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

CUPERTINO, Calif., March 1, 2022 /PRNewswire/ — DURECT Corporation (Nasdaq: DRRX) today announced it dosed the first patient in the European Union 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.

“Dosing the first patient in Europe is an important milestone as we continue to make progress in the AHFIRM trial,” stated James E. Brown, D.V.M., President and CEO of DURECT. “AH is a life-threatening disease in many regions of the world and, accordingly, we now have clinical trial sites open across the U.S., Australia, U.K. and the E.U.”

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 la**R**sucosterol (DUR-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 use and a recent period of increased alcohol consumption (i.e., 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 an analysis of 77 studies published between 1971 and 2016, which included data from a total of 8,184 patients, showed the overall mortality from AH was 26% at 28 days, 29% at 90 days and 44% at 180 days. A subsequent global study published in December 2021, which included 85 tertiary centers in 11 countries across 3 continents, prospectively enrolled 2,581 AH patients with a median MELD score of 23.5, reported mortality at 28 and 90 days of 20% and 30.9% respectively. 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), DURECT’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 alcohol-associated hepatitis (AH) patients. Larsucosterol is in clinical development for the potential treatment of 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 and has been exclusively licensed to Innocoll Pharmaceuticals for development and commercialization in the United States. For more information about DURECT, please

visit www.www.durect.com and follow us on Twitter https://twitter.com/DURECTCorp.

DURECT Forward-Looking Statement. This press release contains forward-looking statements relating to, among other things, DURECT's relationship with Innocoll, statements about 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 the potential benefits of Fast Track Designation. Any statements contained in this press release that are not statements of historical fact may be deemed to be forward-looking statements. Words such as "planned," "will," "may," "expect," "anticipate," and similar expressions are intended to identify these forward-looking statements. These forward-looking statements are based onDURECT's current expectations and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward looking statements as a result of these risks and uncertainties, which include, without limitation, risks and uncertainties that Innocoll may not launch or commercialize POSIMIR successfully, if at all, the risk 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 related toDURECT's ability to obtain capital to fund operations and expenses, risks related to market competition, and other risks described in the "Risk Factors" section of DURECT's Quarterly Report on Form 10-Q for the period ended September 30, 2021 filed with the Securities and Exchange Commission (the "SEC") on November 3, 2021, and in other filings filed from time to time with the SEC. DURECT does not undertake any obligation to update forward-looking statements and expressly disclaims any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein, except as required by law.

NOTE: POSIMIR® is a trademark of Innocoll Pharmaceuticals, Ltd. in the U.S. and a trademark of DURECT Corporation outside of the U.S. SABER® is a trademark 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.

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