DURECT Announces Positive Data from its Phase 2a Clinical Trial of DUR-928 in Alcoholic Hepatitis

CUPERTINO, Calif., Sept. 17, 2019 /PRNewswire/ — DURECT Corporation (Nasdaq: DRRX) today announced that it has completed the Phase 2a clinical trial of its lead product candidate, DUR-928, in patients with alcoholic hepatitis (AH). The final enrollment for the trial consists of 12 severe patients (MELD 21-30) and 7 moderate patients (MELD 11-20) for a total of 19 AH patients.

Clinical data from the trial show that the 19 patients treated with DUR-928 had statistically significantly greater reductions from baseline in bilirubin (day 7 and 28) and MELD (day 28), as well as statistically significantly lower Lille scores, compared with a historical control group (n=15) from a University of Louisville (UL) AH study.[1]

Lille scores are used in clinical practice to help determine the prognosis for AH patients after 7 days of treatment. The lower the Lille score, the better the prognosis is for the AH patient. Patients with a Lille score below 0.45 have an 85% 6-month survival rate vs. those with Lille scores of above 0.45, who have only a 25% 6-month survival rate (Louvet A et al. Hepatology 2007; 45: 1348-54). In our study, the median Lille score for the 18 AH patients treated with DUR-928 who returned for their Day 7 visit[2] was 0.10. Eighty nine percent (16/18) had a Lille score below 0.45. The median Lille score among the UL cohort of 15 patients treated with either supportive care or supportive care with corticosteroids was 0.41, with 53% (8/15) having a Lille score below 0.45.

DUR-928 was well tolerated in all patients, with no drug-related serious adverse events reported at any dose level. Drug exposures were dose proportional and were uninfluenced by the severity of the disease.

“We are excited that the first trial of DUR-928 in AH patients demonstrated superior outcomes compared to historical control data,” said James E. Brown, President and CEO of DURECT. “DUR-928 was well tolerated at all dose levels tested and we have gained valuable information to help support dose selection in the next study. We look forward to completing our analysis and reporting additional data at the upcoming AASLD Liver Meeting in Boston in November.”

“AH is a devastating acute condition with high mortality rates and limited therapeutic options,” continued Dr. Brown. “We are planning to meet with the FDA to discuss the design of the next DUR-928 AH clinical trial as well as the regulatory path to approval.”

About the DUR-928 Alcoholic Hepatitis Phase 2a Trial

Patients with moderate and severe AH were treated with intravenously administered DUR-928 in this open label, dose escalation multi-center U.S., Phase 2a clinical trial. Final enrollment was 19 patients comprised of: 8 patients (4 moderate and 4 severe) dosed at 30 mg, 7 patients (3 moderate and 4 severe) dosed at 90 mg and 4 patients (4 severe) dosed at 150 mg. Throughout the study, prior to initiating a higher dose, safety and PK results of the prior dose level were reviewed by a Dose Escalation Committee (DEC). The DEC also reviewed safety and PK data from the patients treated at the 150mg dose and reported that there were no drug-related serious adverse events throughout the study at any dose. The study objectives included assessment of safety, PK and pharmacodynamic (PD) signals, including liver chemistry and biomarkers.

About DURECT Corporation

DURECT is a biopharmaceutical company actively developing therapeutics based on its Epigenetic Regulator Program and proprietary drug delivery platforms. DUR?928, a new chemical entity in Phase 2 development, is the lead candidate in DURECT’s Epigenetic Regulator Program. An endogenous, orally bioavailable small molecule, DUR-928 has been shown in preclinical studies to play an important regulatory role in lipid homeostasis, inflammation, and cell survival. Human applications may include acute organ injury such as alcoholic Hepatitis (AH) and acute kidney injury (AKI), chronic hepatic diseases such as nonalcoholic steatohepatitis (NASH), and inflammatory skin conditions such as psoriasis and atopic dermatitis. DURECT’s advanced oral and injectable delivery technologies are designed to enable new indications and enhanced attributes for small-molecule and biologic

drugs. Key product candidates in this category include POSIMIR® (bupivacaine extended-release solution), an investigational locally-acting, non-opioid analgesic intended to provide up to 3 days of continuous pain relief after surgery, a long-acting injectable SABER-based HIV product being developed with Gilead, and ORADUR™-Methylphenidate ER Capsules, approved in Taiwan as Methydur Sustained Release Capsules, where it is indicated for the treatment of attention deficit hyperactivity disorder (ADHD). In addition, for the assignment of certain patent rights, DURECT receives single digit sales-based earn-out payments from U.S. net sales of Indivior's PERSERIS™ (risperidone) drug for schizophrenia, which was commercially launched in February 2019. For more information about DURECT, please visit www.www.durect.com.

NOTE: POSIMIR®, SABER® and ORADUR™ are trademarks of DURECT Corporation. Other referenced trademarks belong to their respective owners. DUR-928 and POSIMIR are drug candidates under development and have not been approved for commercialization by the U.S. Food and Drug Administration or other health authorities.

DURECT Forward-Looking Statement

The statements in this press release regarding plans, preliminary data and initial results from the Phase 2a trial of DUR-928 in patients with AH are forward looking statements, which are subject to risks and uncertainties. These risks and uncertainties include, but are not limited to, the risk that results from this clinical trial may not be replicated in future clinical trials, including in trials with larger numbers of patients. This press release also includes additional forward-looking statements, including regarding clinical trial plans for DUR-928, the potential use of DUR-928 to treat AH, AKI, chronic hepatic diseases such as NASH, and inflammatory skin disorders such as psoriasis and atopic dermatitis, as well as statements regarding the use of POSIMIR to treat post-surgical pain, the use of Methydur to treat ADHD, and potential earn-out payments from U.S. sales of PERSERIS. These forward-looking statements involve 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 risk of delays in the enrollment of the ongoing clinical trials of DUR-928 in NASH and psoriasis, potential adverse effects arising from the testing or use of DUR-928, the risk that theFDA may not approve the POSIMIR NDA, the risk that PERSERIS and Methydur will not be successfully commercialized, our ability to avoid infringing patents held by other parties and secure and defend patents of our own patents, and our ability to manage and obtain capital to fund our operations and expenses. Further information regarding these and other risks is included inDURECT's Form 10-Q filed with the Securities and Exchange Commission on August 2, 2019 under the heading "Risk Factors."

[1] Our advisor, Dr. Craig McClain from the University of Louisville (UL), shared anonymized data from his study, in which 15 AH patients with initial MELD scores ranging from 15-30 received either supportive care alone (n=8) or supportive care with corticosteroids (n=7).
[2] One patient did not return for the day 7 visit, so Lille scores could only be calculated for 18 of 19 patients.

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