DURECT Corporation Announces First Quarter 2019 Financial Results and Update of Programs

Live Webcast of Alcoholic Hepatitis KOL and Earnings Call on Wednesday, May 8th at 8:30 a.m. ET

Call will feature discussions by KOLs Steven Flamm, M.D.. Tarek I. Hassanein, M.D., and Paul Kwo, M.D.

CUPERTINO, Calif., May 7, 2019 /PRNewswire/ — DURECT Corporation (Nasdaq: DRRX) today announced financial results for the three months ended March 31, 2019 and provided a corporate update, including preliminary data from the ongoing DUR-928 Phase 2a alcoholic hepatitis (AH) trial.

- Total revenues were $4.1million and net loss was $7.1million for the three months ended March 31, 2019 as compared to total revenues of $3.5 million and net loss of $8.3 million for the three months ended March 31, 2018.
- At March 31, 2019, cash and investments were $28.8 million, compared to cash and investments of $34.5 million at December 31, 2018. Debt at March 31, 2019, including partial accrual for the final payment of our term loan, was $20.7 million.

“Several important development milestones were achieved during the first quarter, including achieving impressive preliminary data in the ongoing AH trial and initiating dosing in the NASH and psoriasis clinical trials. We also made progress toward filing a response to the POSIMIR CRL and strengthened our board with the addition of two new members who bring valuable experience and perspective.” stated James E. Brown, D.V.M., President and CEO of DURECT. “Thanks to the progress made during the quarter, we have four potential major catalysts ahead of us this year: additional AH data, readouts from the NASH and psoriasis DUR-928 clincal trials, and a potential approval for POSIMIR if our filing strategy is successful.”

Update on Selected Programs and Transactions:

Epigenetic Regulator Program. DUR-928, the lead product candidate in the Company’s Epigenetic Regulator Program, is an endogenous, first-in-class small molecule, which may have broad applicability in chronic liver diseases such as NASH, in acute organ injuries such as AH and acute kidney injury (AKI), and in inflammatory skin disorders such as psoriasis and atopic dermatitis.

Clinical Trials

Alcoholic Hepatitis (AH)

- *Preliminary Data*
  - Ten patients have completed dosing with DUR-928 to date in the ongoing Phase 2a open label, dose-escalation, multi-center U.S. trial. Eight patients (4 moderate and 4 severe) have been treated with DUR-98 at the 30 mg dose, and two patients (1 moderate and 1 severe) at the 90 mg dose.
  - Lille scores are used in clinical practice to help determine the prognosis for AH patients after 7 days of treatment. 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 a 25% *6-month* survival rate (*Louvet A et al. Hepatology 2007; 45: 1348-54*). In another study looking at *28-day* survival rates in severe AH patients, a Lille score of ?0.16 is associated with a 91% *28-day* survival rate; a Lille score of 0.16-0.56, 79% *28-day* survival rate and a Lille score of ?0.56 is associated with a 53% *28-day* survival rate. (*Mathurin, et. al., Gut 2011;60:255-260).* The lower the Lille score, the better the prognosis is for the AH patient. Of the 10 AH patients dosed to date with DUR-928, one patient did not return for the day 7 visit, so Lille scores could only be calculated for 9 of 10 patients. In the 9 patients with Lille scores treated with DUR-928, the median Lille score is 0.04, with a range of 0.01 to 0.19.
  - Model of End-Stage Liver Disease (MELD) score is another common scoring system used to assess the severity and prognosis of AH patients. Patients with initial MELD scores of 11-19 are classified as having moderate AH and patients with initial MELD scores of 20-30 are classified as having severe AH. As with Lille scores, the lower the

MELD score, the better the prognosis for the AH patient. Compared to baseline (prior to treatment) (n=10), the median reduction in MELD was 4% at Day 7 (n=9) and 21% at Day 28 (n=8).
    - 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 well the liver is functioning. Compared to baseline (n=10), the median reduction in total bilirubin was 16% at Day 7 (n=9) and 41% at Day 28 (n=8).
    - A more detailed description of the preliminary data from the DUR-928 AH study is provided in a separate press release today and will be presented during the KOL and earnings call tomorrow at 8:30 a.m. ET.
- *About the trial*
    - DURECT is conducting a Phase 2a clinical trial with intravenously administered DUR-928 in patients with AH. This is an open label, dose escalation (30, 90 and 150 mg), multi-center U.S. study, that includes patients with moderate and severe AH (as determined by initial MELD score). Dose escalation may occur following review of safety and pharmacokinetic (PK) results of the prior dose level by a Dose Escalation Committee (DEC). The target number of patients for the study is 4 per dose group. The objectives of this study include assessment of safety, PK and pharmacodynamic (PD) signals, including liver chemistry, and biomarkers.
    - After completing the low-dose 30 mg cohort (n=4) in moderate AH patients, the DEC approved commencement of the 90 mg cohort in moderate AH patients while simultaneously commencing recruitment of severe AH patients with the 30 mg dose.
    - Enrollment of severe AH patients has been more rapid than that of moderate patients. Upon completion the 30 mg cohort (n=4) in severe AH patients, the DEC approved advancement to the 90 mg dosing in severe AH patients. We are now enrolling both moderate and severe AH patients for the 90 mg cohorts.
    - Additional information on the trial design, including eligibility criteria and site locations, can be found at www.clinicaltrials.gov using the NCT Identifier NCT03432260.
- In parallel with our ongoing trial, we are supporting Professor Craig McClain, MD (Chief of Research Affairs, Division of Gastroenterology, Hepatology and Nutrition, University of Louisville) in his efforts to initiate an NIH-funded study of DUR-928 in AH patients at the University of Louisville.
- AH is a syndrome of progressive inflammatory liver injury associated with long-term heavy intake of alcohol, and encompasses a spectrum that ranges from mild injury to severe, life threatening liver damage. The prevalence of AH is estimated to occur in 10-35% of heavy drinkers. According to an article in the *Journal of Clinical Gastroenterology (2015 July; 49(6):506-511)*, there were over 320,000 hospitalizations related to alcoholic hepatitis in the U.S. in 2010, resulting in hospitalization costs of nearly $50,000 per patient. The cost of a liver transplant exceeds $800,000.

Non-Alcoholic Steatohepatitis (NASH)

- In March 2019 we began enrolling patients in a Phase 1b randomized and open-label clinical study being 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. Three doses of DUR-928 (50 mg QD, 150 mg QD and 300 mg BID) will be administered orally for 28 consecutive days with approximately 20 patients per dose group for a total of approximately 60 patients in the trial.
- Key endpoints include safety and pharmacokinetics (PK), clinical chemistry and biomarkers (e.g., bilirubin, lipids, liver enzymes, CK-18s, and inflammatory cytokines) as well as liver imaging (e.g., MRI-PDFF).
- We expect to announce initial data from this study in the second half of 2019.
- In the Company's previous Phase 1b NASH study, reported at the European Association for the Study of the Liver (EASL) in April 2017, exploratory biomarker analysis demonstrated that a single oral dose of DUR-928 in NASH patients, at both dose levels tested (50 mg and 200 mg), resulted in statistically significant reductions from baseline of both full-length and cleaved cytokeratin-18 (CK-18), bilirubin, hsCRP and IL-18.
- 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 about 20% to 30% 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 more than 10% of adults in the United States, Europe, Japan and other developed countries. No drug is currently approved for NAFLD or NASH.

Psoriasis

- We are conducting a Phase 2a, randomized, double-blind, vehicle-controlled proof-of-concept clinical trial, in which DUR-928 is applied topically once-daily for four weeks in patients with mild to moderate plaque psoriasis. The trial is being conducted at multiple clinical sites in the U.S. Twenty patients are planned to be enrolled to obtain approximately 15 evaluable patients.

Patients serve as their own controls, applying DUR-928 to the plaque on one arm and the vehicle to a similar plaque on the other arm. After the treatment period, patients will be followed for an additional four weeks. The primary efficacy endpoint is the change in local psoriasis scores from baseline in the DUR-928-treated plaques compared to that in the vehicle-treated plaques. Additional information on the trial design, including eligibility criteria and site locations, can be found at www.clinicaltrials.gov using the NCT Identifier 03837743.

- We began enrolling patients in March of 2019 and expect to announce top line data from this study in the second half of 2019.
- We previously conducted an exploratory Phase 1b trial in psoriasis patients (9 evaluable patients) in Australia. The trial was randomized, double-blinded, placebo and self-controlled, using a micro-plaque assay with intralesional injections of DUR-928. The results were encouraging and warranted advancing into the current proof-of-concept trial with topically applied DUR-928. In support of the Phase 2a study, we have completed multiple non-clinical safety studies for topically applied DUR-928.
- Psoriasis is an inflammatory skin disease and an immune-mediated condition that causes the body to make new skin cells in days rather than weeks. In the United States, there are about 150,000 new cases of psoriasis every year and it affects an estimated 7.5 million Americans. According to the International Federation of Psoriasis Associations (IFPA), nearly 3% of the world's population has some form of psoriasis or about 125 million people. Psoriasis causes itchiness and irritation and may be painful. There's no cure for psoriasis yet, but currently approved treatment can ease symptoms. Approximately 80% of patients with psoriasis have localized disease, which can be treated with topical therapies. As such, topical agents remain the mainstay of psoriasis treatment.

POSIMIR® (bupivacaine extended-release solution) Post-Operative Pain Relief Depot POSIMIR is our investigational post-operative pain relief depot that utilizes our patented SABER® technology and is designed to deliver bupivacaine to provide up to 3 days of pain relief after surgery.

- After a comprehensive review of the POSIMIR program in light of the issues raised by the FDA in our communications with them, including the Complete Response Letter (CRL), we are planning to submit a full response to the CRL in the second quarter of 2019. As the submission will be a response to a CRL, we expect a 6-month FDA review period.
- The effort to evaluate the program, develop a strategy for filing the response, and the actual writing of key sections of the response, has been under the direction of Dr. Lee Simon, who was formerly FDA's Division Director of Analgesic, Anti-inflammatory and Ophthalmologic Drug Products.
- We believe that the completed inguinal hernia and subacromial decompression (shoulder) clinical trials support the efficacy of POSIMIR in post-operative pain and meet the requirements to be considered as adequate and well-controlled pivotal clinical trials. Both trials demonstrated a significant decrease in pain and opioid use over the 0-72 hour period following surgery as compared to placebo.
- We have completed 16 clinical trials in the POSIMIR program, involving over 1,400 patients, over 850 of whom received POSIMIR with the remainder in control groups. We believe this is a sufficiently sized safety database. We believe that, with the PERSIST safety data included, we now have sufficient data to address FDA's issues raised in the CRL and that the data package meets the requirements for FDA approval.
- POSIMIR has not been approved by the FDA for marketing in the U.S. for any indication and there can be no assurance that FDA will approve the planned submission described above.

Indivior Agreement and PERSERIS™. In September 2017, we entered into a patent purchase agreement with an affiliate of Indivior PLC, whereby we assigned certain of its U.S. patent rights to Indivior. This assignment may provide further intellectual property protection for PERSERIS (risperidone) extended-release injectable suspension for the treatment of schizophrenia in adults.

- Under the terms of the agreement, Indivior has paid us $12.5 million upfront and a $5 million milestone based on NDA approval of PERSERIS. We also receive quarterly earn-out payments based on a single digit percentage of U.S. net sales for certain products covered by the patent rights, including PERSERIS. The patent rights include granted patents extending into at least 2026.
- According to its recent press releases, Indivior has stated that:
    - The PERSERIS commercial launch took place in the last week of February 2019 with a field force of 50 representatives and that modest initial net revenue for Q1 2019 was consistent with their expectations.
    - As of February 14, 2019, payor access was at 38% and Indivior is targeting quality of access comparable with peers.
    - Indivior is targeting appropriate health care providers (HCPs) with high volume Long Acting Injectables (LAI) practices.

- Indivior plans to focus on key differentiating product specific attributes, including the first and only once-monthly risperidone LAI, supplemental oral risperidone or loading dose not recommended, initial peak plasma concentrations achieved in 4 to 6 hours, and just one subcutaneous injection monthly.
- Indivior remained confident in its peak year net revenue goal for PERSERIS of $200 to $300 million.

- U.S. sales of long acting injectables to treat schizophrenia were in excess of $3 billion in 2017.
- Full prescribing information for PERSERIS, including BOXED WARNING, and Medication Guide can be found at www.perseris.com.

Methydur Sustained Release Capsules (ORADUR®-methylphenidate ER Capsules). In September 2018, our licensee, Orient Pharma, informed DURECT that it had obtained marketing authorization from the Ministry of Health and Welfare in Taiwan for Methydur Sustained Release Capsules. This product is indicated for the treatment of attention deficit hyperactivity disorder (ADHD) and Orient Pharma has stated that it expects to make Methydur Sustained Release Capsules commercially available in Taiwan in 2019, while seeking a partner in China and pursuing regulatory approvals in selected other countries where it has commercialization rights and a commercial presence. DURECT retains rights to North America, Europe, Japan and all other countries not specifically licensed to Orient Pharma. DURECT is entitled to receive a royalty on sales of Methydur Sustained Release Capsules by Orient Pharma. Orient Pharma has also committed to supply a portion of the commercial requirements in territories other than the United States for Methydur Sustained Release Capsules.

Earnings Conference Call

A live audio webcast of a conference call to discuss first quarter 2019 results and provide a corporate update will be broadcast live over the internet at 8:30 a.m. Eastern Time on May 8, 2019 and is available by accessing DURECT's homepage at www.www.durect.com and clicking "Investors." A replay of the call will be archived on DURECT's website under Audio Archive in the "Investors" section.

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), 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. Late stage 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, 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, please visit www.www.durect.com.

NOTE: ORADUR®, POSIMIR® and SABER® 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 clinical development plans for DUR-928, including the ongoing Phase 2a trial in AH and its preliminary results, the Phase 2a trial in psoriasis and the Phase 1b trial in patients with NASH, and the anticipated disclosure of data from clinical trials, potential future payments from Indivior and Orient Pharma, potential regulatory approval of POSIMIR, and the potential benefits and uses of our drug candidates, including the potential use of DUR-928 to treat acute organ injury such as AH and AKI, hepatic diseases such as NASH, and inflammatory skin conditions such as psoriasis and atopic dermatitis, 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 future clinical trials of DUR-928 take longer to conduct than anticipated, do not replicate the results from earlier clinical or pre-clinical trials, or do not demonstrate the safety or efficacy of DUR-928 in a statistically significant or clinically meaningful manner, the risk that the FDA will not approve POSIMIR, the risk that Indivior's PERSERIS will not obtain marketplace acceptance, the risk that Orient Pharma will not launch sales of Methydur Sustained Release Capsules as planned, the risk that additional time and resources that may be

required for development, testing and regulatory approval of DUR-928 or POSIMIR, potential adverse effects arising from the testing or use of our drug candidates, our potential failure to maintain our collaborative agreements with third parties or consummate new collaborations 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 Form 10-Q filed with the Securities and Exchange Commission on May 7, 2019 under the heading "Risk Factors."

DURECT CORPORATION
CONDENSED STATEMENTS OF COMPREHENSIVE LOSS
(in thousands, except per share amounts)
(unaudited)

	Three months ended March 31	
	2019	2018
Collaborative research and development and other revenue	$ 1,500	$ 1,096
Product revenue, net	2,631	2,392
Total revenues	4,131	3,488
Operating expenses:		
Cost of product revenues	1,136	1,174
Research and development	6,251	6,952
Selling, general and administrative	3,454	3,194
Total operating expenses	10,841	11,320
Loss from operations	(6,710)	(7,832)
Other income (expense):		
Interest and other income	209	158
Interest and other expense	(629)	(623)
Net other expense	(420)	(465)
Net loss	$ (7,130)	$ (8,297)
Net loss per share		
Basic	$ (0.04)	$ (0.05)
Diluted	$ (0.04)	$ (0.05)
Weighted-average shares used in computing net loss per share		
Basic	162,091	153,558
Diluted	162,091	153,558
Total comprehensive loss	$ (7,134)	$ (8,297)

DURECT CORPORATION
CONDENSED BALANCE SHEETS
(in thousands)

	As of March 31, 2019 (unaudited)	As of December 31, 2018(1)
ASSETS		
Current assets:		
Cash and cash equivalents	$ 27,641	$ 31,644
Short-term investments	989	2,671
Accounts receivable	2,221	1,757
Inventories, net	3,410	3,421
Prepaid expenses and other current assets	2,213	2,247
Total current assets	36,474	41,740
Property and equipment, net	589	605
Operating lease right-of-use assets	7,028	–
Goodwill	6,399	6,399
Long-term restricted Investments	150	150
Other long-term assets	1,105	1,105
Total assets	$ 51,745	$ 49,999
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 1,933	$ 1,589

Accrued liabilities	4,322	4,668
Contract research liability	1,489	1,405
Operating lease liabilities, current portion	1,999	–
Total current liabilities	9,743	7,662
Deferred revenue, noncurrent portion	812	812
Term loan, noncurrent portion, net	20,670	20,533
Operating lease liabilities, noncurrent portion	5,440	–
Other long-term liabilities	722	992
Stockholders' equity	14,358	20,000
Total liabilities and stockholders' equity	$ 51,745	$ 49,999

(1) Derived from audited financial statements.

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SOURCE DURECT Corporation

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