DURECT Corporation Announces Initiation of Patient Recruitment in Phase 2 Safety and Efficacy Study of DUR-928 in COVID-19 Patients with Acute Liver or Kidney Injury

– U.S. Food and Drug Administration (FDA) has authorized the investigational new drug (IND) application

– Acute liver and kidney injury are risk factors for poor outcomes in COVID-19 patients

– The risk of death from multi-organ failure is present in both patients with severe COVID-19 and those with severe Alcoholic Hepatitis (AH)

– Promising Phase 2a clinical results in patients with AH and pre-clinical evidence in multi-organ injury models suggest DUR-928 may be beneficial in COVID-19 patients with acute liver or kidney injury

CUPERTINO, Calif., July 1, 2020 /PRNewswire/ — DURECT Corporation (Nasdaq: DRRX) today announced it has initiated recruiting patients for its randomized, double-blind, placebo-controlled, multi-center Phase 2 study to evaluate the safety and efficacy of DUR-928 in hospitalized COVID-19 infected patients with acute liver or kidney injury. The primary efficacy endpoint is a composite of survival and being free of acute organ failure at Day 28. The trial will enroll approximately 80 patients.

“Unfortunately, acute liver or kidney injury is associated with a significantly increased risk of death in hospitalized COVID-19 patients. Multi-organ failure is the cause of death in many critically ill COVID-19 patients just as it is in severe AH, a life-threatening disease with a 28-day mortality rate of 26%. Based on the positive clinical results of DUR-928 in AH patients from our Phase 2a trial, and our preclinical data in multi-organ failure models, we believe that DUR-928, in combination with standard of care, has the potential to help COVID-19 patients with acute liver or kidney injury,” stated James E. Brown, D.V.M., President and CEO of DURECT. “There is a great need to explore life-saving treatment options for these high risk patients.”

About the Phase 2 Trial

This Phase 2, randomized, double-blind, placebo-controlled, multi-center study is designed to evaluate safety and efficacy of DUR-928 in COVID-19 patients with acute liver or kidney injury. The primary efficacy endpoint is a composite of being alive and free of acute organ failure (free of mechanical ventilation, free of liver failure events and free of renal replacement therapy) at day 28.

A total of approximately 80 patients will be enrolled into two study treatment groups in a 3:1 (DUR-928:placebo) ratio. Patients will receive a dose of 150 mg of DUR-928 or placebo by intravenous infusion on day 1 and day 4 in combination with standard of care therapy, which will be determined by the principal investigator (PI) at each clinical trial site.

Patients will be followed for 60 days. Should any drug product be determined by the FDA to be safe and effective for the treatment of COVID-19 during the trial, such treatments may be offered, at each PI’s discretion, to any remaining and future patients in this trial.

About COVID-19
Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus (SARS-COV-2) infection. The rapid spread of the disease has resulted in a pandemic with millions of confirmed cases and causing hundreds of thousands of deaths worldwide. While most cases result in mild symptoms, including fever, cough and shortness of

breath, some rapidly progress into Acute Respiratory Distress Syndrome (ARDS), multi-organ failure, and death. Many of these patients experience a rapid elevation of inflammation-inducing signaling molecules (cytokine storm) that trigger acute injuries in multiple organs including the liver and the kidney. Organ injury may also occur in hospitalized COVID-19 patients as the result of other complications of the viral infection. In a study of 1,059 adult cases of confirmed COVID-19, 62% of patients presented with at least one elevated liver enzyme. In another study, 36.6% of 5,449 patients admitted with COVID-19 had or developed AKI.

About DUR-928

DUR–928 is a first-in-class, small molecule, new chemical entity and an endogenous epigenetic regulator. It is in Phase 1 and Phase 2 development for three indications and is the lead candidate in DURECT's Epigenetic Regulator Program. DUR-928 has been shown in preclinical studies to play an important regulatory role in lipid metabolism, inflammation, and cell survival. Human applications may include acute organ injury such as alcoholic hepatitis (AH) and acute liver or kidney injury in COVID-19 patients, and chronic metabolic diseases such as nonalcoholic steatohepatitis (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.DURECT's lead candidate, DUR-928, has demonstrated the ability to regulate the expression of genes involved in lipid metabolism, inflammatory responses and cell survival. This drug candidate is currently in Phase 2 development for the treatment of alcoholic hepatitis (AH) and the treatment of COVID-19 patients with acute liver or kidney injury as well as Phase 1 development for the treatment of 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 extended-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 about DURECT, please visit www.www.durect.com.

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, 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, required 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 replicate the results from earlier clinical or pre-clinical trials, or do not demonstrate the safety or efficacy of DUR-928 in a statistically significant manner, the risk that the FDA will not approve POSIMIR, 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 May 11, 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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SOURCE DURECT Corporation

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