DURECT Announces Epigenomic Regulator Program including a New NAFLD/NASH and Acute Organ Injury Product Candidate in Development

Initial Phase 1 Safety Study Successfully Completed, Building on Promising Body of Preclinical Data

CUPERTINO, Calif., March 2, 2015 /PRNewswire/ — DURECT Corporation (Nasdaq: DRRX) today announced its Epigenomic Regulator Program, and the successful completion of a Phase 1 clinical trial with the program's lead product candidate DUR-928. DUR-928 is an endogenous, small-molecule, new chemical entity (NCE), which may have broad applicability in metabolic diseases such as nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH), and in acute organ injuries such as acute kidney injury (AKI).

"We are pleased to add to our pipeline this important product candidate that is in the center of a very active area of research and significant unmet need in inflammation and metabolic disease," said James E. Brown, President and CEO of DURECT. "Preclinical data from 6 different animal models suggest that DUR-928 plays a key regulatory role in lipid homeostasis, inflammatory responses and cell survival. Our plan is to follow our initial successful single-dose safety study with multi-dose Phase 1 trials in 2015 and then continue on to Phase 2 studies for a number of inadequately served orphan and non-orphan diseases, some acute and some chronic."

"The data generated to date with DUR-928 are very powerful and suggestive of utility in a number of indications," stated Thomas P. Bersot, MD, PhD, Director of the Gladstone Lipid Clinic associated with the University of California, San Francisco and contributing author to Goodman & Gilman's The Pharmaceutical Basis of Therapeutics. "What is so compelling about this previously unrecognized molecule is that it appears to be an endogenous epigenomic regulator of a number of interrelated cellular systems and, therefore, may have broad therapeutic effects that would be hard to duplicate with standard single-target drugs."

Epigenomic Regulator Program Overview

DURECT's Epigenomic Regulator Program involves a collaborative effort now in its fourth year between DURECT and the Department of Internal Medicine at Virginia Commonwealth University (VCU), the VCU Medical Center, and the McGuire VA Medical Center. The discoveries from this program are the result of more than 20 years of lipid research by Shunlin Ren, MD, PhD, Associate Professor of Internal Medicine at the VCU Medical Center and a recipient of multiple NIH grants for metabolic disease research. DURECT holds the exclusive worldwide right to develop and commercialize DUR-928 and related molecules discovered in the program.

During the course of this program, a number of compounds have been identified that may have therapeutic utility for various diseases and syndromes for orphan indications as well as for broader patient populations. The lead compound from this program DUR-928 is an endogenous, orally bioavailable small molecule that modulates the activity of various nuclear receptors that play an important regulatory role in lipid homeostasis, inflammation and cell survival. A systems biology study involving over 23,000 genes showed that DUR-928 modulates the activity of more than 240 genes, including ACC, FAS, HMGR, Cyp7A1, LXR, PPAR?, NF?B/I?B, TNF?, IL-1?, IL-6, COX-2, PCSK9, and others.

The biological activity of DUR-928 has been demonstrated in 6 different animal disease models involving three animal species. Three of these models represented acute toxic or ischemic organ injury (kidney and liver) and three represented chronic disorders of hepatic lipid accumulation and dysfunction (NAFLD/NASH).

In pharmacokinetic and toxicity studies conducted in mice, hamsters, rats, dogs and monkeys, DUR-928 has been found to be orally bioavailable and safe at all doses tested to date. These non-clinical results supported the initiation of DUR-928 into human safety trials with an oral formulation. An oral formulation, envisioned for use in chronic conditions, has undergone initial testing. An

injectable formulation, envisioned for use in acute conditions, is undergoing animal testing.

Phase 1 Study

The Phase 1 trial of DUR-928 was a single-site, randomized, double-blinded, placebo-controlled, single-ascending-dose study that evaluated the safety, tolerability and pharmacokinetics of DUR-928 when orally administered. The 30-subject study evaluated DUR-928 in five cohorts of healthy volunteers receiving DUR-928 at escalating doses that resulted in peak plasma concentrations at least 100-fold higher than endogenous levels.

DUR-928 was well-tolerated at all dose levels, with no treatment-related adverse events reported and no subjects withdrawing from the study.

Future Development Plans

DURECT anticipates commencing a Phase 1 multiple-ascending-dose, oral administration trial in healthy subjects in mid-2015, as well as a Phase 1 single-dose, injectable administration trial in healthy subjects in the second half of 2015 as precursor to a multiple-ascending-dose Phase 1 trial. Assuming no undue safety results from these trials, DURECT would then be positioned to commence one or more Phase 2 patient trials in 2016.

DURECT is currently evaluating potential indications for DUR-928 in order to prioritize the development program. Long term opportunities fall into four broad categories: (a) orphan acute indications, (b) broader acute indications, (c) orphan chronic indications, and (d) broader chronic indications. DURECT's initial Phase 2 studies will be designed to show an efficacy signal in patients suffering from one orphan acute condition such as acute kidney injury and one broad chronic indication such as NAFLD/NASH. DURECT plans to provide more detail on the Phase 2 studies later this year.

About DURECT Corporation

DURECT is a specialty pharmaceuticals company with expertise in drug discovery, drug delivery and drug development, applying those skills primarily to therapeutics in the fields of pain management, acute organ injury and metabolic diseases. DURECT's proprietary oral, transdermal and injectable depot delivery technologies enable new indications and superior clinical/commercial attributes such as improved abuse deterrence, convenience, adherence, efficacy and safety for small molecule and biologic drugs. Late stage development programs of this nature include REMOXY® and POSIDUR™. DURECT's Epigenomic Regulator Program includes the lead molecule DUR-928 in Phase I. DUR-928 is an endogenous small molecule that is an epigenomic modulator of cellular activities involved in lipid homeostasis, metabolic disease, inflammation and cell survival. For more information, please visit www.www.durect.com.

DURECT Forward-Looking Statement

The statements in this press release regarding DURECT's Epigenomic Regulator Program and product candidate DUR-928, including the attributes, potential therapeutic effects and commercial potential for DUR-928 and other compounds identified during the course of the program, our development plans for DUR-928, and the timing and nature of future clinical trials 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, DURECT's ability to design, enroll, conduct and complete clinical trials, whether additional human trials for DUR-928 will demonstrate biological activity shown in animal trials and/or will identify safety issues, DURECT's ability to complete the design, development, and manufacturing process development of DUR-928 and other NCE product candidates, obtain product and manufacturing approvals from regulatory agencies and manufacture and commercialize product candidates, and achieve marketplace acceptance of product candidates. Further information regarding these and other risks is included in DURECT's Form 10-Q dated November 4, 2014 filed with the Securities and Exchange Commission under the heading "Risk Factors."

NOTE: POSIDUR™ is a trademark of DURECT Corporation. REMOXY, POSIDUR and DUR-928 are drug candidates under development and have not been approved for commercialization by the U.S. Food and Drug Administration or other health authorities.

To view the original version on PR Newswire, visit:http://www.prnewswire.com/news-releases/durect-announces-epigenomic-regulator-program-including-a-new-nafldnash-and-acute-organ-injury-product-candidate-in-development-300043790.html

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