



DURECT Reaches Enrollment Milestone in Phase 2b AHFIRM Trial

Oct 06, 2022, 08:30 ET

- **AHFIRM enrollment surpasses 200 of the planned 300 AH patients**
- **Enrollment completion now anticipated in Q2 2023**

CUPERTINO, Calif., Oct. 6, 2022 /PRNewswire/ — DURECT Corporation (Nasdaq: [DRRX](#)), a biopharmaceutical company focused on developing epigenetic regulator programs for the treatment of acute organ injury and chronic liver diseases, today announced the enrollment of more than 200 of the planned 300 patients in its Phase2b AHFIRM trial. The AHFIRM trial seeks to evaluate larsucoesterol's potential to serve as a treatment for severe alcohol-associated hepatitis (AH).

"We are very pleased to reach this enrollment milestone in our AHFIRM trial," said James E. Brown, D.V.M., President and CEO of DURECT. "We are proud that the DURECT team continues to drive this important clinical trial forward, and with their hard work and dedication we are now on track to complete enrollment in the second quarter of 2023. We look forward to reading out our topline results in the second half of 2023 and moving closer to attaining our goal of bringing larsucoesterol to AH patients as the first approved treatment for this deadly disease."

About the AHFIRM Trial

Enrollment is ongoing in our Phase 2b randomized, double-blind, placebo-controlled, international, multi-center study in subjects with severe alcohol-associated hepatitis (AH) to evaluate safety and efficacy of larsucoesterol (DUR-928) treatment (AHFIRM). The study is comprised of three arms targeting enrollment of 300 total patients, with approximately 100 patients in each arm: (1) Placebo plus supportive care, with or without methylprednisolone capsules at the investigators' discretion; (2) larsucoesterol (30 mg); and (3) larsucoesterol (90 mg). Patients in the larsucoesterol 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 larsucoesterol compared to those treated with placebo. The Company is enrolling patients at 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 larsucoesterol 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 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 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 20% and 31%, respectively. Stopping alcohol consumption is not sufficient for recovery in many moderate (defined as MELD scores of 11-20) and severe (defined as MELD scores >20) 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 ALD patients, including AH patients, the procedure often involves a long waiting period, a burdensome selection process, costs exceeding \$875,000 on average, and patients requiring lifelong immunosuppressive therapy to prevent organ rejection.



About Larsucosterol (DUR-928)

Larsucosterol is an endogenous sulfated oxysterol and an epigenetic regulator. 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 regulates 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 regulator, 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 (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.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: the clinical trial plans and timelines for larsucosterol, Fast Track designation of larsucosterol, the results and timing of clinical trials, the ability to enroll patients in clinical trials in a timely and cost-effective manner, the possible future enrollment rates and timing of announcements of the results from our clinical trials, the commercial launch of POSIMIR by Innocoll and potential future payments we may receive from Innocoll, the potential to develop larsucosterol for AH, NASH or other indications, the commercialization of POSIMIR by Innocoll, 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 risk that current enrollment rates may not persist, the risk that the AHFIRM trial's enrollment may be slower than we anticipate, the risk that Innocoll may not commercialize POSIMIR successfully, the risk that the AHFIRM trial takes longer to conduct than anticipated due to COVID-19 or other factors, 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, 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 most recent Securities and Exchange Commission (SEC) filings, including its annual report on Form 10-K for the year ended December 31, 2021 and quarterly report on Form 10-Q for the quarter ended June 30, 2022 under the heading "Risk Factors." These reports are available on our website www.durect.com under the "Investors" tab and on the SEC's website at 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 Limited 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.

SOURCE DURECT Corporation