DURECT Announces Presentation of Data from a Phase 1b Study of DUR-928 in Nonalcoholic Steatohepatitis (NASH) at The International Liver Congress™ 2017

Biomarker analysis provides evidence for a potential therapeutic effect of DUR-928 in NASH

CUPERTINO, Calif., April 24, 2017 /PRNewswire/ — DURECT Corporation (Nasdaq: DRRX), a biopharmaceutical company actively developing new therapeutics based on its Epigenetic Regulator Program and proprietary drug delivery platforms, announced that clinical data on DUR-928 were presented at The International Liver Congress™ 2017 (the 52nd annual meeting of the European Association for the Study of the Liver (EASL)) on April 22 in Amsterdam.

“DUR-928 was well tolerated in this study and plasma exposure of the molecule was not significantly increased in NASH patients compared to matched control subjects with normal liver function,” stated James E. Brown, D.V.M., President and CEO of DURECT. “Importantly, treatment with a single dose of DUR-928 was associated with a decrease in cell death markers, an improvement of a biomarker of liver function, and decreases in certain biomarkers associated with inflammation.”

Phase 1b trial in patients with NASH

The study was a Phase 1b single dose ranging (50 mg and 200 mg), safety and pharmacokinetic (PK) study of orally-administered DUR-928 in two cohorts of biopsy-confirmed NASH patients and matched control subjects (MCS) (matched by age, BMI, and gender) with normal liver function. Both cohorts consisted of 10 NASH patients and 6 MCS.

In both cohorts, DUR-928 was well tolerated overall. There was approximately a 10-30% increase in DUR-928 exposure in NASH patients compared to MCS. A single serious adverse event (shortness of breath), designated as possibly related to study drug, was reported in Cohort 2 in a NASH patient with a prior history of arrhythmia and an ongoing viral infection; no unusual abnormal biochemistry was observed and the symptom spontaneously resolved.

Exploratory biomarker analysis indicated that a single oral dose of DUR-928 resulted in reductions from baseline in the levels of both full-length and cleaved cytokeratin-18 (CK-18), bilirubin, hsCRP and IL-18 in NASH patients.

- The decrease of full-length CK-18 (a generalized cell death marker) at 12 hours was approximately 33% in the NASH patients in the low dose cohort and approximately 41% in the high dose cohort. The decrease of cleaved CK-18 (a cell apoptosis marker) at 12 hours was approximately 37% in the NASH patients in the low dose cohort and approximately 47% in the high dose cohort.
- The decrease in total bilirubin (a liver function marker for which a decrease would be seen as positive) at 12 hours in the NASH patients was approximately 27% in the low dose cohort and approximately 31% in the high dose cohort.
- High sensitivity C-Reactive Protein (hsCRP), a marker of inflammation, trended higher at 12 hours in the NASH patients by approximately 3% in the low dose cohort but trended lower by approximately 12% in the high dose cohort.
- IL-18, an inflammatory mediator implicated in both liver and kidney diseases, trended lower at 12 hours by approximately 5% in both the low dose cohort and in the high dose cohort.

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. However, additional studies, including larger controlled trials, will be required to confirm these findings and 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.

The poster that was presented at ILC 2017 will shortly be posted to the “Science & Technologies” section of DURECT’s website at www.www.durect.com

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About DURECT

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 inDURECT'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, chronic metabolic diseases such as nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH) and other liver diseases with both broad and orphan populations, and inflammatory skin conditions such as psoriasis. 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 product candidate in this category is POSIMIR® (SABER®-Bupivacaine), an investigational locally-acting, non-opioid analgesic intended to provide up to 3 days of continuous pain relief after surgery. Another late stage product candidate is REMOXY® ER (oxycodone), an investigational pain control 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 disorders of the liver, acute organ injury, kidney diseases or psoriasis or other inflammatory conditions, the potential use of POSIMIR and REMOXY ER to treat pain, and potential markets 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 risks that future clinical trials of DUR-928 do not replicate results reported here or do not demonstrate the safety or efficacy of DUR-928 in a statistically significant manner, the risk of delays in the commencement, enrollment or completion of clinical 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 our drug candidates, our potential failure to maintain our collaborative agreements with third parties or consummate new collaborations and risks related to our ability to obtain capital to fund operations and expenses. Further information regarding these and other risks is included inDURECT's Form 10-K filed on March 29, 2017 under the heading "Risk Factors."

To view the original version on PR Newswire, visit:http://www.prnewswire.com/news-releases/durect-announces-presentation-of-data-from-a-phase-1b-study-of-dur-928-in-nonalcoholic-steatohepatitis-nash-at-the-international-liver-congress-2017-300443793.html

SOURCE DURECT Corporation

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