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

Webcast of Earnings Call Today, May 4th at 4:30 p.m. ET

CUPERTINO, Calif., May 4, 2021 /PRNewswire/ — DURECT Corporation (Nasdaq: DRRX) today announced financial results for the three months ended March 31, 2021 and provided a corporate update.

Q1 2021 Accomplishments:

- Initiated patient dosing in the Phase 2b AHFIRM clinical study of DUR-928 in severe Alcohol-associated Hepatitis (AH)
- FDA approval of POSIMIR in adults to produce post-surgical analgesia for up to 72 hours following Arthroscopic Subacromial Decompression
- Publication of DUR-928's mechanism of action
- Appointment of two highly experienced biopharmaceutical board members
- Further strengthened our financial position by raising $47.8 million in equity and ending Q1 with $97.2 million in cash and investments

"We are pleased with progress made in opening clinical trial sites in the U.S. and early enrollment in the AHFIRM trial, our Phase 2b clinical trial designed to evaluate the potential life-saving capability of DUR-928 in patients with severe Alcohol-associated Hepatitis," stated James E. Brown, D.V.M, President and CEO of DURECT. "We are also in discussions with multiple potential POSIMIR partners with a goal of enabling the partner to launch the product this year."

Financial highlights for Q1 2021:

- Total revenues were $2.2 million and net loss was $10.1 million for the three months ended March 31, 2021 as compared to total revenues of $1.6 million and net loss of $9.9 million for the three months ended March 31, 2020.
- At March 31, 2021, cash and investments were $97.2 million, compared to cash, cash held in escrow and investments of $56.9 million at December 31, 2020. Debt at March 31, 2021 was $21.0 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 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. Patients receive an intravenous (IV) dose of DUR-928 or placebo (sterile water) on day 1 and a second IV dose on day 4 if they are still hospitalized. The primary outcome measure is 90-day survival rate for patients treated with DUR-928 compared to those treated with placebo plus SOC. Secondary endpoints include 28-day survival, the rate of adverse events, Lille and MELD (prognostic scores) and time in the intensive care unit. The Company is targeting approximately 50-60 clinical trial sites in the U.S., U.K., Europe and Australia.
- 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. The FDA grants Fast Track Designation to facilitate development and expedite the review of therapies with the potential to treat a serious condition where there is an unmet medical need. A therapeutic that receives Fast Track Designation may benefit from early and frequent communication with the agency in addition to a rolling submission of the marketing application, with the objective of getting important new therapies to patients more quickly.

- 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 may support an NDA filing.
- 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).
- During 2019, we completed a 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 May 2020, we reported positive topline results from a Phase 1b randomized and open-label clinical study conducted in the U.S. to evaluate safety, pharmacokinetics and signals of biological activity (including clinical chemistry and biomarkers as well as liver fat content and liver stiffness by imaging) of DUR-928 in NASH patients with stage 1-3 fibrosis. In this 65-patient study, reductions from baseline (pre-treatment) levels were seen in liver enzymes, liver stiffness as measured by imaging, serum lipids and biomarkers. Many of these reductions were statistically significant and DUR-928 was well tolerated at all three doses evaluated.
- We will present additional data from this trial at an upcoming medical conference and we are working with a number of disease experts to determine next steps for DUR-928 in NASH.
- Non-alcoholic fatty liver disease (NAFLD) is the most common form of chronic liver disease in both children and adults. It is estimated that NAFLD affects approximately 30% to 40% of adults and 10% of children in the United States. NASH, a more severe and progressive form of NAFLD, is one of the most common chronic liver diseases worldwide, with an estimated prevalence of 3-5% globally. No drug is currently approved for NAFLD or 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. POSIMIR is the only approved sustained-release bupivacaine product indicated for up to 72 hours of post-surgical analgesia from a single application.
- 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 licensees of commercialization rights to POSIMIR, for which DURECT currently holds worldwide rights. Our goal is to put a commercial license in place in time for the licensee to launch the product in Q4 2021.
- Subacromial decompression is a type of shoulder surgery used to treat impingement syndrome, a common repetitive-use injury that causes pain when the arm is raised over the head. The procedure is typically performed arthroscopically, meaning that several small incisions are made in the skin and muscle of the shoulder through which a camera lens (arthroscope) and surgical instruments are inserted during surgery. Arthroscopic subacromial decompression is generally considered outpatient surgery, and most patients go home within a few hours of surgery. The recovery period may extend from weeks to months, but the most intense pain typically occurs during the first 3 days after surgery and is often managed with oral opioids. There are over 600,000 surgeries involving arthroscopic subacromial decompression performed each year in the U.S.

Conference Call

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

Tuesday, May 4 @ 4:30pm Eastern Time / 1:30 p.m. Pacific Time

Toll Free:	877-407-0784
International:	201-689-8560
Conference ID:	13718713
Webcast:	http://public.viavid.com/index.php?id=144373

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 now 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, 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 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 March 5, 2021 and in our Form 10-Q for the quarter ended March 31, 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 have 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 (in thousands, except per share amounts) (Unaudited)			
		Three months ended March 31	
		2021	2020
Collaborative research and development and other revenue		$ 574	$ (30)
Product revenue, net		1,638	1,625
	Total revenues	2,212	1,595
Operating expenses:			
	Cost of product revenues	352	396
	Research and development	7,975	7,587
	Selling, general and administrative	3,531	3,431
Total operating expenses		11,858	11,414
Loss from operations		(9,646)	(9,819)
Other income (expense):			
	Interest and other income	37	258
	Interest and other expense	(525)	(592)
Net other expense		(488)	(334)
Loss from continuing operations		(10,134)	(10,153)
Income from discontinued operations		–	205
Net loss		$(10,134)	$ (9,948)
Net income (loss) per share			
	Basic and diluted		
	Continuing operations	$ (0.05)	$ (0.05)
	Discontinued operations	$ –	$ 0.00
	Net loss per common share, basic and diluted	$ (0.05)	$ (0.05)
Weighted-average shares used in computing net income (loss) per share, basic and diluted		217,537	195,745
Total comprehensive loss		$(10,143)	$ (9,963)

DURECT CORPORATION CONDENSED BALANCE SHEETS (in thousands)		
	As of March 31, 2021 (unaudited)	As of December 31, 2020[1]
ASSETS		
Current assets:		
Cash and cash equivalents	$ 57,545	$ 21,312
Cash held in escrow	–	14,979
Short-term investments	39,538	19,421
Accounts receivable	993	940
Inventories, net	1,955	1,864
Prepaid expenses and other current assets	4,780	4,545
Total current assets	104,811	63,061
Property and equipment, net	224	251
Operating lease right-of-use assets	4,440	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	$ 116,055	$ 75,641
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 2,150	$ 1,678

Accrued liabilities	4,094		5,801
Contract research liability	384		545
Deferred revenue, current portion	373		–
Term loan, current portion, net	2,895		884
Operating lease liabilities, current portion	1,808		1,795
Total current liabilities	11,704		10,703
Deferred revenue, noncurrent portion	812		812
Operating lease liabilities, noncurrent portion	2,881		3,202
Term loan, noncurrent portion, net	18,062		19,936
Other long-term liabilities	873		873
Stockholders' equity	81,723		40,115
Total liabilities and stockholders' equity	$ 116,055		$ 75,641

(1) Derived from audited financial statements.

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