DURECT Corporation Reports Fourth Quarter and Full Year 2021 Financial Results and Update of Programs

– Webcast of Earnings Call Today, March 7th at 4:30 p.m. ET

– Dosed first patient in Europe in the AHFIRM trial

– Signed a licensing agreement for POSIMIR® for up to $136M

CUPERTINO, Calif., March 7, 2022 /PRNewswire/ — DURECT Corporation (Nasdaq: DRRX) today announced financial results for the three months and year ended December 31, 2021 and provided a corporate update.

“We are pleased with the progress made over the past few months in the larsucosterol (DUR-928) AHFIRM trial, including opening international sites and the enrollment rate of patients with severe alcohol-associated hepatitis (AH),” stated James E. Brown, D.V.M., President and CEO of DURECT. “We also signed a U.S. licensing agreement for POSIMIR® with Innocoll Pharmaceuticals and look forward to their anticipated launch in the second quarter of 2022.”

Fourth Quarter and Recent Business Highlights:

- **Continued progress in AHFIRM enrollment** – DURECT has now dosed over 100 patients in the Phase 2b AHFIRM clinical trial of larsucosterol in severe AH. This includes dosing the first patient in Europe, with 51 global AHFIRM study sites now open, an increase of 15 since our last earnings call. With this progress, our estimated completion of enrollment remains on track for mid-2023.
- **Successful completion of POSIMIR licensing** – DURECT signed an exclusive U.S. licensing agreement for POSIMIR® with Innocoll Pharmaceuticals in late 2021. Under the agreement, DURECT will earn low to mid double-digit royalties from net sales of POSIMIR and is eligible to receive up to $136 million in upfronts and milestones, including the $4 million upfront license fee received in January 2022, and a $2 million milestone payment upon the first commercial sale of POSIMIR, which is anticipated in 2Q22.
- **Increasing awareness of AH market potential** – In collaboration with DURECT, Dr. Suthat Liangpunsakul presented a poster at The Liver Meeting® 2021 showing increased hospitalizations for AH in the U.S., highlighting both significant comorbidities and high hospitalization costs of over $150,000 per hospitalization for those AH patients who died during their hospital stay.
- **Important addition to our team** – In December 2021, DURECT strengthened its board of directors with the appointment of Pete Garcia, a seasoned financial executive in the biopharmaceutical industry.

Financial highlights for Q4 and full year 2021:

- Total revenues were $7.3 million and net loss from continuing operations was $7.0 million for the three months ended December 31, 2021 compared to total revenues of $2.2 million and net loss from continuing operations of $8.8 million for the three months ended December 31, 2020. Total revenues were $14.0 million and net loss from continuing operations was $36.3 million for the year ended December 31, 2021, compared to total revenues of $30.1 million and net loss fromcontinuing operations of $14.3 million for the year ended December 31, 2020.
- At December 31, 2021, cash and investments were $70.0 million, compared to cash, cash held in escrow and investments of $56.9 million at December 31, 2020. Debt at December 31, 2021 was $20.6 million, compared to $20.8 million at December 31, 2020. At December 31, 2021, accounts receivable included $5.3 million due from Innocoll as a result of the $4 million upfront fee and a $1.3 million fee primarily to cover manufacturing supplies and excipients and certain equipment transferred to Innocoll; these funds were received in January 2022.

Upcoming Key Milestones:

- Complete opening of 60 or more global clinical trial sites across the U.S., E.U., U.K., and Australia and continue acceleration of enrollment in the Phase 2b AHFIRM trial of larsucosterol in severe AH
- Provide an update on plans to expand clinical development of larsucosterol in NASH and/or other indications
- Commercial launch of POSIMIR by our licensee, Innocoll Pharmaceuticals; expected in Q2 2022

Earnings Conference Call

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

Monday, March 7 @ 4:30pm Eastern Time / 1:30 p.m. Pacific Time

Toll Free:	877-869-3847
International:	201-689-8261
Conference ID:	13727525
Webcast:	https://themediaframe.com/mediaframe/webcast.html?webcastid=qrEvoVo0

A live audio webcast of the presentation will be also available by accessing DURECT's homepage at www.www.durect.com and clicking "Investors." If you are unable to participate during the live webcast, the call will be archived on DURECT's website under "Event Calendar" in the "Investors" section.

About the AHFIRM Trial

Enrollment is ongoing in our Phase 2b randomized, double-blind, placebo-controlled, international, multi-center study in subjects with severe acute alcohol-associated hepatitis (**AH**) to evaluate sa**F**ety and eff**I**cacy of la**R**sucosterol (DUR-928) treat**M**ent (AHFIRM). The study is comprised of three arms targeting enrollment of 300 total patients, with approximately 100 patients in each arm: (1) Placebo plus standard of care (SOC) which may include the use of methylprednisolone, a corticosteroid, at the discretion of the treating physician; (2) larsucosterol (30 mg); and (3) larsucosterol (90 mg). All patients in the trial receive supportive care. The primary outcome measure is 90-day survival rate for patients treated with larsucosterol compared to those treated with placebo plus SOC. The Company is targeting more than 60 clinical trial sites across the U.S., EU, U.K., and Australia. Reflecting the life-threatening nature of AH and the lack of therapeutic options, the U.S. Food and Drug Administration (FDA) has granted larsucosterol Fast Track Designation for the treatment of AH. We believe demonstration of a robust survival benefit in the AHFIRM trial would support an NDA filing. For more information, refer to ClinicalTrials.gov Identifier: NCT04563026.

About Alcohol-associated Hepatitis (AH)

AH is a life-threatening acute alcohol-associated liver disease (ALD) often caused by chronic heavy alcohol use and a recent period of increased alcohol consumption (i.e., a binge). It is characterized by severe inflammation and destruction of liver tissue (i.e., necrosis), potentially leading to life-threatening complications including liver failure, acute renal injury and multi-organ failure. There are no FDA approved therapies for AH and 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, 29% at 90 days and 44% at 180 days. A subsequent global study published in December 2021, which included 85 tertiary centers in 11 countries across 3 continents, prospectively enrolled 2,581 AH patients with a median MELD score of 23.5, reported mortality at 28 and 90 days of 20% and 31% respectively. Stopping alcohol consumption is not sufficient for recovery in many moderate and severe patients and the use of treatments to reduce liver inflammation, such as corticosteroids, are limited by contraindications and have been shown to provide no

survival benefit at 90 days or 1 year. While liver transplantation is becoming more common for alcoholic liver disease patients, including for AH patients, the procedure involves a long waiting period, a burdensome selection process, and costs more than $875,000 on average.

About Larsucosterol (DUR-928)

Larsucosterol is an endogenous sulfated oxysterol and an epigenetic regulator. Epigenetic regulators are compounds that regulate patterns of gene expression without modifying the DNA sequence. DNA hypermethylation, an example of epigenetic dysregulation, results in transcriptomic reprogramming and cellular dysfunction, and has been found to be associated with many acute (e.g., AH) or chronic diseases (e.g., NASH). As an inhibitor of DNA methyltransferases (DNMT1, DNMT3a and 3b), larsucosterol inhibits DNA methylation, which subsequently regulates expression of genes that are involved in cell signaling pathways associated with stress responses, cell death and survival, and lipid biosynthesis. This may ultimately lead to improved cell survival, reduced inflammation, and decreased lipotoxicity. As an epigenetic regulator, the proposed mechanism of action provides further scientific rationale for developing larsucosterol for the treatment of acute organ injury and certain chronic diseases.

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. Larsucosterol (also known as DUR-928), DURECT's lead drug candidate, binds to and inhibits the activity of DNA methyltransferases (DNMTs), epigenetic enzymes which are elevated and associated with hypermethylation found in alcohol-associated hepatitis (AH) patients. Larsucosterol is in clinical development for the potential treatment of 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 and has been exclusively licensed to Innocoll Pharmaceuticals for development and commercialization in the United States. 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 plans to complete enrollment of the AHFIRM trial in mid-2023, plans to increase the number of clinical trial sites in the AHFIRM trial, the expected commercial launch of POSIMIR by Innocoll and potential future payments we may receive from Innocoll, and the potential to develop larsucosterol for NASH or other indications 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 larsucosterol 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 larsucosterol in a statistically significant manner, risks that Innocoll may not commercialize POSIMIR successfully, if at all, 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 3, 2021 and in our annual report on Form 10-K for the year ended December 31, 2021 when filed with the Securities and Exchange Commission under the heading "Risk Factors." These reports are available on our website www.www.durect.com under the "Investors" tab.

NOTE: POSIMIR® is a trademark of Innocoll Pharmaceuticals, Ltd. in the U.S. and a trademark of DURECT Corporation outside of the U.S. SABER® is a trademark of DURECT Corporation. Other referenced trademarks belong to their respective owners. Larsucosterol (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.

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

	Three months ended December 31, 2021		Twelve months ended December 31, 2021	
	2021	2020	2021	2020[1]
Collaborative research and development and other revenue	$ 4,579	$ 317	$ 6,331	$ 23,941
Product revenue, net	2,718	1,890	7,646	6,170

Total revenues	7,297	2,207	13,977	30,111
Operating expenses:				
Cost of product revenues	880	418	1,955	1,406
Research and development	8,415	6,682	31,846	27,709
Selling, general and administrative	4,514	3,413	14,449	13,611
Total operating expenses	13,809	10,513	48,250	42,726
Loss from operations	(6,512)	(8,306)	(34,273)	(12,615)
Other income (expense):				
Interest and other income	46	40	156	517
Interest and other expense	(542)	(547)	(2,148)	(2,237)
Net other expense	(496)	(507)	(1,992)	(1,720)
Loss from continuing operations	(7,008)	(8,813)	(36,265)	(14,335)
Income from discontinued operations	–	13,173	–	13,753
Net (loss) income	$ (7,008)	$ 4,360	$ (36,265)	$ (582)
Net (loss) income per share				
Basic and Diluted				
Loss from Continuing operations	$ (0.03)	$ (0.04)	$ (0.16)	$ (0.07)
Income from discontinued operations	$ –	$ 0.06	$ –	$ 0.07
Net (loss) income per common share, basic and diluted	$ (0.03)	$ 0.02	$ (0.16)	$ (0.00)
Weighted-average shares used in computing net (loss) income per share				
Basic	227,586	203,272	225,047	199,457
Diluted	227,586	211,497	225,047	199,457
Total comprehensive (loss) income	$ (7,020)	$ 4,337	$ (36,270)	$ (584)

(1) Derived from audited financial statements.

DURECT CORPORATION
CONDENSED BALANCE SHEETS
(in thousands)

	As of December 31, 2021 (unaudited)	As of December 31, 2020(1)
ASSETS		
Current assets:		
Cash and cash equivalents	$ 49,844	$ 21,312
Cash held in escrow	–	14,979
Short-term investments	19,966	19,421
Accounts receivable	6,477	940
Inventories	1,870	1,864
Prepaid expenses and other current assets	3,580	4,545
Total current assets	81,737	63,061
Property and equipment, net	227	251
Operating lease right-of-use assets	3,446	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	$ 91,990	$ 75,641
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 1,311	$ 1,678
Accrued liabilities	6,799	6,346
Deferred revenue, current portion	98	–
Term loan, current portion, net	–	884
Operating lease liabilities, current portion	1,848	1,795
Total current liabilities	10,056	10,703
Deferred revenue, noncurrent portion	812	812
Operating lease liabilities, noncurrent portion	1,824	3,202
Term loan, noncurrent portion, net	20,632	19,936
Other long-term liabilities	884	873
Stockholders' equity	57,782	40,115
Total liabilities and stockholders' equity	$ 91,990	$ 75,641

(1) Derived from audited financial statements.

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Investor Relations (DURECT) – Michael Morabito, PhD, Solebury Trout, +1-646-378-2928, mmorabito@soleburytrout.com; Media Contact (DURECT) – Mónica Rouco Molina, PhD, LifeSci Communications, +1-929-469-3850, mroucomolina@lifescicomms.com