IIb clinical study of ELADUR™ in chronic low back pain. We were also pleased to have established a business relationship that will allow us to generate clinical data around a new ORADUR®-ADHD program and to have established multiple feasibility projects with pharmaceutical and biotechnology companies that apply our SABER™ and DURIN™ technologies to both small molecule and biological agents of interest to our collaborators. These programs move us beyond the pain management field and are intended to add to our product development pipeline over the coming years.

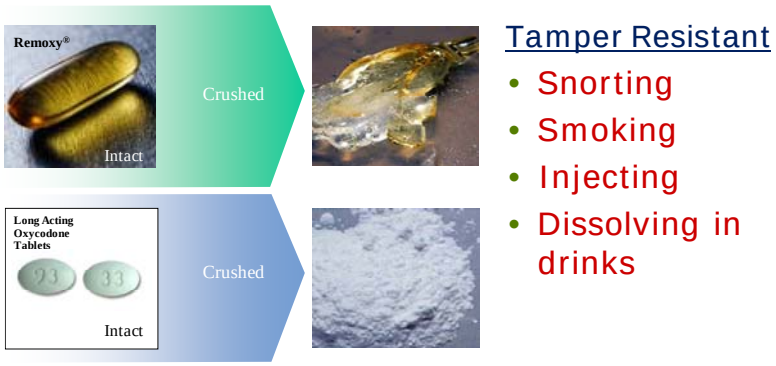
Product Pipeline



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

Highlights for DURECT in Fiscal Year 2009, early Fiscal 2010 and Next Steps:

- **REMOXY®.** In March 2009, King Pharmaceuticals assumed responsibility for the REMOXY New Drug Application (NDA) from Pain Therapeutics. In July 2009, King met with the FDA to discuss the Complete Response Letter received in December 2008 regarding the REMOXY NDA. According to King, it anticipates that in the fourth quarter of 2010 it will resubmit the NDA for REMOXY intended to address all FDA comments in the Complete Response Letter. During the third quarter of 2009, we entered into an exclusive long term excipient supply agreement with King. This agreement stipulates the terms and conditions under which we will supply to King two key excipients used in the manufacture of REMOXY, based on DURECT's manufacturing cost plus a specified percentage mark-up.



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).** In December 2009, we reported positive top-line results from our Phase IIb clinical study in shoulder surgery of 60 patients. In January 2010, we announced that we had commenced our U.S. pivotal Phase III clinical study known as BESST (Bupivacaine Effectiveness and Safety in SABER™ Trial). We expect to complete enrollment of BESST, comprising approximately 300 patients, in the first half of 2011.

POSIDUR is our investigational 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 Nycomed for commercialization in Europe and select other countries, and we have retained commercialization rights in the U.S., Canada and Japan. We are in active discussions with multiple potential partners regarding licensing of the U.S./Canadian and Japanese rights to this program.

- **ELADUR™ (TRANSDUR™-Bupivacaine).** In October 2008, worldwide rights to this program were licensed to Alpharma, which was acquired by King Pharmaceuticals in December 2008. During 2009, we and King focused on details associated with next steps in the clinical program, and in April 2010 King initiated a 260 patient Phase IIb clinical trial in chronic lower back pain.

  ELADUR is our proprietary transdermal patch intended to deliver bupivacaine for a period of up to three days from a single application.

- **TRANSDUR™-Sufentanil.** In February 2009, a successful end-of-Phase II meeting with the FDA was conducted for this program outlining a potential regulatory pathway for the Phase III program and NDA submission. During 2009, we transitioned the program back to our control. We are in discussions with multiple 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 August 2009, we signed a development and license agreement with Orient Pharma related to a drug candidate based on our ORADUR technology and one specified active pharmaceutical ingredient for the treatment of attention deficit hyperactivity disorder (ADHD). Under this agreement, the parties will collaborate to perform a clinical development program through a Phase II study intended to produce a data package that will support later stage development of the drug candidate and subsequent licensing by DURECT. We will be responsible for formulation and study design of the pre-defined clinical program, which Orient Pharma will fund and execute. We expect to commence Phase I studies during 2010 with this program.

- **Feasibility Projects.** During 2009, we signed multiple new feasibility projects with pharmaceutical and biotechnology companies whereby we will apply 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. During 2010, we anticipate establishing and commencing additional feasibility projects with biotechnology and pharmaceutical company collaborators utilizing our drug delivery technologies.

A major priority for DURECT is 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 (U.S., Canada and Japan), as well as various internal programs which we have not described publicly in detail.

Investment Highlights

- **Multiple drug candidates in late stage development.** The value of most pharmaceutical companies ultimately comes down to their products reaching the market. We are fortunate to have multiple drug candidates in late stage development, including one NDA submitted to the FDA, 1 product candidate in Phase III, 2 product candidates in Phase II and 2 programs in Phase I. Each of these product candidates address large market opportunities in the underserved pain management field and have 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 continued progress in 2010 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 our anticipated cash consumption, the potential uses and benefits of our drug candidates, the intended clinical and regulatory approval activities of us and our collaborators relating to our drug candidates, including timing thereof, anticipated requirements for regulatory approval, potential new collaborations with third parties and the anticipated timing of new data and results, 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 possibility that the clinical trials of us and our collaborators will not produce intended results on safety or efficacy or confirm earlier clinical trial results, that possible adverse events or other undesirable side effects will be associated with the use of our drug candidates, that delays and costs may be incurred due to additional work or other requirements imposed by regulatory agencies for continued development, approval or sale of our drug candidates, or that we or our collaborators may fail or have difficulty obtaining approvals from regulatory agencies with respect to clinical trials and other development activities or the marketing of our drug candidates, designing, enrolling, conducting and completing clinical trials, commercializing and obtaining marketplace acceptance of our drug candidates, or avoiding infringing patents held by other parties and securing and defending patents of our own, and that we will fail or have difficulty consummating future collaborative agreements or managing and obtaining capital to fund our growth, operations and expenses. Further information regarding these and other risks is included in DURECT's Form 10-Q filed on May 10, 2010 under the heading "Risk Factors."