DURECT Corporation Announces Second Quarter 2021 Financial Results and Update of Programs

Earnings Call and Webcast Today, July 29th at 4:30 p.m. ET

CUPERTINO, Calif., July 29, 2021 /PRNewswire/ — DURECT Corporation (Nasdaq: DRRX) today announced financial results for the three months ended June 30, 2021 and provided a corporate update.

Q2 2021 Accomplishments:

We expanded the number of U.S. clinical trial sites to 26 in the Phase 2b AHFIRM clinical study of DUR-928 in severe alcohol-associated hepatitis (AH), and we are enrolling at a good rate. We have now opened about 75% of the U.S. sites we plan to open. We expect to open our first ex-U.S. clinical sites (in the UK, Europe and Australia) in the coming months. In addition, we presented further encouraging DUR-928 clinical data from the completed NASH Phase 1b trial showing trends for reduction in insulin resistance and liver fibrosis biomarkers. Data from a Pharmacokinetic trial in patients with moderate and severe liver impairment showed a reduction in an important apoptosis biomarker with no adverse events or dose-limiting toxicity in these severely ill liver patients. We were also invited to present at the 2021 Epigenetic Therapeutic Targets Virtual Summit, which is for leading companies in the field of Epigenetics to present to their peers. To our knowledge, we were the only presenter utilizing an epigenetic regulator to restore function in injured cells as opposed to most who are using epigenetics to kill cancer cells. Our presentation was well received.

“Executing on the AHFIRM trial to the highest level of quality and in a timely fashion is our highest priority and we are pleased with the progress made this quarter,” stated James E. Brown, D.V.M, President and CEO of DURECT. “Discussions with potential POSIMIR partners are ongoing.”

Financial highlights for Q2 2021:

- Total revenues were $2.3 million and net loss was $9.1 million for the three months ended June 30, 2021 as compared to total revenues of $24.5 million and net income of $14.3 million for the three months ended June 30, 2020. Total revenues and net income for the three months ended June 30, 2020 included the recognition of $23.1 million in deferred revenue related to the termination of a license agreement during that period.
- At June 30, 2021, cash and investments were $88.6 million, compared to cash, cash held in escrow and investments of $56.9 million at December 31, 2020. Debt at June 30, 2021 was $20.4 million, compared to $20.8 million at December 31, 2020.

Update on Selected Programs:

Epigenetic Regulator Program. DUR-928, the lead product candidate in the Company’s Epigenetic Regulator Program, is an endogenous, orally bioavailable, first-in-class small molecule, which may have broad applicability in acute organ injuries such as alcohol-associated hepatitis (AH) as well as in chronic liver diseases such as non-alcoholic steatohepatitis (NASH).

Clinical Development

Alcohol-associated Hepatitis (AH)

- Enrollment is ongoing in our Phase 2b study in subjects with severe acute **AH** to evaluate sa**F**ety and eff**I**cacy of DU**R**-928 treat**M**ent **(AHFIRM)**. AHFIRM is a randomized, double-blind, placebo-controlled, international, multi-center Phase 2b study to evaluate the safety and efficacy of DUR-928 in approximately 300 patients with severe AH. The study is comprised of three arms targeting enrollment of approximately 100 patients each: (1) Placebo plus standard of care (SOC, which may

include the use of methylprednisolone, a corticosteroid, at the discretion of the treating physician); (2) DUR-928 (30 mg); and (3) DUR-928 (90 mg). All patients in the trial receive supportive care. The primary outcome measure is 90-day survival rate for patients treated with DUR-928 compared to those treated with placebo plus SOC. The Company is targeting approximately 50 to 60 clinical trial sites in the U.S., U.K., E.U. and Australia.

- Given the high mortality rate in severe AH patients and the absence of an approved therapeutic, we believe demonstration of a robust survival benefit in the AHFIRM trial would support an NDA filing.
- Reflecting the life-threatening nature of AH and the lack of therapeutic options for this devastating condition, the FDA granted DUR-928 Fast Track Designation for the treatment of AH in December 2020.
- In March 2021, a peer-reviewed research paper describing the binding sites and proposed mechanism of action of DUR-928 was published in The Journal of Lipid Research. The publication shows that DUR-928 (referred to in the paper as 25HC3S) binds to and inhibits the activity of DNA methyltransferases (DNMTs) *DNMT-1, 3a and 3b*, epigenetic regulating enzymes that add methyl groups to DNA (a process called DNA methylation). As such, by inhibiting DNMT activity, DUR-928 inhibits DNA methylation, thereby regulating the expression of genes that modulate crucial cellular activities, including those associated with cell death, stress response, and lipid biosynthesis. These modulations may lead to improved cell survival, and reduced lipid accumulation and inflammation, as has been observed in various *in vivo* animal models and in results from DURECT's completed clinical trials in alcohol-associated hepatitis (AH) and non-alcoholic steatohepatitis (NASH).
- In July 2021 we presented DUR-928's mechanism of action, the previously reported positive results from our Phase 2a clinical study in alcohol-associated hepatitis (AH), and an overview of the AHFIRM trial at the 2021 Epigenetic Therapeutic Targets Virtual Summit.
- In the Phase 2a clinical trial of DUR-928 in patients with AH, all 19 patients treated with DUR-928 survived the 28-day follow-up period, 74% of patients (14/19) were discharged in ? 4 days after receiving a single dose of DUR-928, and there were no drug-related serious adverse events.
- Alcohol-associated hepatitis (also called alcoholic hepatitis or AH) is an acute form of alcoholic liver disease (ALD) associated with long-term heavy intake of alcohol, and often occurs after a recent period of increased alcohol consumption. AH is typically characterized by a recent onset of jaundice and hepatic failure. According to the most recent data provided by the Agency for Healthcare Research and Quality (AHRQ), a part of the US Department of Health and Human Services (HHS), there were approximately 132,000 hospitalizations for patients with AH in 2018. From a 2018 publication analyzing the mortality and costs associated with AH, the cost per patient is estimated at over $50,000 in the first year. ALD is one of the leading causes of liver transplants in the U.S., costing over $875,000 per patient. An 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 and 29% at 90 days after admission.

Non-Alcoholic Steatohepatitis (NASH)

- In June 2021, we presented new data showing additional signals of potential efficacy from the NASH Phase 1b study of DUR-928 at the 2021 International Liver Conference (EASL) . This was a randomized and open-label clinical study conducted in the U.S. to evaluate safety, pharmacokinetics and signals of biological activity of DUR-928 in NASH patients with stage 1-3 fibrosis. Subjects in the 50 mg and 150 mg groups had 22% and 18% median reductions (not statistically significant) of homeostatic model assessment (HOMA-IR) from baseline, respectively, after 4 weeks of daily oral dosing of DUR-928. NASH subjects also had improvement from baseline in liver stiffness, assessed by transient elastography (TE), magnetic resonance elastography (MRE) and the liver fibrosis marker pro-C3. Positive topline results from this study were previously reported in May 2020.
- We have also conducted a Phase 1b open-label, multi-center U.S. study to evaluate the safety, tolerability, and pharmacokinetics (PK) of DUR-928 in subjects with moderate (Child-Pugh B scores, n=10) and severe (Child-Pugh C scores, n=7) hepatic function impairment (HI), and matched control subjects (MCS, n=10) with normal hepatic functions. Each subject received a single oral dose of 200 mg DUR-928. Results from this study were presented at the International Liver Conference 2021 (EASL) in June 2021. DUR-928 was safe and well-tolerated by all moderate and severe HI subjects with no adverse events and no dose-limiting toxicity reported throughout the study. As expected, clearance of DUR-928 was decreased in HI subjects compared to MCS with normal hepatic function, resulting in a 4-10 fold higher drug exposure (Cmax and AUC) in HI subjects. Additionally, a single oral dose of 200 mg of DUR-928 in subjects with HI resulted in statistically significant median reductions from baseline of the apoptosis biomarker M30 (cCK-18) at 12 hours post-dose.
- We are working with a number of disease experts to determine next steps for DUR-928 in NASH.

POSIMIR® (bupivacaine solution) Post-Operative Pain Relief Depot. POSIMIR is DURECT's post-operative pain relief depot that uses the Company's patented SABER® technology that delivers bupivacaine to provide up to 3 days of post-surgical analgesia.

- In February 2021, POSIMIR was granted U.S. FDA approval in adults for administration into the subacromial space under direct arthroscopic visualization to produce post-surgical analgesia for up to 72 hours following arthroscopic subacromial decompression.
- The approval was based on positive data from a randomized, multicenter, assessor-blinded, placebo–controlled clinical trial in patients undergoing arthroscopic subacromial decompression surgery with an intact rotator cuff. The primary outcome measures were mean pain intensity and total opioid rescue analgesia administered, both evaluated over the first 72 hours after surgery versus placebo. POSIMIR demonstrated a statistically significant improvement in both primary outcome measures: a 1.3 point, or 20%, reduction in mean pain intensity on a 0-10 point pain scale (p=0.01), and a 67% reduction in I.V. morphine-equivalent rescue opioid use, from a median of 12 mg in the placebo group to 4 mg in the POSIMIR group (p=0.01). In connection with this approval, the Company or its licensee, will be required to conduct two postmarketing non-clinical studies. Full Prescribing Information, including the Boxed Warning, is available at www.POSIMIR.com.
- DURECT is in discussions with potential commercial partners for POSIMIR, for which DURECT currently holds worldwide rights.

Debt Amendment. In May 2021, the Company amended its existing $20 million term loan with Oxford Finance such that principal payments will commence 18 months later than previously scheduled (i.e., commencing June 1, 2023 rather than December 1, 2021) and the final maturity date has been moved back by 16 months (i.e., from May 1, 2024 to September 1, 2025). The interest rate and final payment remain unchanged, and the Company paid Oxford Finance an amendment fee of $712,500.

Conference Call
We will host a conference call today at 4:30 p.m. Eastern Time / 1:30 p.m. Pacific Time to discuss second quarter 2021 results and provide a corporate update:

Thursday, July 29 @ 4:30pm Eastern Time / 1:30 p.m. Pacific Time

Toll Free:	877-407-0784
International:	201-689-8560
Conference ID:	13721980
Webcast:	**http://public.viavid.com/index.php?id=145979**

The conference call will also be available by webcast on DURECT's homepage at www.www.durect.com under the "Investors" tab. If you are unable to participate during the webcast, the call will be archived on DURECT's website under "Event Calendar" in the "Investors" section.

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. DUR-928, the company's lead drug candidate is in clinical development for the potential treatment of alcohol-associated hepatitis (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. Full prescribing information about POSIMIR, including the Boxed Warning, can be found at www.posimir.com. For more information about DURECT, please visit www.www.durect.com and follow us on Twitter https://twitter.com/DURECTCorp.

DURECT Forward-Looking Statement
The statements in this press release regarding the potential for DUR-928 to treat patients with AH and NASH, clinical trial plans, the potential benefits of Fast Track Designation, the potential for the AHFIRM trial to support an NDA filing for DUR-928 in AH, plans to develop DUR-928 in NASH, and plans to seek a commercial licensee for POSIMIR and its commercial launch, 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 AHFIRM trial takes longer to conduct than anticipated due to COVID-19 or other factors, the risk that ongoing and future clinical trials of DUR-928 do not confirm the results from earlier clinical or pre-clinical trials, or do not demonstrate the safety or efficacy or the life-saving potential of DUR-928 in a statistically significant manner, the risk that Fast Track designation for DUR-928 in AH may not actually lead to faster FDA review or an approval, risks that biomarker data in earlier trials of DUR-928 may not predict clinical efficacy, risks that we may not enter a

commercial license for POSIMIR on favorable terms, if at all, risks that we or a licensee may not commercialize POSIMIR successfully, if at all, and risks related to entering into new agreements or our ability to obtain capital to fund operations and expenses. Further information regarding these and other risks is included in DURECT's Form 10-K filed on May 5, 2021 and in our Form 10-Q for the quarter ended June 30, 2021 when filed with the Securities and Exchange Commission under the heading "Risk Factors."

NOTE: POSIMIR® and SABER® are trademarks of DURECT Corporation. Other referenced trademarks belong to their respective owners. 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. Full prescribing information for POSIMIR, including its Boxed Warning, can be found at www.posimir.com.

DURECT CORPORATION

CONDENSED STATEMENTS OF OPERATIONS AND COMPREHENSIVE (LOSS) INCOME
(in thousands, except per share amounts)
(unaudited)

	Three months ended June 30		Six months ended June 30	
	2021	2020	2021	2020
Collaborative research and development and other revenue	$ 735	$ 23,347	$ 1,309	$ 23,317
Product revenue, net	1,568	1,151	3,206	2,776
Total revenues	2,303	24,498	4,515	26,093
Operating expenses:				
Cost of product revenues	359	253	711	649
Research and development	7,433	6,567	15,408	14,154
Selling, general and administrative	3,168	3,337	6,699	6,768
Total operating expenses	10,960	10,157	22,818	21,571
(Loss) income from operations	(8,657)	14,341	(18,303)	4,522
Other income (expense):				
Interest and other income	39	135	76	393
Interest and other expense	(528)	(552)	(1,053)	(1,144)
Net other expense	(489)	(417)	(977)	(751)
(Loss) income from continuing operations	(9,146)	13,924	(19,280)	3,771
Income from discontinued operations	–	414	–	619
Net (loss) income	$ (9,146)	$ 14,338	$ (19,280)	$ 4,390
Net (loss) income per share				
Basic and Diluted				
(Loss) income from Continuing operations	$ (0.04)	$ 0.07	$ (0.09)	$ 0.02
Income from discontinued operations	$ –	$ 0.00	$ –	$ 0.00
Weighted-average shares used in computing net (loss) income per share				
Basic	227,428	196,866	222,510	196,306
Diluted	227,428	207,477	222,510	206,111
Total comprehensive (loss) income	$ (9,133)	$ 14,427	$ (19,276)	$ 4,464

DURECT CORPORATION

CONDENSED BALANCE SHEETS
(in thousands)

	As of June 30, 2021 (unaudited)	As of December 31, 2020[(1)]
ASSETS		
Current assets:		
Cash and cash equivalents	$ 56,073	$ 21,312
Cash held in escrow	–	14,979
Short-term investments	32,357	19,421
Accounts receivable	816	940
Inventories, net	1,918	1,864

Prepaid expenses and other current assets	4,192	4,545
Total current assets	95,356	63,061
Property and equipment, net	211	251
Operating lease right-of-use assets	4,120	4,749
Goodwill	6,169	6,169
Long-term investments	–	1,000
Long-term restricted Investments	150	150
Other long-term assets	261	261
Total assets	$ 106,267	$ 75,641
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 1,086	$ 1,678
Accrued liabilities	5,114	5,801
Contract research liability	192	545
Deferred revenue, current portion	5	–
Term loan, current portion, net	–	884
Operating lease liabilities, current portion	1,821	1,795
Total current liabilities	8,218	10,703
Deferred revenue, noncurrent portion	812	812
Operating lease liabilities, noncurrent portion	2,542	3,202
Term loan, noncurrent portion, net	20,360	19,936
Other long-term liabilities	873	873
Stockholders' equity	73,462	40,115
Total liabilities and stockholders' equity	$ 106,267	$ 75,641

(1) Derived from audited financial statements.

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