# DURECT Corporation Announces Update on DUR-928 Development Program

CUPERTINO, Calif., Jan. 30, 2017 /PRNewswire/ — DURECT Corporation (Nasdaq: DRRX) today provided an update on the DUR-928 development program. DUR-928, our Epigenetic Regulator Program's lead product candidate, is an endogenous, small molecule, new chemical entity (NCE), which may have broad applicability in several metabolic diseases such as nonalcoholic steatohepatitis (NASH) and other liver conditions, and in acute organ injuries such as acute kidney injury (AKI).

**Phase 1b trial in patients with NASH**

Our first patient trial utilizing DUR-928 was an open-label, single-ascending-dose safety and pharmacokinetic (PK) Phase 1b trial in liver function impaired (NASH) patients and matched control subjects (matched by age, body mass index and gender with normal liver function). This study was conducted in Australia in successive cohorts evaluating single-dose levels (first a low dose and then a high dose) of orally administered DUR-928.

An abstract for this study has been accepted and data from the study will be presented at the International Liver Congress™ 2017 organized by the European Association for the Study of the Liver (EASL) in Amsterdam, April 19-23, 2017.

The low dose cohort consisted of 10 subjects with NASH (of which 4 were cirrhotic and 6 were not cirrhotic) and 6 matched control subjects. After a PK/safety review of this cohort, the study proceeded to the high dose cohort utilizing a dose four times larger than the low dose cohort. The high dose cohort consisted of 10 subjects with NASH (of which 2 were cirrhotic and 8 were not cirrhotic) and 6 matched control subjects. One patient (with a prior history of arrhythmia and an ongoing viral infection) in the high dose cohort experienced a serious adverse event (shortness of breath) which occurred without unusual biochemical changes and resolved without intervention but was considered possibly treatment related by the physician due to its temporal association with dosing. In both the low and high dose cohorts, the PK parameters were comparable between the NASH patients and the matched control subjects. In addition, the systemic exposure following the low and high doses of DUR-928 was dose dependent.

While this study was not designed to assess efficacy, we do observe a dose dependent reduction of certain biomarkers after a single oral dose of DUR-928. In both cohorts, IL-18, an inflammatory mediator implicated in both liver and kidney diseases, decreased in the NASH patients. In addition, both full length CK-18 (a generalized cell death marker) and cleaved CK-18 (a cell apoptosis marker) were reduced after DUR-928 treatment, with the effect more pronounced in NASH patients.

Collectively, the reduction of these biomarkers plus results from our animal and cell culture studies suggest potential therapeutic activity of DUR-928 for patients with liver disease. However, additional studies are required to evaluate the safety and efficacy of DUR-928, and there is no assurance that these biomarker effects will be observed in a statistically significant manner, or that DUR-928 will demonstrate safety or efficacy in treating NASH or other liver diseases, in larger controlled trials.

**Phase 1b trial in patients with impaired kidney function**

Our second Phase 1b study with DUR-928, also being conducted in Australia, is an open-label, single-ascending-dose safety and pharmacokinetic study in patients with impaired kidney function (stage 3 and 4 chronic kidney disease) and matched control subjects (matched by age, body mass and gender with normal kidney function). This study is being conducted in successive cohorts evaluating single-dose levels (first a low dose and then a high dose) of DUR-928 administered by intramuscular injection.

The low dose cohort consisted of 6 kidney function impaired patients and 3 matched control subjects. After a PK/safety review of this cohort, the study has proceeded to the high dose cohort utilizing a dose four times larger than the low dose cohort. Data from the low dose cohort showed the PK parameters between the kidney function impaired patients and the matched control subjects were comparable.

The high dose cohort of this study is currently enrolling patients. In addition, we have held a pre-IND meeting with the Cardiovascular and Renal Products Division of the FDA, and we are utilizing feedback from that meeting as well as from our clinical advisors to prepare an IND which is required to enable a future kidney disease clinical trial in the United States.

**Future Development Plans**

We have been working with our clinical advisors to design several Phase 2 studies and are planning to submit INDs which are required to enable these studies to take place in the United States in 2017. We submitted an initial IND in late December 2016 for a proposed Phase 2 liver study. The FDA has requested additional non-clinical information (drug-drug interaction data) and has made suggestions as to modifications to our proposed protocol. We are working to address FDA's request and consulting with our clinical advisors to finalize the study protocol.

**About DURECT Corporation**

DURECT is a biopharmaceutical company actively developing new therapeutics based on its Epigenetic Regulator Program and proprietary drug delivery platforms. DUR?928, a new chemical entity in Phase 1 development, is the lead candidate in DURECT's Epigenetic Regulator Program. An endogenous, orally bioavailable small molecule, DUR-928 has been shown in preclinical studies to play an important regulatory role in lipid homeostasis, inflammation, and cell survival. Human applications may include acute organ injury and chronic metabolic diseases such as nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH). DURECT's advanced oral, injectable, and transdermal delivery technologies are designed to enable new indications and enhanced attributes for small-molecule and biologic drugs. One late-stage development program in this category is POSIMIR® (SABER®-Bupivacaine), an investigational analgesic product intended to address key unmet needs in postoperative pain management. Another is REMOXY® ER (oxycodone), an investigational new drug based on DURECT's ORADUR® technology. For more information, please visit www.www.durect.com.

NOTE: POSIMIR®, SABER®, and ORADUR® are trademarks of DURECT Corporation. Other referenced trademarks belong to their respective owners. POSIMIR, DUR-928, and REMOXY ER are drug candidates under development and have not been approved for commercialization by the U.S. Food and Drug Administration or other health authorities.

**DURECT Forward-Looking Statement**

The statements in this press release regarding the potential benefits and uses of our drug candidates, including the potential use of DUR-928 to treat NASH, other liver disease or kidney disease, plans for an IND and Phase 2 and other clinical trials of DUR-928, the potential use of POSIMIR to treat pain, and potential markets for DUR-928 and POSIMIR, 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 risks that future clinical trials of DUR-928 do not demonstrate the safety or efficacy of DUR-928 in a statistically significant manner, that the PERSIST clinical trial of POSIMIR will take longer to conduct than anticipated or result in data that will not support a successful NDA resubmission or product approval, the risk of delays in the commencement, enrollment or completion of other clinical trials, the risk that prior clinical trials will not be confirmed in subsequent trials, the potential failure of clinical trials to meet their intended endpoints, the risk of adverse decisions by regulatory agencies or delays and additional costs due to requirements imposed by regulatory agencies, additional time and resources that may be required for development, testing and regulatory approval of DUR-928, potential adverse effects arising from the testing or use of DUR-928 or our other drug candidates, and risks related to our ability to obtain capital to fund operations and expenses. Further information regarding these and other risks is included in DURECT's Form 10-Q filed on November 1, 2016 under the heading "Risk Factors."

To view the original version on PR Newswire, visit: http://www.prnewswire.com/news-releases/durect-corporation-announces-update-on-dur-928-development-program-300398345.html

SOURCE DURECT Corporation

Matt Hogan, Chief Financial Officer, DURECT Corporation, 408-777-4936