Dear Fellow Stockholders:

The future value of DURECT is driven by the "sum of the parts" – our pipeline of differentiated products in development, our earlier stage research programs which we anticipate will yield additional product candidates and partnerships, and our ALZET® and LACTEL® product lines which today are strongly cash flow positive. In the last few quarters, we have significantly strengthened our patent portfolio through 13 patent issuances and 2 patent allowances involving major and/or partnered programs that extend patent protection in large market jurisdictions to at least 2025. In particular, we were recently granted four U.S. patents covering our ORADUR® technology, providing intellectual property protection for REMOXY® (oxycodone) Extended-Release Capsules CII and our other ORADUR-based opioids until at least 2025. Similarly, POSIDUR™ has issued patents through at least that date in the U.S. and Europe. While building our pipeline, we have continued to operate in a fiscally conservative manner. Over the last 7 years, our average cash burn rate has been approximately $11 million per year. In 2011, we consumed ~22% less cash than the mid-point of our guidance at the start of the year, and we anticipate a cash burn rate of ~$12 million in 2012, which represents a decrease of about 30% compared to 2011.

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 that is the subject of a Complete Response Letter, one Phase III product candidate, two Phase II product candidates and three Phase I programs. Each of these product candidates addresses large market opportunities and has product features that represent what we believe constitute meaningful improvements 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 make our on-going research and development programs a success. In addition to the later stage programs described above, we have other pre-clinical programs underway that we believe will produce our pipeline of tomorrow.
- **Balanced business model.** Our business model complements the diversification we possess in product candidates and technologies. Certain programs have 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.

In 2012, we look forward to:

- Pfizer conducting a meeting with the FDA to discuss the REMOXY resubmission
- Conducting a pre-NDA meeting with the FDA for POSIDUR, with a potential NDA submission in 2012, depending on FDA feedback
- Supporting Zogenix as they initiate a Phase I study with Relday™
- Selecting a formulation based on our Phase I studies to take forward in our ORADUR-ADHD program
- Potentially entering into additional feasibility studies and collaborations

Update of Programs:

- **REMOXY.** On June 23, 2011, Pfizer received a Complete Response Letter from the U.S. Food and Drug Administration (FDA) for the REMOXY NDA which had been resubmitted in December 2010 by King Pharmaceuticals (acquired by Pfizer in February 2011). The issues raised in the Complete Response Letter relate primarily to manufacturing. Pfizer has efforts underway to resolve these issues and stated in its earnings call on January 31, 2012 that it expects to conduct two bioavailability studies in the second quarter of 2012 and then meet with the FDA in the third quarter to discuss next steps. As a result of its acquisition of King, Pfizer has assumed the development and commercialization rights and obligations to REMOXY and to the three other licensed ORADUR-based opioid drug candidates (hydrocodone, hydromorphone and oxymorphone). This family of potential products is now covered by recently issued patents extending out to at least 2025.

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 discourage common methods of tampering associated with prescription opioid analgesic misuse and abuse. DURECT is eligible for a potential royalty on REMOXY of between 6.0% to 11.5% of net sales depending on the sales volumes. In addition, we supply to Pfizer two of the key excipients used in the manufacture of REMOXY for which we are paid our manufacturing cost plus a specified percentage mark-up.

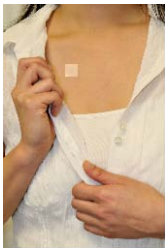
- **POSIDUR (SABER™-Bupivacaine).** We have conducted an extensive clinical development program for POSIDUR, comprising 13 completed studies with over 680 patient exposures in multiple surgical procedures including hernia, appendectomy, shoulder, hysterectomy and various abdominal procedures. After preparation of integrated safety and efficacy summaries combining our previous well-controlled studies with data from the BESST trial, a Phase III clinical trial for POSIDUR, we intend to hold a pre-NDA meeting with the FDA in the summer of 2012, with a potential NDA submission later in the year, depending on FDA feedback.

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. DURECT currently holds worldwide commercialization rights to this program.

- **Transdermal Development Candidates.** DURECT has two transdermal products that are Phase II assets with features that may be superior to currently available patches. TRANSDUR-Sufentanil is our proprietary transdermal patch intended to deliver sufentanil to chronic pain patients for a period of up to 7 days from a single application; this compares favorably against existing fentanyl patches which are typically effective for 2-3 days and which are substantially larger. ELADUR, for topical neuropathic conditions such as post-herpetic neuralgia (PHN), is our proprietary transdermal patch intended to deliver bupivacaine for a period of up to three days from a single application; existing lidocaine patches for this condition can be worn for 12 hours with a rest period of 12 hours during which time many patients experience breakthrough pain. We are in discussions with potential partners regarding licensing development and commercialization rights to these programs to which we hold worldwide rights.

ELADUR
(left)

TRANSDUR-Sufentanil
(right)



- **ORADUR-ADHD Program.** We are developing a drug candidate (ORADUR-ADHD) based on DURECT's ORADUR technology for the treatment of Attention Deficit Hyperactivity Disorder. This drug candidate is intended to provide once-a-day dosing with added tamper-resistant characteristics to address common methods of abuse and misuse of these types of drugs. We and Orient Pharma have completed several Phase I pharmacokinetic studies funded by Orient Pharma with multiple formulations. Based on information from those studies, we are continuing to evaluate our lead formulations. Orient Pharma is our licensee for certain Asian and South Pacific countries, while we retain the rights to the rest of the world.

- **Relday (Risperidone Program).** In July 2011, we signed a development and license agreement with Zogenix to develop Relday, a product candidate targeting the antipsychotic market. Zogenix expects to initiate clinical studies for Relday in patients with schizophrenia in 2012. Relday is a proprietary, long-acting (once-monthly) injectable formulation of 0.5 mL of risperidone using DURECT's SABER controlled-release formulation technology in combination with Zogenix's DosePro® needle-free, subcutaneous drug delivery system.

- **Feasibility Projects.** During 2011, we continued work on several 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. The Zogenix program, described above, was one such project which has matured into a development and license agreement.

- **ALZET and LACTEL products.** The wide use and applications of our ALZET line of osmotic pumps used for research purposes is evidenced by the more than 12,000 scientific references that now exist. We also design, develop and manufacture a line of biodegradable polymers under the LACTEL brand name, and several of these polymers are incorporated in FDA-approved therapeutics. In 2011, these product lines generated $10.6 million in revenue and a gross profit of $6.2 million for DURECT.

alzet® OSMOTIC PUMPS

LACTEL® Absorbable Polymers

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

On behalf of everyone at DURECT, we thank you for your continued support and look forward to reporting on our progress in 2012 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 stockholder letter regarding DURECT's anticipated 2012 cash burn, potential regulatory meetings and submissions for REMOXY and POSIDUR, anticipated clinical trials (including timing and results) for Relday and our other drug candidates, the potential benefits and uses of our drug candidates, our ability to prevent others from infringing our patents, collaborations with third parties and potential business development activities 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 rejection of meeting requests, requests for additional information or 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 operations and expenses. Further information regarding these and other risks is included in DURECT's Form 10-Q on May 4, 2012 under the heading "Risk Factors."