Dear Fellow Stockholders:

Many of our shareholders have been with us a long time on our journey to develop improved drugs that make a difference. Some investors are more recent shareholders who recognize the risks and also the associated opportunities in front of us. We thank all of our shareholders for their commitment, which is shared by our employees. Over the last year or so, many of our officers and directors have bought shares in the open market or volunteered to take reduced pay in return for additional stock options. Over the years, DURECT has had a very stable workforce as our employees have shown great dedication to overcoming the obstacles that inevitably arise in drug development. This commitment stems from the recognition that success with just one of our multiple programs would be transformative.

Our R&D programs are addressing very real medical needs which are supported by very positive industry trends. For example, REMOXY® is designed to provide effective opioid treatment for chronic pain sufferers with an abuse-resistant formulation. The importance of this has recently been emphasized by the FDA's actions to support abuse-resistant claims for narcotics as well as preventing the approval of generics for the original OxyContin® for safety reasons. In the case of POSIDUR™, we have developed an extended release post-surgical pain product that may significantly reduce the need for opioids, with their attendant risks and side-effects, in this important patient setting. Both opioid abuse and dealing with post-surgery side-effects have enormous associated healthcare costs, where we aspire to make a difference. The U.S. Food and Drug Administration (FDA) recognizes the need for opioids, but recent actions by the FDA also suggest that they wish to see more tamper-resistant formulations created for opioids and that they would look favorably on non-opioid alternatives where they can be safe and efficacious.

Major accomplishments since the start of 2012:

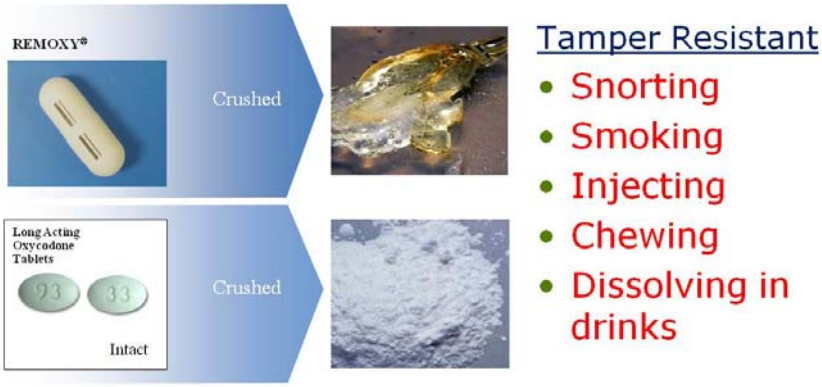
- **REMOXY Progress.** With support as appropriate from DURECT, Pfizer has devoted considerable efforts to resolve the issues raised in the Complete Response Letter, which are primarily related to manufacturing. Pfizer held a meeting with the FDA in late March 2013 to discuss their proposed resubmission plan for REMOXY. On April 30, 2013, Pfizer stated that they had a productive meeting with the FDA and received guidance that is helping to inform the next steps in addressing the issues raised by the FDA in the Complete Response Letter. The extended release oxycodone market is ~$3 billion, and the royalty we would receive on Pfizer sales of REMOXY range from 6% to 11.5%.

- **POSIDUR NDA Submission.** In mid-2012, DURECT had pre-NDA communications with the FDA. Incorporating feedback received from the FDA, we submitted the NDA in April 2013 and expect to hear whether the FDA accepts our submission in June 2013. If accepted for filing, the FDA would be expected to assign a PDUFA target date (the date the FDA expects to complete its review of the POSIDUR NDA) in the first quarter of 2014. We hold worldwide commercialization rights to POSIDUR, but are engaged in licensing efforts as this letter goes to print.

- **Patent Issuances.** We have had multiple important patents issue in the U.S. and other important commercial markets over the last 18 months. In addition to these issuances, we continue to file new applications protecting our technologies and programs, and are pursuing existing applications which may extend the patent life of several key programs. REMOXY is now covered in the U.S. by issued patents that go out to at least 2031 and in Europe to at least 2026. POSIDUR is now covered by issued patents that go out to at least 2025 in the U.S. and Europe. ELADUR® now has an issued patent expiring in 2031 and in Europe expiring in at least 2027. For TRANSDUR®-sufentanil, we have received issuance of three patents with coverage in the U.S. until at least 2025 and in Europe, we also received issuance of a patent with coverage until at least 2025.

Update of Programs:

- **REMOXY.** On June 23, 2011, Pfizer received a Complete Response Letter from the 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. On April 30, 2013, Pfizer stated that they had a productive meeting regarding REMOXY with the FDA and received guidance that is helping to inform the next steps in addressing the issues raised by the FDA in the Complete Response Letter. 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 a recently issued U.S. patent extending to at least 2031.



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. In April 2013, we submitted the POSIDUR NDA and expect to hear whether the FDA accepts our submission in June 2013. If accepted for filing, the FDA would be expected to assign a PDUFA date in the first quarter of 2014.

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, although we are in discussions with multiple parties regarding licensing commercialization rights to POSIDUR.

- **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 effective for only 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 January 2013, Zogenix (our licensee) announced positive single-dose pharmacokinetic (PK) results from a Phase 1 clinical trial of Relday**.** Based on the favorable safety and PK profile demonstrated with the 25 mg and 50 mg once-monthly doses tested in the Phase 1 trial, Zogenix extended the study to include a 100 mg dose of the same formulation. In May 2013, Zogenix announced positive results with the 100 mg arm, demonstrating dose proportionality across the full dose range that would be anticipated to be used in clinical practice.

- **Feasibility Projects.** During 2012, 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 nearly 14,000 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 2012, these product lines generated $10.5 million in revenue and a gross profit of $5.9 million for DURECT.

alzet® OSMOTIC PUMPS

LACTEL® Absorbable Polymers

In 2013, we look forward to:

- Pfizer working toward a REMOXY resubmission
- Interacting with the FDA on the POSIDUR NDA, with a possible PDUFA date in Q1 2014
- Supporting Zogenix in the development of Relday
- Potentially entering into additional feasibility studies and collaborations

On behalf of everyone at DURECT, we thank you for your continued support and look forward to reporting on our progress in 2013 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 regulatory meetings and submissions for REMOXY and POSIDUR, potential regulatory approvals of REMOXY and POSIDUR, the potential benefits and uses of our drug candidates, the FDA's view on opioids, our ability to prevent others from infringing our patents, potential extensions of existing 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 that Pfizer might discontinue development of REMOXY, the risk of adverse decisions by regulatory agencies, including requests for additional information or product non-approval or non-acceptance of our POSIDUR or other NDA submissions, 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 risks related to 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 product candidates, obtain marketplace acceptance of 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 for the quarterly period ending on March 31, 2013 under the heading "Risk Factors."

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