
UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Form 8-K

Current Report
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

November 12, 2019

Date of Report
(Date of earliest event reported)

DURECT CORPORATION
(Exact name of Registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

000-31615
(Commission
File Number)

94-3297098
(I.R.S. Employer
Identification No.)

10260 Bubb Road
Cupertino, CA 95014
(Address of principal executive offices) (Zip code)

(408) 777-1417
(Registrant's telephone number, including area code)

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- ☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- ☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- ☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- ☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class
Common Stock \$0.0001 par value per share
Preferred Share Purchase Rights

Trading Symbol
DRRX

Name of Each Exchange
The NASDAQ Stoc
(The Nasdaq Cap

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01 Other Events

On November 12, 2019, DURECT Corporation (the "Company") announced the results of its Phase 2a clinical trial of DUR-928 (the "Trial") in alcoholic hepatitis (AH), presented as a late-breaking oral presentation at The Liver Meeting®. Additionally, the Trial results were selected for inclusion in the 'Best of The Liver Meeting' summary slide presentation in the alcohol-related liver disease category.

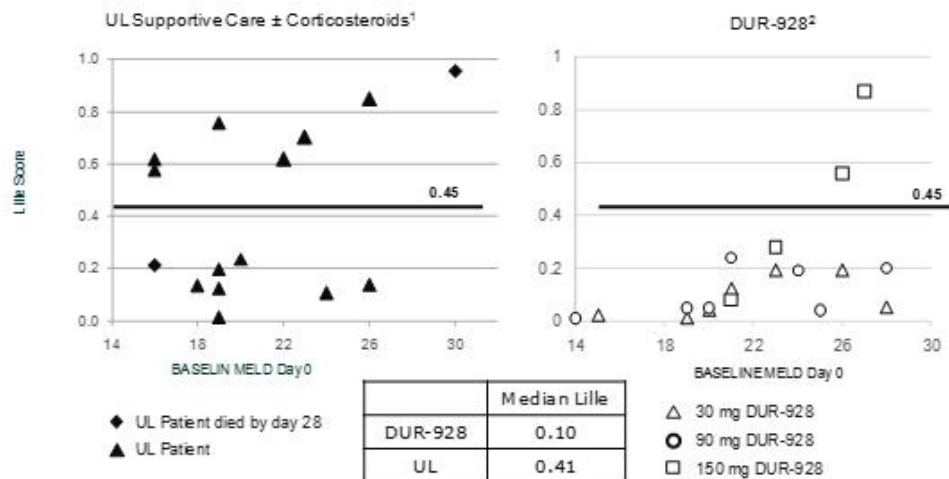
Results

All patients treated with DUR-928 in the Trial survived the 28-day follow-up period and there were no drug-related serious adverse events. Patients treated with DUR-928 had a statistically significant reduction from baseline in bilirubin at day 7 and 28, and MELD at day 28. Lille scores were also statistically significantly lower than those from a well-matched group of patients in a contemporary ongoing trial as well as several published historical controls. 74% of all DUR-928 treated patients and 67% of those with severe AH were discharged from the hospital within four days of receiving a single dose of DUR-928.

Lille

Lille scores are used in clinical practice to help determine the prognosis and response of AH patients after seven days of treatment. The lower the Lille score, the better the prognosis. Patients with a Lille score below 0.45 have a six-month survival rate of 85% compared to those with Lille scores above 0.45, with only a 25% six-month survival rate.¹ The chart below shows the Lille scores for individual AH patients treated with DUR-928 plotted as a function of their baseline MELD scores. In the Trial, the median Lille score for patients treated with DUR-928 was 0.10. The median Lille score among a cohort of 15 patients treated with standard of care at the University of Louisville (UL) was 0.41 (shown as historical control).

The chart below shows individual patient Lille scores plotted as a function of their baseline MELD scores.



- 1) The Company's 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 moderate AH patients) or supportive care with corticosteroids (n=7 severe AH patients). Two of the UL patients died by day 28.
- 2) One patient in the DUR-928 group did not return for the day 7 visit.

¹ Louvet A et al. Hepatology 2007; 45: 1348-54.

3) Lille scores in the DUR-928 patients were significantly lower than that of the UL patients ($p=0.01$; Wilcoxon's Rank Sum Test).

As shown below, 100% of patients in the 30mg and 90mg DUR-928 dosing groups were treatment responders based on their Lille scores. 89% of the overall DUR-928 patient population were treatment responders. Patients with severe AH, as defined by Maddrey's Discriminant Function >32 or MELD 21-30, and baseline serum bilirubin above 8 mg/dL, had similarly high response rates to DUR-928 treatment.

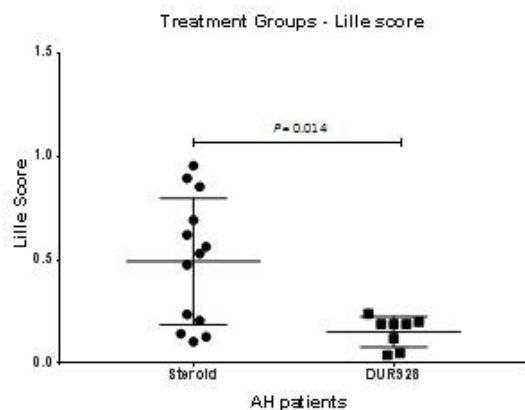
AH Patient Category	n¹	Responders (Lille<0.45)	Lille Median (Quartile)
All Patients ²	18	89%	0.10 (0.04, 0.20)
30 or 90mg DUR-928 ³	14	100%	0.05 (0.04, 0.19)
DF >32 (SAH) ²	15	87%	0.19 (0.05, 0.22)
30 or 90mg DUR-928 ³	11	100%	0.12 (0.05, 0.19)
MELD 21-30 ²	12	83%	0.19 (0.11, 0.25)
30 or 90mg DUR-928 ³	8	100%	0.19 (0.10, 0.19)
Baseline bilirubin >8 mg/dl ²	11	82%	0.10 (0.05, 0.20)
30 or 90mg DUR-928 ³	8	100%	0.10 (0.05, 0.19)

¹ One patient did not return for Day 7 visit; ² Including patients receiving 30, 90 and 150mg of DUR-928; ³ Excluding patients receiving 150mg of DUR-928.

Maddrey's Discriminant Function (DF) is calculated using the patient's prothrombin time and serum bilirubin level.

The Lille scores of patients treated with DUR-928 in the Trial were also significantly lower than several selected published historical studies (*Hepatology* 2007, 45:1348-1354; *Gut* 2011, 60:255-260), in which patients had similar baseline bilirubin, albumin, Creatinine, prothrombin time and DF scores, and were treated with standard of care with or without corticosteroids. Notwithstanding the foregoing, such comparisons should be taken cautiously due to the historical nature of the studies.

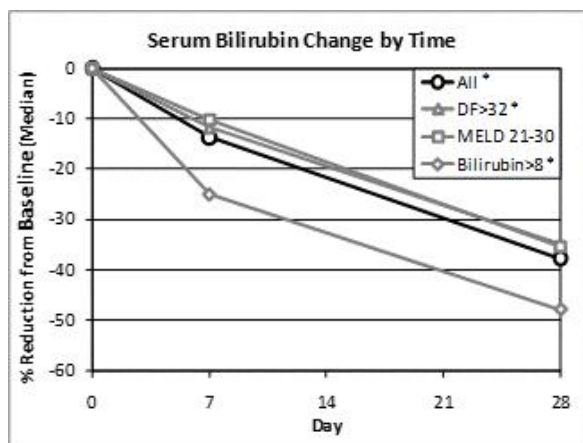
A sub-group analysis was conducted to compare severe AH patients in the 30mg and 90mg dosing groups (n=8) with well-matched severe AH patients (n=13) who received corticosteroids for 28 days in a contemporaneous study at the University of Louisville (UL). Patients shown below in the UL steroid group had a mean baseline MELD of 24.46 and mean baseline Maddrey's DF score of 62.98. The eight patients in the DUR-928 group had baseline mean MELD of 24.50 and mean baseline Maddrey's DF score of 61.25. All patients treated with DUR-928 survived the 28-day follow up period, while three patients in the UL steroid group died within the first 28 days.



The steroid group in the above graph includes the seven severe AH patients treated with steroids from the UL group shown in the MELD vs Lille graph above plus an additional 6 severe AH patients subsequently treated in the UL study.

Bilirubin

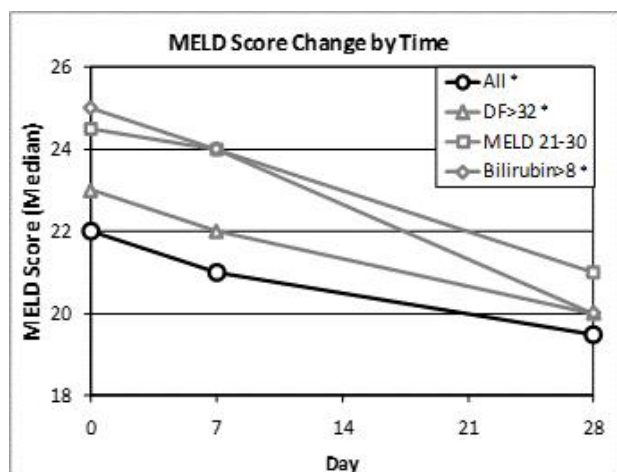
Bilirubin is formed by the breakdown of red blood cells in the body. The level of total bilirubin in the blood is an indication of how the liver is functioning. In the Trial, patients treated with DUR-928 had a significant early reduction from baseline in bilirubin by day 7. Patients with more elevated bilirubin at baseline (serum bilirubin >8 mg/dL) had a median reduction from baseline of 25% by day 7 and 48% by day 28.



* $p < 0.05$ compared to baseline (Wilcoxon's Signed Rank Test)

Model of End-Stage Liver Disease (MELD)

MELD is another common scoring system used to assess the severity and prognosis of AH patients. Patients with MELD scores of 11-20 are classified as having moderate AH and patients with MELD scores of 21-30 are classified as having severe AH. As with Lille scores, the lower the MELD score, the better the prognosis for the AH patient. In the Trial (shown in the chart below), the median reduction from baseline in MELD among all DUR-928 treated patients was over two points and among those with baseline bilirubin levels >8 mg/dL was five points by day 28.



* $p < 0.05$ compared to baseline (Wilcoxon's Signed Rank Test)

MELD is calculated based on (a) bilirubin, (b) serum creatinine (sCr), and (c) International Normalized Ratio (INR), which is a measure of prothrombin time.

Safety and Pharmacokinetics

DUR-928 was well tolerated at all doses tested. There were no drug-related serious adverse events and only three adverse events designated as possibly related to DUR-928: one occurrence of moderate generalized pruritus, one mild rash and one grade two alkaline phosphatase. There were no discontinuations, early withdrawals or termination of study drug or study participation due to adverse events. All patients treated with DUR-928 survived through the 28-day follow-up period. Drug exposures were dose proportional and were not affected by the severity of the disease.

About the DUR-928 Alcoholic Hepatitis Phase 2a Trial

The open-label, dose escalation, multi-center trial was designed to determine the safety, pharmacokinetics and pharmacodynamics of DUR-928 in AH patients following treatment. This included assessing liver biochemistry, biomarkers, and prognostic scores such as the Lille score. Final enrollment included 19 patients with moderate and severe AH, who were administered DUR-928 intravenously at three different doses. Eight patients (four moderate and four severe) were dosed at 30mg, seven patients (three moderate and four severe) were dosed at 90mg and four patients (all severe) were dosed at 150mg. After being discharged on day two, one patient did not return for the scheduled day 7 and day 28 follow-up visits; therefore Lille, bilirubin and model of end-stage liver disease (MELD) data reported above are based on 18 patients.

Next Steps

DURECT is planning to conduct a double-blind, placebo-controlled, Phase 2b clinical trial evaluating DUR-928 in AH patients beginning mid-2020. Assuming reasonable enrollment rates, top line data from the Trial would be available in 2022.

Cautionary Note Regarding Forward-looking Statements

To the extent that statements in this Current Report on Form 8-K are not strictly historical, including statements as to the potential benefits and uses of DUR-928 to treat AH, such statements are forward-looking, and are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. The forward-looking statements contained in this Current Report on Form 8-K are subject to certain risks and uncertainties that could cause actual results to differ materially from the statements

made. Such risks and others are further described in the Company's filings with the Securities and Exchange Commission including the most recent reports on Forms 10-K, 10-Q and 8-K, and any amendments thereto. Any forward-looking statement made by the Company in this Current Report on Form 8-K is based only on information currently available to it and speaks only as of the date on which it is made. The Company undertakes no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

DURECT Corporation

Date: November 12, 2019

By: /s/ Michael H. Arenberg

Michael H. Arenberg
Chief Financial Officer