DURECT Corporation Announces Fourth Quarter and Full Year 2018 Financial Results and Update of Programs

Advancing To Next Dosing Cohort in Severe Alcoholic Hepatitis (AH) Patients

Live Webcast of Earnings Call Today at 4:30 p.m. Eastern Time

CUPERTINO, Calif., March 7, 2019 /PRNewswire/ — DURECT Corporation (Nasdaq: DRRX) today announced financial results for the three months and year ended December 31, 2018 and provided a corporate update.

- Total revenues were $3.6 million and net loss was $7.3 million for the three months ended December 31, 2018 as compared to total revenues of $19.5 million and net profit of $8.2 million for the three months ended December 31, 2017. Revenues for the three months ended December 31, 2017 included the recognition of $15.4 million in deferred revenue from the $20 million upfront fee associated with our terminated agreement with Sandoz AG.
- Total revenues were $18.6 million and net loss was $25.3 million for the year ended December 31, 2018, compared to total revenues of $49.2 million and net loss of $3.7 million for the year ended December 31, 2017. Revenues for the year ended December 31, 2018 included a $5 million milestone payment from Indivior related to the NDA approval of PERSERIS™ (risperidone); revenues for the year ended December 31, 2017 included a $20 million upfront fee from Sandoz AG and a $12.5 million upfront payment from Indivior.
- At December 31, 2018, cash and investments were $34.5 million, compared to cash and investments of $36.9 million at December 31, 2017. Debt at December 31, 2018, including partial accrual for the final payment of our term loan, was $20.5 million.

“Based on encouraging data from both of the completed moderate and severe alcoholic hepatitis (AH) 30 mg cohorts, the relatively rapid enrollment of severe AH patients, and strong encouragement from several of our key expert advisors and clinical trial investigators, we have decided to continue our AH trial by conducting the next cohort of severe AH patients at the 90 mg dose. In parallel, we are continuing to recruit patients in the moderate AH 90 mg cohort and work with Dr. McClain at the University of Louisville on enabling initiation of his NIH-funded DUR-928 AH trial. We also look forward to generating and reporting data this year from the NASH and psoriasis trials in which patients will receive daily doses of DUR-928 for 28 days,” stated James E. Brown, D.V.M., President and CEO of DURECT. “In addition, we will be requesting approval of POSIMIR when we submit to the FDA a full response to the Complete Response Letter. If successful, this could lead to FDA approval this year. Also, Indivior announced that the commercial launch of PERSERIS in the U.S. took place in February 2019. We receive quarterly earn-out payments on U.S. net sales of PERSERIS.”

Potential milestones in 2019:

- Reporting initial data from a DUR-928 multi-dose trial in NASH patients
- Reporting top-line data from a DUR-928 Phase 2a proof-of-concept trial in mild to moderate plaque psoriasis patients
- Completing the 90 mg cohort in severe AH patients
- Submission to and acceptance by the FDA of a full response to the CRL for POSIMIR and potential NDA approval following an expected six-month review period
- Commercial launch of PERSERIS by Indivior in the U.S.
- Commercial launch of Methydur by Orient Pharma in Taiwan
- New license and collaboration agreements

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 several hepatic and renal 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

Non-Alcoholic Steatohepatitis (NASH)

- This will be an open-label, Phase 1b study conducted in the U.S. to evaluate safety, pharmacokinetics and signals of biological activity of DUR-928 in patients with NASH. Three doses of oral DUR-928 (low, middle and high) will be administered daily for 28 consecutive days. We plan to enroll approximately 20 patients per dose group for a total of approximately 60 patients in the trial. We expect to begin enrolling patients during the first quarter of 2019 and 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.

Alcoholic Hepatitis (AH)

- DURECT is conducting a Phase 2a clinical trial with intravenously administered DUR-928 in patients with alcoholic hepatitis (AH). This is an open label, dose escalation, multi-center U.S. study, originally designed to be conducted in two sequential parts. Part A includes patients with moderate AH (as determined by the Model of End-Stage Liver Disease (MELD) scores, a common scoring system to assess the severity and prognosis of AH patients), and Part B includes patients with severe AH. Three dose levels (30, 90 and 150 mg) were planned for testing in Part A. 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 biochemistry and biomarkers.
- After completing dosing for the low-dose 30 mg cohort (n=4) of Part A (moderate AH patients), the DEC approved commencement of the 90 mg cohort in Part A while simultaneously commencing recruitment for Part B (severe AH patients) with the 30 mg dose.
- We have now completed dosing of the 30 mg cohort (n=4) of Part B, the enrollment of which was much more rapid than Part A. After reviewing the safety and PK data, the DEC has approved commencement of the 90 mg cohort in Part B. Based on the encouraging data from both the moderate and severe 30 mg cohorts, the relatively rapid enrollment of severe AH patients, and strong encouragement from several of our key expert advisors and clinical trial investigators, we have decided to continue our trial by conducting the next cohort of severe AH patients at the 90 mg dose.
- In parallel with our recruitment of patient for both of the 90 mg cohorts in our trial, we are supporting Dr. Craig McClain's efforts to initiate his NIH-funded study 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 2010, resulting in hospitalization costs of nearly $50,000 per patient.

Psoriasis

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

in local psoriasis scores from baseline in the DUR-928-treated plaques compared to that in the vehicle-treated plaques. We expect to begin enrolling patients during the first quarter of 2019 and announce top line data from this study in the second half of 2019. Additional information on the trial design, including eligibility criteria and site locations, can be found at www.clinicaltrials.gov using the NCT Identifier 03837743.

- The Company 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, the Company has 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 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 the Company's investigational post-operative pain relief depot that utilizes the Company's 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 first half 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, the Company entered into a patent purchase agreement with an affiliate of Indivior PLC, whereby the Company 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 the Company $12.5 million upfront and a $5 million milestone based on NDA approval of PERSERIS. The Company also receives 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.
- Through press releases on December 18, 2018, and February 14 and 27, 2019, Indivior has stated that:
    - PERSERIS was made available in the U.S. in late November 2018.
    - The PERSERIS commercial launch took place in February 2019 with a field force of 50 representatives.
    - 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.

Debt Amendment. In November 2018, the Company amended its existing $20 million term loan with Oxford Finance such that principal payments now commence 18 months later than previously scheduled (i.e., commencing June 1, 2020 rather than December 1, 2018) and the final maturity date is moved back by 30 months (i.e., from August 1, 2020 to November 1, 2022). The interest rate and final payment remain unchanged, and the Company paid Oxford Finance an amendment fee of $900,000.

Earnings Conference Call
A live audio webcast of a conference call to discuss fourth quarter 2018 and year ended December 31, 2018 results and provide a corporate update will be broadcast live over the internet at 4:30 p.m. Eastern Time on March 7 and is available by accessing DURECT's homepage at www.www.durect.com and clicking "Investor Relations." A replay of the call will be archived on DURECT's website under Audio Archive in the "Investor Relations" 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 approved in July 2018. 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 continuation of the Phase 2a trial in AH, plans for a Phase 2a trial in psoriasis and a 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 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, 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 are not started when anticipated, 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 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 on November 8, 2018 under the heading "Risk Factors."

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

	Three months ended December 31		Twelve months ended December 31	
	2018	2017	2018	2017
Collaborative research and development and other revenue	$ 775	$16,273	$ 8,207	$23,577
Product revenue, net	2,852	3,265	10,357	13,093
Revenue from sale of intellectual property rights	–	–	–	12,500
Total revenues	3,627	19,538	18,564	49,170
Operating expenses:				
Cost of product revenues	1,093	1,061	4,263	6,633
Research and development	5,887	6,604	25,501	31,609
Selling, general and administrative	3,539	3,303	12,419	13,165
Total operating expenses	10,519	10,968	42,183	51,407
Income (loss) from operations	(6,892)	8,570	(23,619)	(2,237)
Other income (expense):				
Interest and other income	238	287	870	967
Interest and other expense	(645)	(622)	(2,573)	(2,425)
Net other expense	(407)	(335)	(1,703)	(1,458)
Net income (loss)	$ (7,299)	$ 8,235	$(25,322)	$ (3,695)
Net income (loss) per share				
Basic	$ (0.05)	$ 0.06	$ (0.16)	$ (0.03)
Diluted	$ (0.05)	$ 0.05	$ (0.16)	$ (0.03)
Weighted-average shares used in computing net income (loss) per share				
Basic	162,040	149,428	159,834	145,273
Diluted	162,040	150,759	159,834	145,273
Total comprehensive income (loss)	$ (7,299)	$ 8,234	$(25,321)	$ (3,693)

DURECT CORPORATION
CONDENSED BALANCE SHEETS
(in thousands)

	As of December 31, 2018 (unaudited)	As of December 31, 2017[1]
ASSETS		
Current assets:		
Cash and cash equivalents	$ 31,644	$ 29,375
Short-term investments	2,671	7,384
Accounts receivable	1,757	2,376
Inventories, net	3,421	3,163
Prepaid expenses and other current assets	2,247	3,060
Total current assets	41,740	45,358
Property and equipment, net	605	929
Goodwill	6,399	6,399
Long-term restricted Investments	150	150

Other long-term assets	1,105			277	
Total assets	$	49,999		$	53,113
LIABILITIES AND STOCKHOLDERS' EQUITY					
Current liabilities:					
Accounts payable	$	1,589		$	1,520
Accrued liabilities	4,668			5,511	
Contract research liability	1,405			834	
Deferred revenue, current portion	–			682	
Term loan, current portion, net	–			7,281	
Total current liabilities	7,662			15,828	
Deferred revenue, noncurrent portion	812			1,093	
Term loan, noncurrent portion, net	20,533			13,578	
Other long-term liabilities	992			1,126	
Stockholders' equity	20,000			21,488	
Total liabilities and stockholders' equity	$	49,999		$	53,113

(1) Derived from audited financial statements.

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