April 28, 2014

Dear Fellow Stockholders:

Our mission is to build a leading specialty pharmaceuticals company. When investors think of DURECT, they inevitably think of REMOXY® and POSIDUR™ – our two NDA-stage product candidates that address large market opportunities in the field of pain management. These two product candidates address a major medical need driven by the widespread abuse and misuse of opioids, but in different ways. REMOXY is designed to provide effective opioid treatment for chronic pain sufferers but in an abuse-deterrent formulation. We developed POSIDUR as an extended release pain product intended to cover the first full three days after surgery while also significantly reducing the need for opioids and their attendant risks and side-effects in this important patient setting.

Many investors don't look beyond these two programs, but we're not just a two product company – there is much more at DURECT that can create value for us over time. Assessing the true future value of DURECT requires a real look into 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. Our pipeline of products is protected by an extensive patent portfolio involving major and partnered programs that extend patent protection in large market jurisdictions to at least 2025, and in several cases past 2030.

Major accomplishments since the start of 2013:

- **REMOXY Progress.** The abuse of opioids remains a major public health concern, as reiterated on multiple occasions by the FDA. REMOXY, an investigational drug, is a unique long-acting formulation of oxycodone that is based on DURECT's ORADUR® technology. Through this formulation, REMOXY is designed to discourage common methods of tampering associated with misuse and abuse. Pfizer met with the FDA in March 2013, and this meeting provided a path forward for the resubmission of REMOXY along the lines that Pfizer proposed. Pfizer currently has four studies for REMOXY posted on Clintrials.gov, with work toward a resubmission actively underway. The extended release oxycodone market is ~$3 billion, and we are 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..

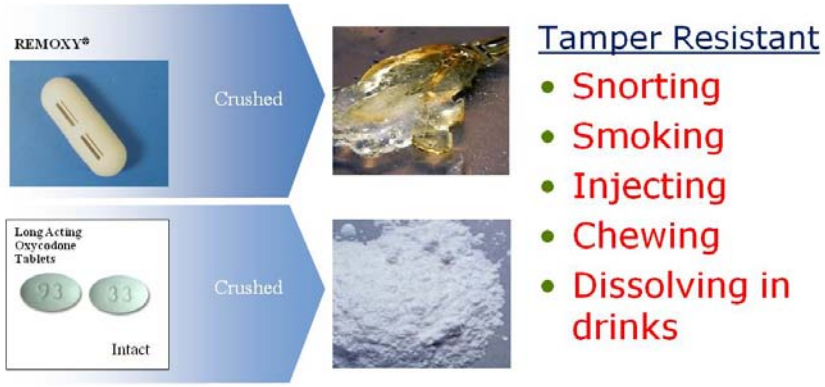
- **POSIDUR (SABER®-bupivacaine) New Drug Application (NDA).** In April 2013 we submitted an NDA with the FDA, and in February 2014 we received a Complete Response Letter (CRL), meaning that the FDA is not prepared to approve the NDA in its present form. We are evaluating the issues and recommendations described in the CRL and plan to have further discussions with the FDA around them. We hold worldwide commercialization rights to POSIDUR.

- **ELADUR® (TRANSDUR®-bupivacaine).** In January 2014, we signed an agreement with Impax Laboratories, Inc. (Impax) granting them the rights to develop and commercialize ELADUR. Per the agreement, Impax paid DURECT an upfront fee of $2 million, with the potential for up to $61 million in additional milestone payments, and a tiered royalty on product sales. We are pleased to have this Phase 2 product candidate back in development.

- **Relday™ (Risperidone program).** In 2013, Zogenix, Inc. (our licensee) announced positive results from a single-dose Phase 1 clinical trial of Relday at the full dose range anticipated to be used in clinical practice. With our assistance, Zogenix is planning to commence a multi-dose trial in the fourth quarter of 2014. We are eligible to receive up to $103 million in future milestone payments and a tiered royalty on product sales.

Update of Programs:

- **REMOXY.** On June 23, 2011, Pfizer received a CRL 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 CRL relate primarily to manufacturing. Pfizer has stated that they had a productive meeting regarding REMOXY with the FDA in March 2013, and this meeting provided a path forward for the resubmission of REMOXY along the lines that Pfizer proposed. As previously disclosed, the complete response submission is not expected to occur prior to mid-2015. REMOXY is covered by issued U.S. patents, including one extending to at least 2031.



REMOXY, an investigational drug, is a unique long acting oral formulation of oxycodone intended to treat pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. 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.

- **POSIDUR (SABER-Bupivacaine).** In April 2013 we submitted an NDA with the FDA, and in February 2014 we received a Complete Response Letter. Based on its review, the FDA has determined that they cannot approve the NDA in its present form, stating the NDA does not contain sufficient information to demonstrate that POSIDUR is safe when used in the manner described in the proposed label, and the FDA has indicated that additional clinical safety studies need to be conducted. We are evaluating the issues and recommendations described in the CRL and plan to have further discussions with the FDA around them. POSIDUR is covered by issued U.S. patents extending to at least 2025.

POSIDUR is our post-operative pain relief depot that utilizes our patented SABER technology and is intended 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.

- **ELADUR (TRANSDUR-bupivacaine).** 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. As described earlier, we licensed this program to Impax in January 2014, and Impax is now driving forward this asset which is in Phase 2.

- **Relday™ (Risperidone Program).** Relday is a proprietary, long-acting, once-monthly subcutaneous injectable formulation of risperidone. An existing long-acting injectable risperidone product, which achieved $1.3 billion in global net sales in 2013, requires twice-monthly, intramuscular injections and drug reconstitution prior to use. In 2013, Zogenix (our licensee) announced positive results from a single-dose Phase 1 clinical trial of Relday at the full dose range anticipated to be used in clinical practice. According to Zogenix, the positive results from this study positions Zogenix to begin a multi-dose clinical trial, which would provide the required steady-state pharmacokinetic and safety data prior to initiating Phase 3 development studies, and Zogenix plans to commence this multi-dose trial in the fourth quarter of 2014.

- **ORADUR-ADHD Program.** In 2013, we selected a lead formulation for the initial program in our Attention Deficit Hyperactivity Disorder (ADHD) program, ORADUR-Methylphenidate. This formulation was chosen based on its potential for rapid onset of action, long duration with once-a-day dosing and target pharmacokinetic profile as demonstrated in a Phase 1 trial. In addition, this product candidate utilizes a small capsule size relative to the leading existing long acting products on the market and incorporates our ORADUR anti-tampering technology. Our licensee, Orient Pharma, has met with the Taiwan Food and Drug Administration (TFDA) to discuss the Phase 3 program in that market and is developing its plans for further development in the defined Asian and South Pacific countries to which it has rights from us. We retain rights to all other markets in the world, notably including the U.S., Europe and Japan, and have initiated licensing discussions with other companies now that the lead formulation has been selected.

- **Other ORADUR-based Opioids.** We have licensed three other ORADUR-based opioids (hydrocodone, hydromorphone and oxymorphone) to Pain Therapeutics. Phase I clinical trials have been conducted for ORADUR-hydrocodone and ORADUR-hydromorphone, and an Investigational New Drug (IND) application has been accepted by the FDA for ORADUR-oxymorphone. During the first quarter of 2014, we conducted research and development activities on these programs under approved workplans with Pain Therapeutics.

- **Feasibility Projects.** During 2013, 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 Relday 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 2013, these product lines generated $11.4 million in revenue and $6.8 million in gross profit for DURECT.

alzet® OSMOTIC PUMPS

LACTEL® Absorbable Polymers

Potential key drivers for DURECT over the next 12-24 months:

- Pfizer working toward a REMOXY resubmission target of mid-2015, followed by a 6 month review by the FDA and then, pending a favorable outcome, commercial launch of REMOXY
- Meeting with the FDA to gain clarity on the POSIDUR NDA and potentially licensing commercialization rights of POSIDUR if we feel it is with the right party and on terms that reflect the value of this asset
- Impax potentially commencing and conducting the Phase 3 program for ELADUR
- Supporting Zogenix in the development of Relday, targeted to initiate a multi-dose clinical study in the fourth quarter of 2014, which would be the precursor to Phase 3
- Potentially entering into new collaborations and announcing new development programs

On behalf of everyone at DURECT, we thank you for your continued support and look forward to reporting on our progress in 2014 and beyond including the potential resubmission and approval of REMOXY next year.

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, discussions and submissions for REMOXY and POSIDUR, potential FDA approval of REMOXY, POSIDUR, or any of our other product candidates, anticipated clinical trials (including timing and results) for ELADUR, Relday, ORADUR-Methylphenidate and our other drug candidates, potential royalties or milestone payments from Pfizer, Impax and Zogenix, the potential benefits and uses of our drug candidates and pipeline of products, collaborations with third parties and potential business development, licensing and commercialization activities, including potential commercial product launches, and cash flows, creation of value, new development programs and other results of operations 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 will discontinue development of REMOXY, the risk of adverse decisions by regulatory agencies, including rejection of meeting requests, requests for additional information or product non-approval or non-acceptance of the REMOXY, 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 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 our (and our third party collaborators where applicable) ability to design, enroll, conduct and complete clinical trials, complete the design, development, and manufacturing process development of 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 Annual Report on Form 10-K for the year ended December 31, 2014 under the heading “Risk Factors.”

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