



# DURECT Corporation Announces Last Patient Last Visit in Phase 2b AHFIRM Trial of Larsucosterol in Alcohol-Associated Hepatitis

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Company on track to report topline data from AHFIRM in Q4 2023

CUPERTINO, Calif., Sept. 7, 2023 /PRNewswire/ — DURECT Corporation (Nasdaq: [DRRX](#)), a late-stage biopharmaceutical company pioneering the development of epigenetic therapies to transform the treatment of serious and life-threatening conditions, including acute organ injury and cancer, today announced that the last patient has completed the study protocol in the Company's AHFIRM trial. AHFIRM is a Phase 2b randomized, double-blind, placebo-controlled trial evaluating the safety and efficacy of lasucosterol in subjects with severe alcohol-associated hepatitis (AH). A total of 301 patients were randomized and dosed in AHFIRM and DURECT plans to report topline data in the fourth quarter of 2023.

"We are pleased to have completed follow-up of all patients in our Phase 2b AHFIRM trial, bringing us one step closer to reporting topline data from the study which we anticipate in the fourth quarter of 2023," stated James E. Brown, D.V.M., President and CEO of DURECT. "Assuming a positive outcome from AHFIRM, we plan to review the results with the U.S. Food and Drug Administration (FDA) in the first quarter of 2024. We designed AHFIRM to be a potentially pivotal trial and hope to expedite regulatory discussions through the Fast Track Designation that the FDA previously granted. If approved, lasucosterol would be the first FDA-approved treatment for alcohol-associated hepatitis (AH) and would represent a paradigm shift in the management of this life-threatening disease."

## About the AHFIRM Trial

Enrollment was completed in June 2023 in our Phase 2b randomized, double-blind, placebo-controlled, international, multi-center study in subjects with severe acute alcohol-associated hepatitis (AH) to evaluate saFety and efflcacy of laRsucosterol treatMent (AHFIRM). The study is comprised of three arms, and 301 total patients were randomized and dosed, with approximately 100 patients in each arm: (1) Placebo plus supportive care, with or without methylprednisolone capsules at the investigators' discretion; (2) lasucosterol (30 mg); and (3) lasucosterol (90 mg). Patients in the lasucosterol arms receive the same supportive care without steroids. In order to maintain blinding, patients in the two active arms receive matching placebo capsules if the investigator prescribes steroids. The primary outcome measure will be the 90-Day incidence of mortality or liver transplantation for patients treated with lasucosterol compared to those treated with placebo. The Company has enrolled patients at 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 lasucosterol Fast Track Designation for the treatment of AH. We believe a positive outcome in the AHFIRM trial could support a New Drug Application filing. For more information, refer to ClinicalTrials.gov Identifier: NCT04563026.

## About Alcohol-associated Hepatitis (AH)

AH is an acute form of alcohol-associated liver disease (ALD), associated with long-term heavy intake of alcohol and often occurs after a recent period of increased alcohol consumption (i.e., a binge). AH is typically characterized by severe inflammation and destruction of liver tissue (i.e., necrosis), potentially leading to life-threatening complications including liver failure, acute kidney injury and multi-organ failure. There are no FDA approved therapies for AH and a retrospective 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 Model of End-Stage Liver Disease (MELD) score of 23.5, reported mortality at 28 and 90 days of approximately 20% and 31%, respectively. Stopping alcohol consumption is necessary, but frequently not sufficient for recovery in many moderate (defined as MELD scores of 11-20) and severe (defined as MELD scores >20) patients and therapies that reduce liver inflammation, such as corticosteroids, are limited by contraindications, have not been shown to improve survival at 90 days or one year, and have demonstrated an increased risk of infection. While liver transplantation is becoming more common for ALD patients, including AH patients, the total number of such



transplants is still relatively small. Average charges for a liver transplant exceed \$875,000, and patients require lifelong immunosuppressive therapy to prevent organ rejection.

#### **About Larsucosterol**

Larsucosterol is an endogenous sulfated oxysterol and an epigenetic modulator. Epigenetic regulators are compounds that regulate patterns of gene expression without modifying the DNA sequence. DNA hypermethylation, an example of epigenetic dysregulation, results in transcriptomic reprogramming and cellular dysfunction, and has been found to be associated with many acute (e.g., AH) or chronic diseases (e.g., NASH). As an inhibitor of DNA methyltransferases (DNMT1, DNMT3a and 3b), larsucosterol inhibits DNA methylation, which subsequently modulates expression of genes that are involved in cell signaling pathways associated with stress responses, cell death and survival, and lipid biosynthesis. This may ultimately lead to improved cell survival, reduced inflammation, and decreased lipotoxicity. As an epigenetic modulator, the proposed mechanism of action provides further scientific rationale for developing larsucosterol for the treatment of acute organ injury and certain chronic diseases.

#### **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, DURECT's lead drug candidate, binds to and inhibits the activity of DNA methyltransferases (DNMTs), epigenetic enzymes that 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 commercialization in the United States. For more information about DURECT, please visit [www.durect.com](http://www.durect.com) and follow us on Twitter <https://twitter.com/DURECTCorp>.

#### **DURECT Forward-Looking Statements**

This press release contains forward-looking statements, including statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, relating to: our plans to report topline data in the fourth quarter of 2023, our plans to meet with the FDA to review the results of AHFIRM trial in the first quarter of 2024, the potential FDA approval of larsucosterol for the treatment of AH, the ability of a positive outcome in the AHFIRM trial to support a New Drug Application filing, our plans to commercialize larsucosterol if approved, the commercialization of POSIMIR by Innocoll, the potential to develop larsucosterol for AH, NASH or other indications, and the potential benefits, if any, of our product candidates. Actual results may differ materially from those contained in the forward-looking statements contained in this press release, and reported results should not be considered as an indication of future performance. The potential risks and uncertainties that could cause actual results to differ from those projected include, among other things, the risks that the AHFIRM trial takes longer to complete than anticipated, the risk that ongoing and future clinical trials of larsucosterol do not confirm the results from earlier clinical or pre-clinical trials, or do not demonstrate the safety or efficacy of larsucosterol in a statistically significant manner, the risk that the FDA or other government agencies may require additional clinical trials for larsucosterol before approving it for the treatment of AH even if the results of the AHFIRM trial are successful, risks that Innocoll may not commercialize POSIMIR successfully, and risks related to the sufficiency of our cash resources, our anticipated capital requirements and capital expenditures, our need or desire for additional financing, our ability to obtain capital to fund our operations and expenses and our ability to continue to operate as a going concern. Further information regarding these and other risks is included in DURECT's most recent Securities and Exchange Commission (SEC) filings, including its annual report on Form 10-K for the year ended December 31, 2022 and quarterly report on Form 10-Q for the quarter ended June 30, 2023 under the heading "Risk Factors." These reports are available on our website [www.durect.com](http://www.durect.com) under the "Investors" tab and on the SEC's website at [www.sec.gov](http://www.sec.gov). All information provided in this press release and in the attachments is based on information available to DURECT as of the date hereof, and DURECT assumes no obligation to update this information as a result of future events or developments, 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 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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