May 2, 2018

Dear Fellow Stockholders:

Making a difference - what we strive for as individuals and as a company. We believe that DUR-928, in particular, has created a unique opportunity for DURECT to make a profound difference in the lives of people suffering from a range of acute and chronic conditions. In addition, several other programs, based on our drug delivery technologies and patent estate, are advancing. We have two potential product approvals in 2018, with PDUFA (Prescription Drug User Fee Act) action dates set for late July and early August. As we've advanced our pipeline and prioritized efforts around DUR-928, DURECT is a different company today than it was a few years ago.

Epigenetic Regulator Program*:*

DUR-928, the lead product candidate in our Epigenetic Regulator Program, is a naturally occurring small molecule that plays an important regulatory role in the vital functions of lipid homeostasis, inflammation and cell survival. As such, this small molecule may have therapeutic benefits in several metabolic and liver diseases such as primary sclerosing cholangitis (PSC) and nonalcoholic steatohepatitis (NASH), in acute organ injuries such as liver and kidney injury, and in inflammatory skin diseases such as psoriasis and atopic dermatitis.

In 2017, we reported encouraging results at The International Liver Congress™ from our first patient trial utilizing DUR-928. Twenty NASH patients and 12 matched control subjects received single oral doses. DUR-928 was well tolerated in this Phase 1b study and plasma exposure was not significantly increased in NASH patients compared to matched control subjects with normal liver function. While this study was not designed to assess efficacy, treatment with a single dose of DUR-928 was associated with a decrease in full length and cleaved CK-18 (cell death markers), an improvement of bilirubin (a biomarker of liver function), and decreases in certain biomarkers associated with inflammation. Collectively, the reduction of these biomarkers, together with results from DURECT's animal and cell culture studies, suggest potential therapeutic activity of DUR-928 in patients with liver disease.

We have also conducted a Phase 1b single-ascending-dose, injectable administration trial in renal-function-impaired patients (11 chronic kidney disease patients and 6 matched controls). DUR-928 was well tolerated and plasma exposure was not significantly increased in these chronic kidney disease patients compared to matched control subjects with normal kidney function. While the number of subjects involved was small and the trial not designed to assess efficacy, once again we observed decreases in bilirubin and CK-18 when those levels were meaningfully elevated pre-treatment, although these results were not statistically significant.

We also completed an initial exploratory Phase 1b trial in psoriasis patients (9 evaluable patients). The decision to proceed with clinical testing in psoriasis was based on the anti-inflammatory and cell survival properties of DUR-928, as well as the results of a psoriasis study with DUR-928 in mice. The Phase 1b trial was conducted with intradermal micro injections of DUR-928, and the results demonstrated promising activity and warrant further investigation.

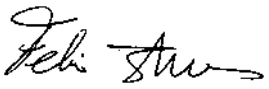
An important goal in 2018 is to advance DUR-928 into initial Phase 2 studies. We have begun a Phase 2a open label trial in patients with the orphan disease PSC with orally administered DUR-928 and a Phase 2a open label trial in patients with Alcoholic Hepatitis with intravenously infused DUR-928. We anticipate soon beginning a third Phase 2 trial in psoriasis patients with topically applied DUR-928. If recruitment proceeds as planned, we will receive preliminary data from one or more of these studies during 2018.

Given space constraints, just a brief mention of a few other programs and products at DURECT:

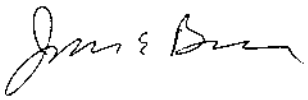
- **Indivior Agreement and RBP-7000**. In September 2017, we entered into a patent purchase agreement with an affiliate of Indivior PLC, whereby we assigned certain of our U.S. patent rights to Indivior. This assignment may provide further intellectual property protection for RBP-7000, Indivior's investigational once-monthly injectable risperidone product for the treatment of schizophrenia. Under the terms of the agreement, Indivior made an upfront non-refundable payment to DURECT of $12.5 million, with the potential for an additional $5 million payment based on NDA approval of RBP-7000, as well as quarterly earn-out payments that are based on a single digit percentage of U.S. net sales for certain products covered by the patent rights, including RBP-7000. Indivior submitted an NDA for RBP-7000 to the FDA, which has been accepted for review. The PDUFA target action date is July 28, 2018. Indivior has stated that it has set up a separate business unit to market RBP-7000, if approved, with an anticipated launch in the fourth quarter of 2018 and a peak sales projection of $200-300 million.

- **REMOXY® ER.** Based on our ORADUR® technology, REMOXY ER is a unique long-acting formulation of oxycodone designed to discourage common methods of tampering associated with opioid misuse and abuse. In January 2018, Pain Therapeutics announced positive results from a human abuse potential study using nasal administration of REMOXY ER and that they had completed all studies necessary to resubmit the REMOXY ER NDA to the FDA. In February 2018, Pain Therapeutics resubmitted the REMOXY ER NDA. This was followed in March 2018 by an announcement from Pain Therapeutics that the FDA has determined that the NDA is sufficiently complete to permit a substantive review. The FDA has set a PDUFA action date of August 7, 2018. Pain Therapeutics also announced that the FDA will hold an Advisory Committee Meeting to discuss the NDA for REMOXY ER, and the tentative date for this meeting is June 26, 2018. The extended release oxycodone market remains substantial, and we are eligible for a $1.5 million milestone payment upon FDA approval and a potential royalty on REMOXY ER of between 6.0% to 11.5% of net sales.
- **POSIMIR.** POSIMIR is our investigational post-operative pain relief depot that utilizes our patented SABER technology and is designed to deliver bupivacaine to provide up to 3 days of pain relief after surgery. In 2017, we were pleased to sign an agreement with Sandoz whereby Sandoz would commercialize POSIMIR in the U.S. Under the terms of the agreement, Sandoz made a non-refundable upfront payment of $20 million, and we remain eligible for up to an additional $30 million in milestone payments based on successful development and regulatory milestones, up to an additional $230 million in sales-based milestones, and a tiered double-digit royalty on U.S. sales. Unfortunately, not everything goes according to plan when conducting pain trials. In October 2017, we reported that PERSIST, a Phase 3 clinical trial for POSIMIR, did not meet its primary efficacy endpoint of reduction in pain on movement as compared to standard bupivacaine HCl over the first 48 hours after surgery. While the results trended in favor of POSIMIR versus the comparator, they did not achieve statistical significance. As of this writing, we are working with Sandoz to consider potential next steps.
- **ALZET® and LACTEL® products.** The wide use and many research applications of our ALZET line of osmotic pumps are supported by over 16,000 references in the scientific literature. 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 2017, these product lines generated record results with over $13 million in revenue for DURECT and over $8 million in gross profit.

We are as optimistic as we've ever been about our prospects for making a difference; we have two potential approvals in 2018 and our therapeutic candidate DUR-928 is a compelling opportunity. DUR-928 is an endogenous molecule that appears to be safe and yet with regulatory activities in the important functions of lipid homeostasis, inflammation and cell survival that could yield multiple indications. Our focus is on driving DUR-928 forward to demonstrate further proof-of-concept in several different patient populations. On behalf of everyone at DURECT, we thank you for your continued support and look forward to reporting on our progress in 2018 and beyond.



Felix Theeuwes, D.Sc.
Chairman and Distinguished Scientist



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

Forward-Looking Statements: The statements in this stockholder letter regarding regulatory matters, including potential FDA approval of RBP-7000 and REMOXY ER, anticipated clinical trials (including timing and results) for DUR-928 and our other drug candidates, potential milestones and royalties from Sandoz and Pain Therapeutics and potential milestones and earn-out payments from Indivior, the potential benefits and uses of our drug candidates and pipeline of products, collaborations with third parties, and market opportunities for our product 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 unexpected delays in the regulatory review of, or adverse decisions by, the FDA, for RBP-7000 or REMOXY ER, requests for additional information or product non-approval or non-acceptance of the RBP-7000, REMOXY ER or other NDA submissions, delays and additional costs due to requirements imposed by regulatory agencies, failure of initial safety and efficacy indications for DUR-928 to be demonstrated in larger controlled trials, additional time and resources that may be required for development, testing and regulatory approval of our Epigenetic Regulator Program, 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, 2017 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.