DURECT Corporation Announces Additional Safety Data and Efficacy Signals from Phase 1b Clinical Trial of DUR-928 in NASH Patients at The Liver Meeting Digital Experience™ 2020

CUPERTINO, Calif., Nov. 13, 2020 /PRNewswire/ — DURECT Corporation (Nasdaq: DRRX) today presented additional safety data and efficacy signals from its Phase 1b clinical trial of DUR-928 in nonalcoholic steatohepatitis (NASH) patients in a poster presentation at The AASLD Liver Meeting Digital Experience ™ (TLMdX) 2020.

“The additional safety and efficacy data presented, including improvements in multiple biomarkers of liver health such as a significant reduction in cytokeratin-18 among the patients who also experienced at least a 10% reduction in liver fat, continue to strengthen the promising profile of DUR-928 for NASH,” stated Eric Lawitz, M.D., Texas Liver Institute, University of Texas Health San Antonio and principal investigator of the study. “Together with previously reported overall global reduction from baseline of liver enzymes, liver fat, stiffness as measured by imaging and serum lipids, this additional biomarker data suggests that epigenetic modulation by DUR-928 is worthy of further study in NASH patients.”

James E. Brown, D.V.M., President and CEO of DURECT, added, “The safety and efficacy profiles demonstrated with DUR-928 not only in this NASH trial but in our Phase 2a trial in alcoholic hepatitis, demonstrate potential of this epigenetic regulator to treat multiple acute organ injury and chronic liver diseases. We look forward to continuing the evaluation of DUR-928 in our clinical studies and potentially bringing a life-saving treatment option to patients in need.”

Data presented at The Liver Meeting further demonstrated that DUR-928 was well tolerated at all three doses (50mg, 150mg, and 600mg) with no serious adverse events reported.

Improvements in Biomarkers Data Summary (Day 28 vs Baseline)

% change from baseline at the end of dosing (median at day 28)

Biomarker	Daily Dose (mg)		
	50	150	600
Cytokeratin 18 M30	-14.6	-8.6	-16.1
Cytokeratin 18 M65	-18.1	-9.9	-35.0
C Reactive Protein	-13.9	-11.8	1.7
Plasminogen Activator Inhibitor-1	-13.5	-13.7	-8.2
Interleukin 1 Beta	-0.1	-0.6	-0.2
Interleukin 6	-6.0	1.7	5.4
Interleukin 12	0.0	0.0	0.0
Interleukin 17	-1.3	-16.4	-0.8
Interleukin 18	-8.9	-5.0	-2.1
Tumor Necrosis Factor	-3.2	-2.9	-7.9
Bile Acid	0.0	0.0	1.6
Adiponectin	-1.6	-3.8	3.9
Adiponectin, HMW	0.0	1.0	1.0

Biomarker Data Along With Previously Reported Improvements in Liver Enzymes, Imaging and Serum Levels (Day 28 vs Baseline)

** Indicates p-value <0.05; ** indicates p < 0.01; *** indicates p <0.001*

Median at Day 28		All Subjects			Patients with ? 10% Reduction in MRI-PDFF		
		50 mg QD *(n=21-23)*	150 mg QD *(n=20-21)*	300 mg BID *(n=20-21)*	50 mg QD *(n=9)*	150 mg QD *(n=8)*	300 mg BID *(n=9)*
Liver Enzymes	**ALT**	-16%*	-10%	-17%***	-21%**	-19%*	-32%***
	AST	-14%	-9%	-18%**	-24%**	-21%	-39%***
	GGT	-6%	-1%	-8%*	-13%***	-16%*	-14%
Imaging	**MRI-PDFF**	-7%	-7%	-4%	-18%***	-19%***	-23%***
	FibroScan	-10%**	-9%	-1%	-7%	-9%**	-9%
Serum Lipids	**LDL-C**	-6%	-11%*	-7%	-7%	-11%	-8%*
	Non-HDL-C	-8%	-5%	-1%	-10%	-8%*	-12%*
	Triglycerides	-13%*	-3%	-2%	-9%	0%	-8%
Biomarkers	**CK-18, M30**	-14.6%	-8.6%	-16.1%	-22.8%***	-3.8%	-42.1%*
	CK-18, M65	-18.1%	-9.9%	-35.0%	-28.1%***	-8.7%	-55.8%*

ALT *(alanine aminotransferase);* ***AST*** *(aspartate aminotransferase);* ***GGT*** *(gamma-glutamyl transferase);* ***MRI-PDFF*** *(Magnetic Resonance Imaging – Proton Density Fat Fraction) is a non-invasive measure of the proportion of liver tissue which is composed of fat;* ***FibroScan*** *is a specialized ultrasound machine that measures the stiffness of liver tissue.* ***LDL-C*** *(Low-Density Lipoprotein – Cholesterol);* ***Non-HDL-C*** *(Total cholesterol excluding High-Density Lipoprotein-Cholesterol);* ***QD*** *(once a day);* ***BID*** *(twice a day);* ***CK-18*** *(cytokeritin 18)*

Additionally, in subjects with baseline triglyceride (TG) levels ?200mg/dL (n=16), there was a 24% reduction at the end of the 4-week dosing period (p<0.01).

About DUR-928 Phase 1b Trial

The study was a randomized, open label, multi center US study to evaluate safety, pharmacokinetics and signals of biological activity of DUR-928 in NASH patients with stage 1-3 fibrosis. A total of 65 patients completed the study. DUR-928 was orally administered daily at 50 mg (n=23), 150 mg (n=21), or 600 mg (300 mg BID (n=21)). Patients in this trial were dosed daily for 4 weeks and followed up for an additional 4 weeks.

About DUR-928

DURECT's lead drug candidate, DUR-928, is an endogenous sulfated oxysterol and an epigenetic regulator. It represents a new class of therapeutics with a unique mechanism of action. DUR-928 epigenetically modulates the expression of multiple clusters of master genes that are involved in many important cell signaling pathways, through which it stabilizes mitochondria, reduces lipotoxicity, regulates inflammatory or stress responses, and promotes cell survival.

About NASH

Nonalcoholic steatohepatitis (NASH) is the most severe and progressive form of nonalcoholic fatty liver disease (NAFLD) and the most common chronic liver disease worldwide, with an estimated prevalence of more than 10% of adults inthe United States, Europe, Japan, and other developed countries, expected to double by 2030. No drug is currently approved for treatment of NAFLD or NASH.

About DURECT Corporation

DURECT is a biopharmaceutical company committed to transforming the treatment of acute organ injury and chronic liver diseases by advancing novel and potentially lifesaving therapies based on its endogenous epigenetic regulator program. DUR-928, the company's lead drug candidate is in clinical development for the potential treatment of alcoholic hepatitis (AH), COVID-19 patients with acute liver or kidney injury, and nonalcoholic steatohepatitis (NASH). DURECT's proprietary drug 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® (bupivacaine sustained-release solution), an investigational locally-acting, non-opioid analgesic intended to provide up to three days of continuous pain relief after surgery. For more information aboutDURECT, please visit www.www.durect.com and follow us on Twitter https://twitter.com/DURECTCorp.

DURECT Forward-Looking Statement

The statements in this press release regarding clinical development plans for DUR-928, including the potential use of DUR-928 to treat COVID-19 patients with liver or kidney injury, the potential use of DUR-928 to treat acute organ injuries, such as AH, and chronic liver diseases, such as NASH, the life saving potential of DUR-928, and the potential use of POSIMIR to provide pain relief after surgery 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 the clinical trial of DUR-928 in COVID-19 patients is delayed or stopped because of changes to the standard of care, the availability of alternative therapies, protocol changes or lack of available patients, the risk that future clinical trials of DUR-928 are not started when anticipated, take longer to conduct than anticipated, do not confirm the results from earlier clinical or pre-clinical trials, or do not demonstrate the safety or efficacy or the life saving potential of DUR-928 in a statistically significant manner, the risk that the FDA will not approve POSIMIR or approve POSIMIR with a limited label, the risk that additional time and resources may be required for development, testing and regulatory approval of DUR-928 or the Company's other product candidates, potential adverse effects arising from the testing or use of our drug candidates, our potential failure to maintain our collaborative agreements with third parties 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 3, 2020 under the heading "Risk Factors."

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

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