DURECT Corporation Doses First ex-U.S. Patient in Phase 2b AHFIRM Study of Larsucosterol (DUR-928) in Severe Alcohol-Associated Hepatitis

CUPERTINO, Calif., Nov. 10, 2021 /PRNewswire/ — DURECT Corporation (Nasdaq: DRRX) today announced it dosed the first ex-U.S. patient in Australia as part of its AHFIRM randomized, double-blind, placebo-controlled, multi-center Phase 2b study to evaluate the safety and efficacy of larsucosterol in severe alcohol-associated hepatitis (AH) patients.

“AH is a global condition and we are excited to have started dosing severe AH patients in the AHFIRM trial outside ofthe United States. We recently opened the first ex-U.S. clinical trial sites in Australia and are pleased that the first Australian subject has now been dosed,” stated James E. Brown, D.V.M., President and CEO of DURECT. “We continue working to open 60 or more clinical trial sites across the U.S., Australia, EU, and U.K.”

About the AHFIRM Trial
Enrollment is ongoing in our Phase 2b randomized, double-blind, placebo-controlled, international, multi-center study in subjects with severe acute alcohol-associated hepatitis (**AH**) to evaluate sa**F**ety and eff**I**cacy of larsucosterol (DU**R**-928) treat**M**ent (AHFIRM). The study is comprised of three arms targeting enrollment of 300 total patients, with approximately 100 patients in each arm: (1) Placebo plus standard of care (SOC) which may include the use of methylprednisolone, a corticosteroid, at the discretion of the treating physician); (2) larsucosterol (30 mg); and (3) larsucosterol (90 mg). All patients in the trial receive supportive care. The primary outcome measure is 90-day survival rate for patients treated with larsucosterol compared to those treated with placebo plus SOC. The Company is targeting more than 60 clinical trial sites across the U.S., EU, U.K., and Australia. Reflecting the life-threatening nature of AH and the lack of therapeutic options, the U.S. Food and Drug Administration (FDA) has granted larsucosterol Fast Track Designation for the treatment of AH. We believe demonstration of a robust survival benefit in the AHFIRM trial would support an NDA filing. For more information, refer to ClinicalTrials.gov Identifier: NCT04563026.

About alcohol-associated hepatitis (AH)
AH is a life-threatening acute alcohol-associated liver disease (ALD) often caused by chronic heavy alcohol and a recent period of increased alcohol consumption (e.g., a binge). It is characterized by severe inflammation and destruction of liver tissue (i.e., necrosis), potentially leading to life-threatening complications, including liver failure, acute renal injury and multi-organ failure. There are no FDA approved therapies for AH and the overall average mortality of AH patients in clinical trials has been reported to be 26% at 28 days, 29% at 90 days and 44% at 180 days. Stopping alcohol consumption is not sufficient for recovery in many moderate and severe patients and the use of treatments to reduce liver inflammation, such as corticosteroids, are limited by contraindications and have been shown to provide no survival benefit at 90 days or 1 year. While liver transplantation is becoming more common for alcoholic liver disease patients, including for AH patients, the procedure involves a long waiting period, a burdensome selection process and costs more than $875,000 on average.

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. Larsucosterol (also known as DUR-928), the Company’s lead drug candidate, binds to and inhibits the activity of DNA methyltransferases (DNMTs), epigenetic enzymes which are elevated and associated with hypermethylation found in AH patients. Larsucosterol is in clinical development for the potential treatment of alcohol-associated hepatitis (AH) for which FDA has granted a Fast Track Designation; non-alcoholic steatohepatitis (NASH) is also being explored. In addition, POSIMIR® (bupivacaine solution) for infiltration use, a non-opioid analgesic utilizing the innovative SABER® platform technology, is FDA-approved. Full prescribing information about POSIMIR, including the Boxed Warning, can be found at www.posimir.com. For more information about DURECT, 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 the potential for larsucosterol (also known as DUR-928) to treat patients with AH, NASH, multiple acute organ injury, chronic liver diseases and other diseases, ongoing clinical trials of larsucosterol and plans to

open 60 or more clinical trial sites, the potential benefits of Fast Track Designation, and the commercial potential of 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 the clinical trial of larsucosterol in AH takes longer to conduct than anticipated due to COVID-19 or other factors, the risk that clinical trials of larsucosterol, including AHFIRM, do not confirm the results from earlier clinical or pre-clinical trials, or do not demonstrate the safety or efficacy or the lifesaving potential of larsucosterol in a statistically significant manner, the risk that Fast Track Designation for larsucosterol in AH may not lead to faster FDA review or an approval, risks that we or a third-party licensee may not commercialize POSIMIR successfully, if at all, 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, 2021 under the heading "Risk Factors."

NOTE: POSIMIR® and SABER® are trademarks of DURECT Corporation. Other referenced trademarks belong to their respective owners. Larsucosterol (DUR-928) is an investigational drug candidate under development and has not been approved for commercialization by the U.S. Food and Drug Administration or other health authorities for any indication. Full prescribing information for POSIMIR, including its Boxed Warning, can be found at www.posimir.com.

View original content:https://www.prnewswire.com/news-releases/durect-corporation-doses-first-ex-us-patient-in-phase-2b-ahfirm-study-of-larsucosterol-dur-928-in-severe-alcohol-associated-hepatitis-301421128.html

SOURCE DURECT Corporation

Corporate Contact – Mike Arenberg, DURECT, Chief Financial Officer, +1-408-346-1052, mike.arenberg@durect.com; Media Contact – Mónica Rouco Molina, PhD, LifeSci Communications, +1-929-469-3850, mroucomolina@lifescicomms.com