UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-Q

☒ **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the quarterly period ended September 30, 2022

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from _____ to

Commission file number 000-31615

DURECT CORPORATION
(Exact name of registrant as specified in its charter)

Delaware	**94-3297098**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

10260 Bubb Road
Cupertino, California 95014
(Address of principal executive offices, including zip code)

(408) 777-1417
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	**Trading Symbol**	**Name of Each Exchange on Which Registered**
Common Stock $0.0001 par value per share	**DRRX**	**The NASDAQ Stock Market LLC (The Nasdaq Capital Market)**

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by a check mark whether the registrant a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer", "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
Emerging growth company	☐		

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

As of November 1, 2022, there were 227,859,838 shares of the registrant's common stock outstanding.

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Special Note Regarding Forward-Looking Statements

This Form 10-Q contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, and Section 27A of the Securities Act of 1933, as amended. When used in this Quarterly Report on Form 10-Q, the words "believe," "anticipate," "intend," "plan," "estimate," "expect," "may," "will," "could," "potentially" and similar expressions are forward-looking statements. Such forward-looking statements are based on current expectations and beliefs. Any such forward-looking statements are not guarantees of future performance and involve risks and uncertainties. Actual events or results may differ materially from those discussed in the forward-looking statements as a result of various factors. Forward-looking statements made in this report include, but are not limited to, statements about:

- the clinical trial plans and timelines for larsucosterol;
- potential uses and benefits of larsucosterol to treat alcohol-associated hepatitis (also called "alcoholic hepatitis" or "AH"), non-alcoholic steatohepatitis, or other conditions;
- the results and timing of clinical trials, the ability to enroll patients in clinical trials in a timely and cost-effective manner;
- the likelihood of future clinical trial results of larsucosterol being positive and/or similar to results from previous trials, the possible commencement of future clinical trials, enrollment rates and timing of announcements of the results from our clinical trials;
- the possibility of filing for marketing approval for larsucosterol for the treatment of AH if the **AH** to evaluate sa**F**ety and eff**I**cacy of la**R**sucosterol treat**M**ent (AHFIRM) trial is successful and the likelihood of the U.S. Food and Drug Administration ("FDA") or other regulatory bodies granting such marketing approval;
- our intention to seek, and ability to enter into and maintain strategic alliances and collaborations;
- the potential benefits and uses of our products, product candidates and technologies, including larsucosterol, POSIMIR, and our SABER and CLOUD technologies;
- the potential milestone and royalty payments we may receive from Innocoll related to POSIMIR, earn-out payments we may receive from Indivior UK Limited ("Indivior") related to the commercialization of PERSERIS, and milestone, sub-license fees and royalty payments we may receive from Orient Pharma Co., Ltd. ("Orient Pharma");
- the progress of our third-party collaborations, including estimated milestones;
- responsibilities of our third-party collaborators, including the responsibility to make cost reimbursement, milestone, royalty and other payments to us, and our expectations regarding our collaborators' plans with respect to our products and product candidates and continued development of our products and product candidates;
- our responsibilities to our third-party collaborators, including our responsibilities to conduct research and development, clinical trials and/or manufacture excipients, products or product candidates;
- market opportunities for product candidates in our product development pipeline;
- potential regulatory filings for or approval of larsucosterol or any of our or any third parties' other product candidates;
- the progress and results of our research and development programs and our evaluation of additional development programs;
- requirements for us to purchase pre-clinical, clinical trial and commercial supplies of product candidates and/or products, as well as raw materials or active pharmaceutical ingredients from third parties, and the ability of third parties to provide us with our requirements for such supplies and raw materials;
- conditions for obtaining regulatory approval of our product candidates;
- submission and timing of applications for regulatory approval and timing of responses to our regulatory submissions;
- the impact of FDA, European Medicines Agency ("EMA") and other government regulation on our business;
- our ability to obtain, assert and protect patents and other intellectual property rights, including intellectual property licensed to our collaborators, as well as avoiding the intellectual property rights of others;
- products and companies that will compete with our products and the product candidates we develop and/or license to third-party collaborators;

•the possibility we may commercialize our own products and build up our commercial, sales and marketing capabilities and other required infrastructure;

•the possibility that we may develop additional manufacturing capabilities;

•our employees, including the number of employees and the continued services of key management, technical and scientific personnel;

•our future performance, including our anticipation that we will not derive meaningful revenues from our products and product candidates in development for at least the next twelve months, potential for future inventory write-offs and our expectations regarding our ability to achieve profitability;

•sufficiency of our cash resources, anticipated capital requirements and capital expenditures, our ability to comply with covenants of our term loan, and our need or desire for additional financing, including potential sales under our shelf registration statement;

•our expectations regarding research and development expenses, and selling, general and administrative expenses;

•the composition of future revenues; and

•accounting policies and estimates.

We caution you that the foregoing list may not contain all of the forward-looking statements made in this Quarterly Report on Form 10-Q. Forward-looking statements are not guarantees of future performance and involve risks and uncertainties. Actual events or results may differ materially from those discussed in the forward-looking statements as a result of various factors. For a more detailed discussion of such forward looking statements and the potential risks and uncertainties that may impact upon their accuracy, see the "Risk Factors" section and "Overview" section of this Management's Discussion and Analysis of Financial Condition and Results of Operations. These forward-looking statements reflect our view only as of the date of this report. We undertake no obligations to update any forward-looking statements. You should also carefully consider the factors set forth in other reports or documents that we file from time to time with the Securities and Exchange Commission.

PART I. FINANCIAL INFORMATION

Item 1. Financial Statements

DURECT CORPORATION

CONDENSED BALANCE SHEETS
(in thousands)
(unaudited)

	September 30, 2022	December 31, 2021
ASSETS		
Current assets:		
Cash and cash equivalents	$ 50,394	$ 49,844
Short-term investments	1,499	19,966
Accounts receivable, net	3,229	6,477
Inventories, net	2,269	1,870
Prepaid expenses and other current assets	1,955	3,580
Total current assets	59,346	81,737
Property and equipment, net	211	227
Operating lease right-of-use assets	2,340	3,446
Goodwill	6,169	6,169
Long-term restricted investments	150	150
Other long-term assets	256	261
Total assets	$ 68,472	$ 91,990
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 2,139	$ 1,311
Accrued liabilities	6,240	6,799
Deferred revenue, current portion	—	98
Term loan, current portion, net	3,106	—
Operating lease liabilities, current portion	1,872	1,848
Total current liabilities	13,357	10,056
Deferred revenue, non-current portion	812	812
Operating lease liabilities, non-current portion	639	1,824
Term loan, non-current portion, net	17,928	20,632
Other long-term liabilities	882	884
Commitments and contingencies		
Stockholders' equity:		
Common stock	23	23
Additional paid-in capital	585,752	583,818
Accumulated other comprehensive loss	(8)	(10)
Accumulated deficit	(550,913)	(526,049)
Stockholders' equity	34,854	57,782
Total liabilities and stockholders' equity	$ 68,472	$ 91,990

The accompanying notes are an integral part of these condensed financial statements.

DURECT CORPORATION

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

	Three months ended September 30,		Nine months ended September 30,	
	2022	2021	2022	2021
Collaborative research and development and other revenue	$ 10,585	$ 443	$ 11,686	$ 1,752
Product revenue, net	1,392	1,722	4,282	4,928
Total revenues	11,977	2,165	15,968	6,680
Operating expenses:				
Cost of product revenues	345	364	1,073	1,075
Research and development	9,881	8,023	26,909	23,431
Selling, general and administrative	3,883	3,236	11,570	9,935
Total operating expenses	14,109	11,623	39,552	34,441
Loss from operations	(2,132)	(9,458)	(23,584)	(27,761)
Other income (expense):				
Interest and other income	284	34	465	110
Interest and other expenses	(623)	(553)	(1,745)	(1,606)
Net other expense	(339)	(519)	(1,280)	(1,496)
Net loss	(2,471)	(9,977)	(24,864)	(29,257)
Net change in unrealized loss on available-for-sale securities, net of reclassification adjustments and taxes	17	3	2	7
Total comprehensive loss	$ (2,454)	$ (9,974)	$ (24,862)	$ (29,250)
Net loss per share				
Basic	$ (0.01)	$ (0.04)	$ (0.11)	$ (0.13)
Diluted	$ (0.01)	$ (0.04)	$ (0.11)	$ (0.13)
Weighted-average shares used in computing net loss per share				
Basic	227,774	227,499	227,735	224,191
Diluted	227,774	227,499	227,735	224,191

The accompanying notes are an integral part of these condensed financial statements.

DURECT CORPORATION

CONDENSED STATEMENTS OF STOCKHOLDERS' EQUITY
(in thousands, except per share amounts)
(unaudited)

	Common Stock		Additional Paid-In	Accumulated Other Comprehensive	Accumulated	Total Stockholders'
	Shares	Amount	Capital	loss	Deficit	Equity
Balance at December 31, 2021	227,680	$ 23	$ 583,818	$ (10)	$ (526,049)	$ 57,782
Issuance of common stock upon exercise of stock options	14	—	8	—	—	8
Stock-based compensation expense from stock options and ESPP shares	—	—	678	—	—	678
Net loss	—	—	—	—	(10,842)	(10,842)
Net change in unrealized loss on available-for-sale securities, net of reclassification adjustments and taxes	—	—	—	(19)	—	(19)
Balance at March 31, 2022	227,694	$ 23	$ 584,504	$ (29)	$ (536,891)	$ 47,607
Issuance of common stock upon exercise of stock options	70	—	27	—	—	27
Stock-based compensation expense from stock options and ESPP shares	—	—	617	—	—	617
Net loss	—	—	—	—	(11,551)	(11,551)
Net change in unrealized loss on available-for-sale securities, net of reclassification adjustments and taxes				4	—	4
Balance at June 30, 2022	227,764	$ 23	$ 585,148	$ (25)	$ (548,442)	$ 36,704
Issuance of common stock upon equity financings, net of issuance costs of $506	30	—	25	—	—	25
Stock-based compensation expense from stock options and ESPP shares			579			579
Net loss	—	—	—	—	(2,471)	(2,471)
Net change in unrealized loss on available-for-sale securities, net of reclassification adjustments and taxes	—	—	—	17	—	17
Balance at September 30, 2022	227,794	$ 23	$ 585,752	$ (8)	$ (550,913)	$ 34,854
Balance at December 31, 2020	203,533	$ 20	$ 529,884	$ (5)	$ (489,784)	$ 40,115
Issuance of common stock upon exercise of stock options	2,502	1	3,262	—	—	3,263
Issuance of common stock upon equity financings, net of issuance costs of $269	21,315	2	47,784	—	—	47,786
Stock-based compensation expense from stock options and ESPP shares	—	—	702	—	—	702
Net loss	—	—	—	—	(10,134)	(10,134)
Net change in unrealized loss on available-for-sale securities, net of reclassification adjustments and taxes	—	—	—	(9)	—	(9)
Balance at March 31, 2021	227,350	$ 23	$ 581,632	$ (14)	$ (499,918)	$ 81,723
Issuance of common stock upon exercise of stock options, ESPP purchases and other	146	—	163	—	—	163
Stock-based compensation expense from stock options and ESPP shares	—	—	710	—	—	710
Net loss	—	—	—	—	(9,146)	(9,146)
Unrealized gain on available-for-sale securities, net of tax	—	—	—	13	—	13
Balance at June 30, 2021	227,496	$ 23	$ 582,505	$ (1)	$ (509,064)	$ 73,463
Issuance of common stock upon equity financings, net of issuance cost of $126	—	—	(126)	—	—	(126)
Issuance of common stock upon exercise of stock options	10	—	11	—	—	11
Stock-based compensation expense from stock options and ESPP shares	—	—	653	—	—	653
Net loss	—	—	—	—	(9,977)	(9,977)
Change in unrealized loss on available-for-sale securities, net of tax	—	—	—	3	—	3
Balance at September 30, 2021	227,506	$ 23	$ 583,043	$ 2	$ (519,041)	$ 64,027

The accompanying notes are an integral part of these condensed financial statements

DURECT CORPORATION

CONDENSED STATEMENTS OF CASH FLOWS
(in thousands)
(unaudited)

	Nine months ended September 30,	
	2022	2021
Cash flows from operating activities		
Net loss	$ (24,864)	$ (29,257)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	109	92
Stock-based compensation	1,874	2,065
Amortization of debt issuance cost	358	330
Net amortization on investments	16	(80)
Changes in operating lease liabilities	(55)	(12)
Changes in assets and liabilities:		
Accounts receivable	3,248	(6)
Inventories	(399)	(406)
Prepaid expenses and other assets	1,630	1,307
Accounts payable	828	216
Accrued liabilities	(516)	(449)
Deferred revenue	(98)	-
Total adjustments	6,995	3,057
Net cash used in operating activities	(17,869)	(26,200)
Cash flows from investing activities		
Purchases of property and equipment	(93)	(184)
Purchases of available-for-sale securities	—	(44,812)
Proceeds from maturities of available-for-sale securities	18,453	39,936
Net proceeds from sale of LACTEL product line	—	14,979
Net cash provided by investing activities	18,360	9,919
Cash flows from financing activities		
Payments on equipment financing obligations	(1)	(2)
Payment for long-term debt amendment fee	—	(713)
Net proceeds from issuances of common stock	60	51,096
Net cash provided by financing activities	59	50,381
Net increase in cash, cash equivalents, and restricted cash	550	34,100
Cash, cash equivalents, and restricted cash, beginning of the period (1)	49,994	21,462
Cash, cash equivalents, and restricted cash, end of the period (1)	$ 50,544	$ 55,562

(1) Includes restricted cash of $150,000 (in long term restricted investments) included in the condensed balance sheets at September 30, 2022 and December 31, 2021.

The accompanying notes are an integral part of these condensed financial statements.

Note 1. Summary of Significant Accounting Policies

Nature of Operations

DURECT Corporation (the "Company") was incorporated in the state of Delaware on February 6, 1998. The Company is a biopharmaceutical company with research and development programs broadly falling into two categories: (i) new chemical entities derived from our Epigenetics Regulator Program, in which the Company attempts to discover and develop molecules which have not previously been approved and marketed as therapeutics, and (ii) Proprietary Pharmaceutical Programs, in which the Company applies its formulation expertise and technologies largely to active pharmaceutical ingredients whose safety and efficacy have previously been established but which the Company aims to improve in some manner through a new formulation. The Company has several product candidates under development by itself and with third party collaborators. The Company also manufactures and sells osmotic pumps used in laboratory research, and manufactures certain excipients for certain clients for use as raw materials in their products. In addition, the Company conducts research and development of pharmaceutical products in collaboration with third party pharmaceutical and biotechnology companies.

Basis of Presentation

These condensed financial statements have been prepared in accordance with the rules and regulations of the Securities and Exchange Commission (the "SEC"), and therefore do not include all the information and footnotes necessary for a complete presentation of the Company's results of operations, financial position and cash flows in conformity with U.S. generally accepted accounting principles ("U.S. GAAP"). The unaudited condensed financial statements reflect all adjustments (consisting only of normal recurring adjustments) which are, in the opinion of management, necessary for a fair presentation of the financial position at September 30, 2022, the operating results and comprehensive loss, and stockholders' equity for the three and nine months ended September 30, 2022 and 2021, and cash flows for the nine months ended September 30, 2022 and 2021. The balance sheet as of December 31, 2021 has been derived from audited financial statements at that date but does not include all of the information and footnotes required by U.S. GAAP for complete financial statements. These financial statements and notes should be read in conjunction with the Company's audited financial statements and notes thereto, included in the Company's annual report on Form 10-K for the fiscal year ended December 31, 2021 filed with the SEC.

The results of operations for the interim periods presented are not necessarily indicative of results that may be expected for any other interim period or for the full fiscal year.

Liquidity and Need to Raise Additional Capital

As of September 30, 2022, the Company had an accumulated deficit of $550.9 million as well as negative cash flows from operating activities.

The Company generally has had negative cash flows from operating activities and expects its negative cash flows to continue. The Company will continue to require substantial funds to continue research and development, including clinical trials of its product candidates. In order to meet its operating cash flow requirements beyond the next 12 months from the date the financial statements are filed, management's plans may include seeking additional collaborative agreements for certain of the Company's programs, receiving funds from collaboration and licensing agreements as well as pursuing financing activities such as public offerings and private placements of its common stock, preferred stock offerings, issuances of debt and convertible debt instruments.

There are no assurances that such additional funding will be obtained or that the Company will succeed in its future operations. If the Company cannot successfully raise additional capital when needed and implement its strategic development plan, its liquidity, financial condition and business prospects will be materially and adversely affected.

The Company believes its existing cash, cash equivalents, and investments are sufficient to fund its operating cash flow requirements for a period greater than 12 months from the date of issuance of these financial statements.

Inventories

Inventories are stated at the lower of cost or net realizable value, with cost determined on a first-in, first-out basis. The Company capitalizes inventories produced in preparation for product launches after receiving regulatory approval on a product. The Company may be required to expense previously capitalized inventory costs upon a change in management's judgment due to new information that suggests that the inventory will not be saleable. If the Company is able to subsequently sell products made with raw materials that were previously written down, the Company will report an unusually high gross profit as there will be no or little associated cost of goods for these materials.

The Company's inventories consist of the following (in thousands):

	September 30, 2022	December 31, 2021
Raw materials	$ 148	$ 143
Work in process	1,035	712
Finished goods	1,086	1,015
Total inventories	$ 2,269	$ 1,870

Revenue Recognition

Product Revenue, Net

The Company sells osmotic pumps used in laboratory research and manufactures certain excipients for pharmaceutical clients for use as raw materials in their products.

Revenues from product sales are recognized when the customer obtains control of the Company's product, which occurs at a point in time, typically upon shipment to the customer. The Company expenses incremental costs of obtaining a contract as and when incurred if the expected amortization period of the asset that the Company would have recognized is one year or less.

Trade Discounts and Allowances: The Company provides certain customers with discounts that are explicitly stated in the Company's contracts and are recorded as a reduction of revenue in the period the related product revenue is recognized.

Product Returns: The Company generally offers customers a limited right of return for products that have been purchased. The Company estimates the amount of its product sales that are probable of being returned by its customers and records this estimate as a reduction of revenue in the period the related product revenue is recognized. The Company currently estimates product return liabilities primarily using its historical sales information. The Company expects product returns to be minimal.

Collaborative Research and Development and Other Revenue

The Company enters into license agreements, under which it licenses certain rights to its product candidates or products to third parties. The terms of these arrangements typically include payment to the Company of one or more of the following: non-refundable, up-front license fees; reimbursement of development costs incurred by the Company under approved work plans; development, regulatory, intellectual property and commercial milestone payments; payments for manufacturing supply services the Company provides itself or through its contract manufacturers; and royalties on net sales of licensed products. Each of these payments results in collaborative research and development revenues, except for revenues from royalties on net sales of licensed products, which are classified as other revenues.

In determining the appropriate amount of revenue to be recognized as it fulfills its obligations under each of its agreements, the Company performs the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. For arrangements that are determined to include multiple performance obligations, the Company must develop assumptions that require judgment to determine the estimated stand-alone selling price for each performance obligation identified. These assumptions may include: forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success. The Company expects to recognize revenue for the variable consideration currently being constrained when it is probable that a significant revenue reversal will not occur.

Licenses of intellectual property: If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes the transaction price associated with the license as revenues when the license is transferred to the customer and the customer is able to use and benefit from the license. For performance obligations comprised of licenses that are bundled with other promises, the Company utilizes its judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the Company applies an appropriate method of measuring progress for purposes of recognizing related revenues. For performance obligations recognized over time, the Company evaluates the measure of progress each reporting period and recognizes revenues on a cumulative catch-up basis as collaborative research and development revenues and net income (loss).

Milestone Payments: At the inception of each arrangement that includes development milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company

re-evaluates the probability of achievement of such development milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price.

Manufacturing Supply Services: Arrangements that include a promise for future supply of raw materials or drug product for either clinical development or commercial supply at the customer's discretion are generally considered as options. The Company assesses if these options provide a material right to the customer and if so, they are accounted for as separate performance obligations and allocated a portion of the transaction price based on the estimated standalone selling price of the material right. If the Company is entitled to additional payments when the customer exercises these options, the deferred transaction price and any additional payments are recorded in collaborative research and development revenue when the customer obtains control of the goods.

Royalties and Earn-outs: For arrangements that include sales-based royalties or earn-outs, including milestone payments based on first commercial sale or the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized material royalty revenue resulting from the Company's collaborative arrangements or material earn-out revenues from any of the Company's patent purchase agreements.

Research and development services: Revenue from research and development services that are determined to represent a distinct performance obligation with the Company's third-party collaborators is recognized over time as the related research and development services are performed using an appropriate method of measuring progress. The Company evaluates the measure of progress each reporting period and recognizes revenue on a cumulative catch-up basis, as collaborative research and development revenues and net income (loss). Research and development expenses under the collaborative research and development agreements generally approximate or exceed the revenue recognized under such agreements over the term of the respective agreements. Deferred revenue may result when the Company does not expend the required level of effort during a specific period in comparison to funds received under the respective agreement.

The Company receives payments from its customers based on development cost schedules established in each contract. Up-front payments are recorded as deferred revenue upon receipt or when due and may require deferral of revenue recognition to a future period until the Company performs its obligations under these arrangements. Amounts are recorded as accounts receivable when the Company's right to consideration is unconditional. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the customer and the transfer of the promised goods or services to the customer will be one year or less.

Total revenue by geographic region based on customers' locations for the three and nine months ended September 30, 2022 and 2021 are as follows (in thousands):

	Three months ended September 30,		Nine months ended September 30,	
	2022	2021	2022	2021
Europe	$ 10,433	$ 297	$ 11,185	$ 880
United States	1,246	1,442	3,851	4,374
Japan	136	303	502	948
Other	162	123	430	478
Total	$ 11,977	$ 2,165	$ 15,968	$ 6,680

Prepaid and Accrued Contract Research Expenses

The Company incurs significant costs associated with third party consultants and organizations for pre-clinical studies, clinical trials, contract research and manufacturing, validation, testing, regulatory advice and other research and development-related services. The Company is required to estimate periodically the cost of services rendered but unbilled based on management's estimates of project status. If these good faith estimates are inaccurate, actual expenses incurred could materially differ from these estimates.

Research and development expenses

Research and development expenses are primarily comprised of salaries and benefits associated with research and development personnel, overhead and facility costs, preclinical and non-clinical development costs, clinical trial and related clinical manufacturing costs, contract services, and other outside costs. Research and development costs are expensed as incurred. Research and development costs paid to third parties under sponsored research agreements are recognized as the related services are performed. In addition, research and development expenses incurred that are reimbursed by the Company's partners are recorded as collaborative research and development revenue.

Comprehensive Loss

Components of other comprehensive loss are comprised entirely of unrealized gains and losses on the Company's available-for-sale securities for all periods presented. Total comprehensive loss has been disclosed in the Company's Statements of Operations and Comprehensive Loss.

Net Loss Per Share

Basic net loss per share is calculated by dividing the net loss by the weighted-average number of common shares outstanding. Diluted net loss per share is computed using the weighted-average number of common shares outstanding and common stock equivalents (i.e., options to purchase common stock) outstanding during the period, if dilutive, using the treasury stock method for options.

The numerators and denominators in the calculation of basic and diluted net loss per share were as follows (in thousands except per share amounts):

	Three months ended September 30,		Nine months ended September 30,	
	2022	2021	2022	2021
Numerators:				
Net loss	$ (2,471)	$ (9,977)	$ (24,864)	$ (29,257)
Denominator:				
Weighted average shares used to compute basic net loss per share	227,774	227,499	227,735	224,191
Dilutive common shares from stock options and ESPP	—	—	—	—
Weighted average shares used to compute diluted net loss per share	227,774	227,499	227,735	224,191
Net loss per share:				
Basic	$ (0.01)	$ (0.04)	$ (0.11)	$ (0.13)
Diluted	$ (0.01)	$ (0.04)	$ (0.11)	$ (0.13)

Options to purchase approximately 26.4 million and 26.2 million shares of common stock were excluded from the denominator in the calculation of diluted net loss per share for the three and nine months ended September 30, 2022, respectively, as the effect would be antidilutive. Options to purchase approximately 9.6 million and 8.0 million shares of common stock were excluded from the denominator in the calculation of diluted net loss per share for the three and nine months ended September 30, 2021, respectively, as the effect would be anti-dilutive.

Recent Accounting Pronouncements

In June 2016, the FASB issued Accounting Standards Update No. 2016-13 (ASU 2016-13) “Financial Instruments - Credit Losses: Measurement of Credit Losses on Financial Instruments.” ASU 2016-13 requires measurement and recognition of expected credit losses for financial assets. This standard is effective for fiscal years beginning after December 15, 2022 for small reporting companies, including interim reporting periods within those years and must be adopted using a modified retrospective approach, with certain exceptions. Early adoption is permitted. The Company does not expect the adoption of this standard to have a material effect on its financial statements.

In March 2020, the FASB issued ASU 2020-04, Reference Rate Reform (Topic 848): Facilitation of the Effects of Reference Rate Reform on Financial Reporting. In response to concerns about structural risks of the cessation of London Interbank Offered Rate (LIBOR), the amendments in this ASU provide optional guidance for a limited time to ease the potential burden in accounting for (or recognizing the effects of) reference rate reform on financial reporting. The amendments in this ASU provide optional expedients and exceptions for applying GAAP to contracts, hedging relationships and other transactions affected by reference rate reform if certain criteria are met. The amendments in this ASU apply only to contracts and hedging relationships that reference LIBOR or another reference rate expected to be discontinued due to reference rate reform. The expedients and exceptions provided by the amendments do not apply to contract modifications made and hedging relationships entered into or evaluated after December 31, 2022. The amendments in this ASU are elective and are effective for all entities as of March 12, 2020 through December 31, 2022. The adoption of this standard did not have a material effect on the Company’s financial statements.

Note 2. Strategic Agreements

The collaborative research and development and other revenues associated with our major collaborators or counterparties were $10.6 million and $11.7 million for the three and nine months ended September 30, 2022 compared with $443,000 and $1.8 million for the corresponding periods in 2021. The collaborative research and development and other revenues in the three and nine months ended September 30, 2022 included $8.0 million of patent milestone revenue and $2.0 million of first commercial sale milestone revenue compared with zero in the corresponding periods in 2021. In addition, the collaborative research and development and other revenues included (a) amounts related to earn-out revenue from Indivior UK Limited (Indivior) with respect to PERSERIS net sales; (b) feasibility programs and research and development activities funded by our collaborators, (c) royalty revenue from Orient Pharma

with respect to Methydur net sales and (d) royalty revenue from Innocoll with respect to POSIMIR net sales.

Agreement with Innocoll

On December 21, 2021, the Company entered into a license agreement (the "Innocoll Agreement") with Innocoll Pharmaceuticals Limited ("Innocoll"). Pursuant to the Innocoll Agreement, the Company has granted Innocoll an exclusive, royalty-bearing, sublicensable right and license to develop, manufacture and commercialize in the United States, POSIMIR®, the Company's FDA-approved post-surgical pain product, with respect to all uses and applications in humans. The Innocoll Agreement provides for the assignment of the Company's supply agreement with its contract manufacturing organization to Innocoll and also provides Innocoll with the right, within the United States, to expand the approved indications of POSIMIR. The Company retains, outside the United States, all of the global rights to POSIMIR.

Upon execution of the Innocoll Agreement, Innocoll paid the Company an initial nonrefundable, upfront fee of $4.0 million as well as a fee in the amount of $1.3 million primarily to cover the manufacturing supplies and excipients and certain equipment transferred to Innocoll pursuant to the terms of the Innocoll Agreement, and certain recently incurred DURECT expenses the parties negotiated for Innocoll to reimburse. The Innocoll Agreement includes customary representations and warranties on behalf of the Company and Innocoll, including representations as to the licensed intellectual property, regulatory matters and compliance with applicable laws. The Innocoll Agreement also provides for certain mutual indemnities for breaches of representations, warranties and covenants.

The Company also evaluated Innocoll's future purchases of an excipient from the Company and concluded that these purchases are option rights, and are at market rates, and do not constitute a material right performance obligation. As such, these future purchases have been excluded from the allocation of transaction price and the Company will account for them as separate contracts when and if Innocoll elects to issue purchase orders for the excipient.

During December 2021, the upfront fee of $4.0 million as well as a fee in the amount of $1.2 million to cover reimbursed expenses, the manufacturing supplies and excipients transferred to Innocoll pursuant to the terms of the Innocoll Agreement was recognized as revenue when the performance obligations were satisfied in December 2021 and $0.1 million was recorded as a net reduction in equipment in December 2021. At December 31, 2021, the Company included $5.3 million due from Innocoll in accounts receivable on its balance sheet; these funds were received in January 2022.

In August 2022, the Company was issued a new patent by the U.S. Patent and Trademark Office, extending U.S. patent coverage of POSIMIR to at least 2041, resulting in an $8.0 million milestone payment by Innocoll to the Company. In September 2022, Innocoll launched POSIMIR in the U.S., triggering a $2.0 million milestone payment to the Company for the first commercial sale of POSIMIR. As the commercial launch of POSIMIR progresses, the Company will receive tiered, low double-digit to mid-teen royalties on net product sales of POSIMIR in the United States. The Company may earn additional milestone payments of up to $122.0 million in the aggregate, depending on the achievement of certain regulatory, commercial, and intellectual property milestones with respect to POSIMIR. Thus, the Company recognized $10.0 million of milestone revenue under the agreement with Innocoll during the three and nine months ended September 30, 2022.

Patent Purchase Agreement with Indivior

In September 2017, we entered into an agreement with Indivior (the "Indivior Agreement"), under which we assigned to Indivior certain patents that may provide further intellectual property protection for PERSERIS, Indivior's extended-release injectable suspension for the treatment of schizophrenia in adults. In consideration for such assignment, Indivior made non-refundable upfront and milestone payments to DURECT totaling $17.5 million. Additionally, under the terms of the agreement with Indivior, DURECT receives quarterly earn-out payments into 2026 that are based on a single digit percentage of U.S. net sales of PERSERIS. Indivior commercially launched PERSERIS in the U.S. in February 2019. The Indivior Agreement contains customary representations, warranties and indemnities of the parties. Amounts recognized in the three and nine months ended September 30, 2022 and 2021 related to earn-out revenues from PERSERIS have been immaterial and are included in collaborative research and development and other revenue.

Note 3. Financial Instruments

Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. The Company's valuation techniques used to measure fair value maximize the use of observable inputs and minimize the use of unobservable inputs. The Company follows a fair value hierarchy based on three levels of inputs, of which the first two are considered observable and the last unobservable, that may be used to measure fair value. These levels of inputs are the following:

•Level 1—Quoted prices in active markets for identical assets or liabilities.

•Level 2—Inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

•Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

The Company's financial instruments are valued using quoted prices in active markets or based upon other observable inputs. Money market funds are classified as Level 1 financial assets. Certificates of deposit, commercial paper, municipal bonds, corporate debt securities, and U.S. Government agency securities are classified as Level 2 financial assets. The fair value of the Level 2 assets is estimated using pricing models using current observable market information for similar securities. The Company's Level 2 investments include U.S. government-backed securities and corporate securities that are valued based upon observable inputs that may include benchmark yields, reported trades, broker/dealer quotes, issuer spreads, two-sided markets, benchmark securities, bids, offers and reference data including market research publications. The fair value of commercial paper is based upon the time to maturity and discounted using the three-month treasury bill rate. The average remaining maturity of the Company's Level 2 investments as of September 30, 2022 is less than twelve months and these investments are rated by S&P and Moody's at AAA or AA- for securities and A1, A2, P1 or P2 for commercial paper.

The following is a summary of available-for-sale securities as of September 30, 2022 and December 31, 2021 (in thousands):

	September 30, 2022			
	Amortized Cost	Unrealized Gain	Unrealized Loss	Estimated Fair Value
Money market funds	$ 712	$ —	$ —	$ 712
Certificates of deposit	150	—	—	150
Commercial paper	48,944	—	(8)	48,936
	$ 49,806	$ —	$ (8)	$ 49,798
Reported as:				
Cash and cash equivalents	$ 48,157	$ —	$ (8)	$ 48,149
Short-term investments	1,499	—	—	1,499
Long-term restricted investments	150	—	—	150
	$ 49,806	$ —	$ (8)	$ 49,798

	December 31, 2021			
	Amortized Cost	Unrealized Gain	Unrealized Loss	Estimated Fair Value
Money market funds	$ 2,089	$ —	$ —	$ 2,089
Certificates of deposit	150	—	—	150
Commercial paper	62,505	—	(10)	62,495
Corporate debt	1,293	—	—	1,293
	$ 66,037	$ —	$ (10)	$ 66,027
Reported as:				
Cash and cash equivalents	$ 45,913	$ —	$ (2)	$ 45,911
Short-term investments	19,974	—	(8)	19,966
Long-term restricted investments	150	—	—	150
	$ 66,037	$ —	$ (10)	$ 66,027

The following is a summary of the cost and estimated fair value of available-for-sale securities at September 30, 2022, by contractual maturity (in thousands):

	September 30, 2022	
	Amortized Cost	Estimated Fair Value
Mature in one year or less	$ 48,944	$ 48,936
Mature after one year through five years	150	150
	$ 49,094	$ 49,086

There were no securities that have had an unrealized loss for more than 12 months as of September 30, 2022.

As of September 30, 2022, unrealized losses on available-for-sale investments are not attributed to credit risk and are considered to be temporary. The Company believes that it is more-likely-than-not that investments in an unrealized loss position will be held until maturity or the recovery of the cost basis of the investment. To date, the Company has not recorded any impairment charges on marketable securities related to other-than-temporary declines in market value.

Note 4. Accrued Liabilities

Accrued liabilities as of September 30, 2022 and December 31, 2021 were comprised as follows (in thousands):

	September 30, 2022	December 31, 2021
Accrued compensation and benefits	$ 3,221	$ 4,099
Accrued contract research and manufacturing costs	1,406	757
Accrued clinical costs	391	97
Others	1,222	1,846
Total	$ 6,240	$ 6,799

Note 5. Stock-Based Compensation

As of September 30, 2022, the Company has two stock-based compensation plans. The stock-based compensation cost that has been included in the statements of comprehensive loss is shown as below (in thousands):

	Three months ended September 30,		Nine months ended September 30,	
	2022	2021	2022	2021
Cost of product revenues	$ 5	$ 6	$ 15	$ 17
Research and development	292	317	918	952
Selling, general and administrative	281	330	941	1,096
Total stock-based compensation	$ 578	$ 653	$ 1,874	$ 2,065

As of September 30, 2022 and December 31, 2021, $17,000 of stock-based compensation cost was capitalized in inventory on the Company's balance sheets for each period.

The Company uses the Black-Scholes option pricing model to value its stock options. The expected life computation is based on historical exercise patterns and post-vesting termination behavior. The Company considered its historical volatility in developing its estimate of expected volatility.

The Company used the following assumptions to estimate the fair value of stock options granted and shares purchased under its employee stock purchase plan for the three and nine months ended September 30, 2022 and 2021:

	Three months ended September 30,		Nine months ended September 30,	
	2022	2021	2022	2021
Stock Options				
Risk-free rate	2.7-3.2%	—	1.8-3.2%	0.8-1.3%
Expected dividend yield	—	—	—	—
Expected life of option (in years)	7.3	—	7.0-7.3	7.0-7.3
Volatility	85-86%	—	83-86%	74-86%

	Three months ended September 30,		Nine months ended September 30,	
	2022	2021	2022	2021
Employee Stock Purchase Plan				
Risk-free rate	1.49%	0.04%	0.04-1.49%	0.04-0.1%
Expected dividend yield	—	—	—	—
Expected life of option (in years)	0.5	0.5	0.5	0.5
Volatility	80%	71%	56-80%	71-78%

Note 6. Term Loan

In July 2016, the Company entered into a $20.0 million secured single-draw term loan (as amended, the "Loan Agreement") with Oxford Finance LLC ("Oxford Finance"). The Company and Oxford Finance entered into five subsequent amendments to the Loan Agreement in February 2018, November 2018, December 2019, March 2021 and May 2021. For amendments 1-3 and 5, the Company paid Oxford Finance loan modification fees of $100,000, $900,000, $825,000 and $712,500, respectively. As amended, the Loan Agreement provides for interest only payments through June 1, 2023, followed by consecutive monthly payments of principal and interest in arrears starting on June 1, 2023 and continuing through the maturity date of the term loan of September 1, 2025. The Loan Agreement provides for a floating interest rate (7.95% initially and 9.86% as of September 30, 2022) based on an index rate plus a spread. In addition, a payment equal to 10% of the principal amount of the term loan is due when the term loan becomes due or upon the prepayment of the facility. If the Company elects to prepay the loan, there is also a prepayment fee of between 0.75% and 2.5% of the principal amount of the term loan depending on the timing of prepayment. The $150,000 facility fee that was paid at the original closing, the loan modification fees and other debt offering/issuance costs have been recorded as debt discount on the Company's balance sheets and together with the final $2.0 million payment are being amortized to interest expense using the effective interest method over the revised term of the loan.

The term loan is secured by substantially all of the assets of the Company, except that the collateral does not include any intellectual property (including licensing, collaboration and similar agreements relating thereto), and certain other excluded assets. The 2016 Loan Agreement contains customary representations, warranties and covenants by the Company, which covenants limit the Company's ability to convey, sell, lease, transfer, assign or otherwise dispose of certain assets of the Company; engage in any business other than the businesses currently engaged in by the Company or reasonably related thereto; liquidate or dissolve; make certain management changes; undergo certain change of control events; create, incur, assume, or be liable with respect to certain indebtedness; grant certain liens; pay dividends and make certain other restricted payments; make certain investments; and make payments on any subordinated debt.

The Loan Agreement also contains customary indemnification obligations and customary events of default, including, among other things, the Company's failure to fulfill certain obligations of the Company under the Loan Agreement and the occurrence of a material adverse change which is defined as a material adverse change in the Company's business, operations, or condition (financial or otherwise), a material impairment of the prospect of repayment of any portion of the loan, or a material impairment in the perfection or priority of lender's lien in the collateral or in the value of such collateral. In the event of default by the Company under the Loan Agreement, the lender would be entitled to exercise its remedies thereunder, including the right to accelerate the debt, upon which the Company may be required to repay all amounts then outstanding under the Loan Agreement, which could harm the Company's financial condition. The conditionally exercisable call option related to the event of default is considered to be an embedded derivative which is required to be bifurcated and accounted for as a separate financial instrument. In the periods presented, the value of the embedded derivative is not material, but could become material in future periods if an event of default became more probable than is currently estimated.

The fair value of the term loan approximates the carrying value. Future maturities due under the term loan as of September 30, 2022, are as follows (in thousands):

Three months ended December 31, 2022	$ —
2023	5,000
2024	8,571
2025	8,429
Total minimum payments	22,000
Less unamortized debt discount and accrued final payment	(966)
Carrying value of term loan, net	21,034

As of September 30, 2022, the Company was in compliance with all material covenants under the Loan Agreement and there had been no material adverse change.

Note 7. Commitments

Operating Leases

The Company has lease arrangements for its facilities as follows.

Location	Approximate Square Feet	Operation	Expiration
Cupertino, CA	30,149 sq. ft.	Office, Laboratory and Manufacturing	Lease expires 2024 (with an option to renew for an additional five years)
Cupertino, CA	20,100 sq. ft.	Office and Laboratory	Lease expires 2024 (with an option to renew for an additional five years)
Vacaville, CA	24,634 sq. ft.	Manufacturing	Lease expires 2023

Under these leases, the Company is required to pay certain maintenance expenses in addition to monthly rent. Rent expense is recognized on a straight-line basis over the lease term for leases that have scheduled rental payment increases. The lease expense includes the amortization of the right-of-assets with the associated interest component estimated by applying the effective interest method. Rent expenses under all operating leases were $478,000 and $1.4 million for both the three and nine months ended September 30, 2022 and 2021, respectively.

Future minimum payments under these noncancelable leases are as follows (in thousands):

	Operating Leases
Three months ended December 31, 2022	$ 496
2023	1,970
2024	275
	$ 2,741

Note 8. Stockholders' Equity

In August 2018, the Company filed a shelf registration statement on Form S-3 with the SEC (the "2018 Registration Statement") (File No. 333-226518), which upon being declared effective in October 2018 allowed the Company to offer up to $175.0 million of securities from time to time in one or more public offerings, inclusive of up to $75.0 million of the Company's common stock which the Company could have sold, subject to certain limitations, pursuant to a sales agreement dated November 3, 2015 with Cantor Fitzgerald & Co. (the "2015 Sales Agreement").

In February 2021, the Company completed an underwritten public offering of 20,364,582 shares of its common stock at a price of $2.2386 per share pursuant to an underwriting agreement with Cantor Fitzgerald & Co., raising total gross proceeds to the Company of approximately $45.6 million before deducting estimated offering expenses payable by the Company. Total stock issuance costs related to this financing were approximately $195,000. After deducting estimated offering expenses payable by the Company, the net proceeds to the Company were approximately $45.4 million.

In July 2021, the Company filed a shelf registration statement on Form S-3 with the SEC (the "2021 Registration Statement") (File No. 333-258333), which upon being declared effective in August 2021, terminated the 2018 Registration Statement and allows the Company to offer up to $250.0 million of securities from time to time in one or more public offerings, inclusive of up to $75.0 million of shares of the Company's common stock which the Company may sell, subject to certain limitations, pursuant to a sales agreement dated July 30, 2021 with Cantor Fitzgerald & Co. (the "2021 Sales Agreement"). The 2021 Sales Agreement replaced the 2015 Sales Agreement.

During the three and nine months ended September 30, 2022, the Company raised net proceeds (net of commissions) of approximately $25,000 from the sale of 30,000 shares of the Company's common stock in the open market at a weighted average price of $0.84 per share pursuant to the 2021 Registration Statement and the 2021 Sales Agreement. During the three months ended September 30, 2021, the Company did not issue any shares pursuant to the 2018 Registration Statement and the 2015 Sales Agreement. During the nine months ended September 30, 2021, the Company raised net proceeds (net of commissions) of approximately $2.4 million from the sale of 950,009 shares of the Company's common stock in the open market at a weighted average price of $2.60 per share pursuant to the 2018 Registration Statement and the 2015 Sales Agreement.

As of November 1, 2022, the Company had up to $250.0 million of the Company's securities available for sale under the 2021 Registration Statement, of which $75.0 million of the Company's common stock are available pursuant to the 2021 Sales Agreement.

Note 9. Subsequent Event

None.

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations

This Management's Discussion and Analysis of Financial Condition and Results of Operations for the three and nine months ended September 30, 2022 should be read in conjunction with (i) our unaudited condensed financial statements and related notes appearing elsewhere in this Quarterly Report on Form 10-Q and (ii) our annual report on Form 10-K for the year ended December 31, 2021 filed with the Securities and Exchange Commission ("SEC") as well as the "Risk Factors" section included elsewhere in Part II, Item IA of this Quarterly Report on Form 10-Q. References to the "Company," "DURECT," "we," "us" and "our" refer to DURECT Corporation.

Overview

We are a biopharmaceutical company advancing novel and potentially lifesaving investigational therapies derived from our Epigenetic Regulator Program. Larsucosterol (also known as "DUR 928"), a new chemical entity in clinical development, is the lead candidate in our Epigenetic Regulator Program. An endogenous, orally bioavailable small molecule, larsucosterol has been shown in both *in vitro* and *in vivo* studies to play an important regulatory role in lipid metabolism, stress and inflammatory responses, and cell death and survival. We are developing larsucosterol for alcohol-associated hepatitis ("AH"), a life-threatening acute liver condition with no approved therapeutics and a 28-Day and 90-Day historical mortality rate of 20%-26% and 29%-31%, respectively. After completing a Phase 2a trial in which 100% of AH patients treated with larsucosterol survived the 28-Day study period, we are now conducting a ~300-patient, double-blind, placebo-controlled Phase 2b clinical trial called AHFIRM (trial in **AH** to evaluate sa**F**ety and eff**I**cacy of la**R**sucosterol treat**M**ent). Through our AHFIRM trial, we are evaluating larsucosterol's potential to reduce mortality or liver transplantation compared to a placebo with or without steroids at the investigators' discretion. Currently we anticipate dosing the last patient in the AHFIRM trial in the second quarter of 2023. If the AHFIRM trial is successful, it may support a New Drug Application ("NDA") filing and we may decide to develop our own commercial, sales and marketing organization. We have also investigated larsucosterol in patients with nonalcoholic steatohepatitis ("NASH") with encouraging results in a Phase 1b clinical trial and are considering further development for this and other indications.

In addition to our Epigenetic Regulator Program, we developed a novel and proprietary post-surgical pain product called POSIMIR that utilizes our innovative SABER platform technology to enable continuous sustained delivery of bupivacaine, a non-opioid local analgesic, over three days in adults. In February 2021, POSIMIR received U.S. FDA approval for post-surgical pain reduction for up to 72 hours following arthroscopic subacromial decompression. In December 2021, we entered into a license agreement (the "Innocoll Agreement") with Innocoll Pharmaceuticals Limited ("Innocoll"), pursuant to which the Company granted to Innocoll an exclusive, royalty-bearing, sublicensable right and license to develop, manufacture and commercialize POSIMIR in the United States. In January 2022, we received a $4.0 million upfront license fee as well as a payment in the amount of $1.3 million primarily to cover the manufacturing supplies and excipients and certain equipment transferred to Innocoll pursuant to the terms of the Innocoll Agreement, and certain incurred DURECT expenses the parties negotiated for Innocoll to reimburse under the Innocoll Agreement. In August 2022, we were issued a new patent by the U.S. Patent and Trademark Office, extending U.S. patent coverage of POSIMIR to at least 2041, resulting in an $8.0 million milestone payment to us by Innocoll. In September 2022, Innocoll launched POSIMIR in the U.S., triggering a $2.0 million milestone payment to us for the first commercial sale of POSIMIR. We will also earn low double-digit to mid-teen royalties on net product sales of POSIMIR in the U.S. We may earn additional milestone payments up to $122.0 million in the aggregate, depending on the achievement of certain commercial, regulatory and intellectual property milestone payments with respect to POSIMIR.

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®, CLOUD™, ORADUR™ and ALZET® are trademarks of DURECT Corporation. Other trademarks referred to belong to their respective owners. Full prescribing information for POSIMIR, including BOXED WARNING and Medication Guide can be found at www.posimir.com. Full prescribing information for PERSERIS, including BOXED WARNING and Medication Guide can be found at www.perseris.com.

As a result of the assignment of certain patent rights, we also receive single digit sales-based earn-out payments from U.S. net sales of Indivior UK Limited ("Indivior")'s PERSERIS™(risperidone) drug for schizophrenia and single-digit royalties from net sales of Orient Pharma Co., Ltd. ("Orient Pharma")'s Methydur Sustained Release Capsules (Methydur) for the treatment of attention deficit hyperactivity disorder (ADHD) in Taiwan. We also manufacture and sell ALZET osmotic pumps used in laboratory research and have several early-stage development programs with corporate collaborators on terms which typically call for our collaborator to fund all or a substantial portion of future development costs and then pay us milestone payments based on specific development or commercial achievements plus royalties on product sales.

Additional details of these programs and related strategic agreements are contained in our annual report on Form 10-K for the year ended December 31, 2021 and in Note 2 of the financial statements included in Item 1 above.

Epigenetic Regulator Program and New Chemical Entities

Epigenetic regulation influences the expression of genes through the silencing or initiation of gene activity without modifying the DNA sequence. For instance, methylation of cytosine nucleotides in promoter regions of DNA, facilitated by DNMTs, will generally result in downregulation of gene expression, while demethylation generally results in upregulation. DNA methylation/demethylation can thus regulate the expression of relevant genes, especially clusters of master genes that further modulate crucial cellular activities.

Our Epigenetic Regulator Program involves a multi-year collaborative effort with the Department of Internal Medicine at Virginia Commonwealth University ("VCU"), the VCU Medical Center and the McGuire VA Medical Center. The knowledge base supporting this program is a result of more than 30 years of lipid research by Shunlin Ren, M.D., Ph.D., Professor of Internal Medicine at the VCU Medical Center. The lead compound from this program, larsucosterol, is an endogenous sulfated oxysterol, which acts as an epigenetic regulator. Under a license with VCU, we hold the exclusive royalty-bearing worldwide right to develop and commercialize larsucosterol and related molecules discovered in the program.

In March 2021, a peer-reviewed research paper proposed mechanism of action of larsucosterol was published in The Journal of Lipid Research. The publication showed that larsucosterol (referred to in the paper as "25HC3S") bound to and inhibited the activities of DNA methyltransferases (DNMTs) 1, 3a and 3b, enzymes that add methyl groups to DNA (a process called "DNA methylation"), as well as reduced DNA hypermethylation. DNMT1 and 3a have been shown to be over-expressed in the livers of patients with severe AH. As such, by inhibiting DNMT activities, larsucosterol may inhibit DNA hypermethylation, thereby modulating the expression of genes and pathways that are involved in crucial cellular activities, including those associated with cell death, stress response, and lipid biosynthesis. These modulations may lead to improved cell survival, reduced lipid accumulation or lipotoxicity, minimized inflammation, and enhanced liver regeneration, as has been observed in various *in vivo* animal models and in results from our completed clinical trials in AH and NASH patients.

The biological activity of larsucosterol has been demonstrated in over a dozen different animal disease models involving three animal species. Some of these models represent acute organ injuries (e.g., LPS-induced endotoxin shock, drug-induced acute oxidative stress injury, ischemic-reperfusion-induced kidney and brain injury, and some represent chronic metabolic disorders (e.g., diabetes-NASH and NAFLD).

Our major product research and development efforts for larsucosterol are described in the following table:

Summary of DUR-928 Clinical Trials

Indication	Preclinical	Phase 1	Phase 2	Design / Timing	Patient Population
Alcohol-associated Hepatitis (Injectable)				Ongoing Phase 2b double-blind, placebo-controlled, multi-center safety and efficacy trial (AHFIRM) planning to enroll ~300 severe AH patients. If robust reduction in mortality or liver transplantation is shown, may support NDA filing.	~137,000 annual U.S. hospitalizations[1]
NASH (Oral)				Top line Phase 1b data, n=65: Reductions in liver enzymes, liver stiffness, serum lipids, certain biomarkers.	9-16 million in the U.S.[2]

(1) US Department of Health and Human Services' Healthcare Cost and Utilization Project reports https://hcupnet.ahrq.gov. (2) Estes C, et al. Hepatology 2018;67:123-133.

In pharmacokinetic ("PK") and toxicology studies conducted in mice, rats, rabbits, dogs, minipigs and monkeys, larsucosterol has been found to be well tolerated and safe by all routes of administration tested to date. These results support the use of larsucosterol in completed and ongoing human safety, PK, proof-of-concept, and efficacy trials. The chronic toxicity of larsucosterol was further assessed in a 6-month oral study in rats and in a 9-month oral study in dogs. These studies support the use of larsucosterol in long duration human trials.

Acute Organ Injury Program with Injectable larsucosterol

Market Opportunity. Alcohol-associated hepatitis (also called "alcoholic hepatitis" or "AH"), an acute form of alcohol-associated liver disease, is associated with long-term heavy intake of alcohol and often occurs after a recent period of increased alcohol consumption. AH is typically characterized by recent onset jaundice and hepatic failure. A Model of End-Stage Liver Disease ("MELD") score is a commonly used scoring system to assess the severity and prognosis of AH patients. AH was associated with approximately 158,000 U.S. hospitalizations in 2020 according to the available data published for the year. A retrospective 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 30.9% respectively.

There are no FDA approved therapies for AH and stopping alcohol consumption is necessary, but frequently not sufficient for recovery in many moderate and severe patients. Corticosteroids do not improve survival at 90 days or one year, and have demonstrated an increased risk of infection. In addition, fewer than 50% of AH patients are eligible for corticosteroids. According to a recent study, the healthcare costs associated with treating hospitalized AH patients and their length of hospital stay are significant.

Each hospitalization episode with AH diagnosis for patients who:	**Average length of stay**	**Average total charges during hospital stay**
Died during the hospitalization	9 days	$147,000
Were discharged	6 days	$53,000
Marlowe, N., Lam, D., Krebs, W., Lin, W. & Liangpunsakul, S. (2022) Prevalence, co-morbidities, and in-hospital mortality of patients hospitalized with alcohol-associated hepatitis in the United States from 2015 to 2019. *Alcoholism: Clinical and Experimental Research.*		

The rate of AH patients undergoing liver transplantation has been increasing in recent years, although the total number of such transplants is still relatively small. Average charges for a liver transplant exceed $875,000, and patients require lifelong immunosuppressive therapy to prevent organ rejection.

Clinical Program. In 2019, we completed a Phase 2a clinical trial evaluating safety and PK of intravenously infused larsucosterol in patients with moderate and severe AH. Severity of AH was determined by MELD scores with moderate defined as MELD 11-20 and severe as MELD 21-30. This was an open label, dose escalation (30 mg, 90 mg and 150 mg), multi-center U.S. study, designed to be conducted in two sequential parts. Part A included patients with moderate AH and Part B included patients with severe AH.

In this Phase 2a trial, dose escalation was permitted following review of safety and PK results of the prior dose level by a Dose Escalation Committee. The target number of patients for the study was 4 per dose group. Final enrollment included 19 patients with moderate (7 of 19) and severe AH (12 of 19), who received larsucosterol intravenously at 30 mg, 90 mg, or 150 mg doses. Eight patients (four moderate and four severe) were dosed at 30mg, seven patients (three moderate and four severe) were dosed at 90mg and four patients (all severe) were dosed at 150mg. After being discharged on Day 2, one patient did not return for the scheduled Day 7 and Day 28 follow-up visits; therefore Lille, bilirubin and MELD data reported below are based on 18 patients. The objectives of this study included assessment of safety, PK and pharmacodynamic signals, including liver biochemistry, biomarkers, and prognostic scores, including the Lille score, following larsucosterol treatment.

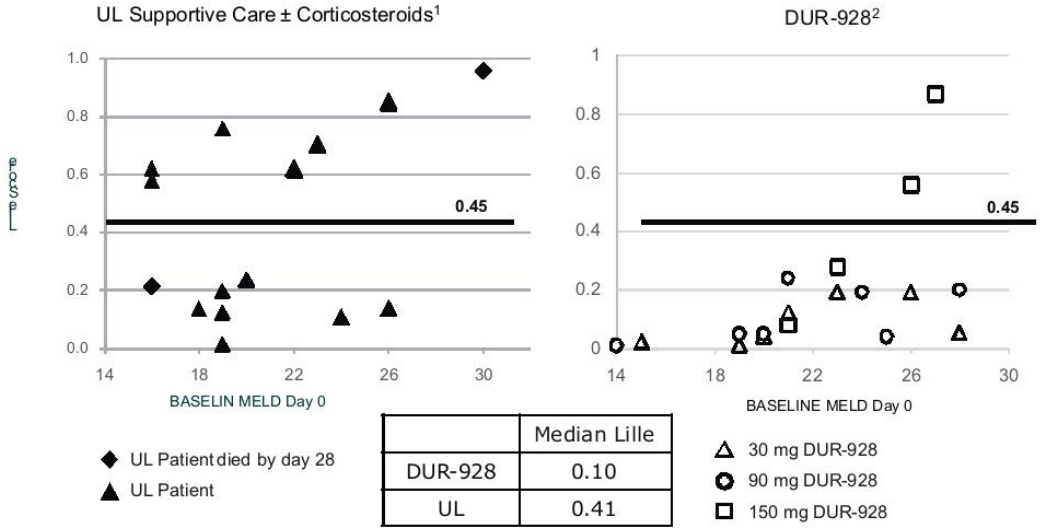
In November 2019, the results from this Phase 2a clinical trial of larsucosterol in AH were presented as a late-breaking oral presentation at The Liver Meeting®. The study summary results were also selected for inclusion in the 'Best of The Liver Meeting' presentation in the alcohol-related liver disease category.

All 19 patients treated with larsucosterol in this trial survived the 28-day follow-up period and there were no drug-related serious adverse events. Using an alternative measure of AH severity to MELD, Maddrey's Discrimination Function ("DF"), 15 of the 19 patients had DF scores of 32 or greater, indicating that they had severe AH. Patients treated with larsucosterol had a statistically

significant reduction from baseline in bilirubin at Day 7 and 28 and MELD at Day 28. Lille scores, described below, were also statistically significantly lower than those from a well-matched group of patients in a contemporary trial as well as several published historical controls. 74% of all larsucosterol treated patients and 67% of those with severe AH were discharged from the hospital within 4 days after receiving a single dose of larsucosterol.

Lille

Lille scores are used in clinical practice to help determine the prognosis and response of AH patients after 7 days of treatment. The lower the Lille score, the better the prognosis. Patients with a Lille score below 0.45, treatment responders, have a six-month survival rate of 85% compared to those with Lille scores above 0.45, who have only a 25% six-month survival rate. The chart below shows the Lille scores for individual AH patients treated with larsucosterol plotted as a function of their baseline MELD scores. In our study, the median Lille score for patients treated with larsucosterol was 0.10. The median Lille score among a cohort of 15 patients treated with standard of care at the University of Louisville ("UL") was 0.41 (shown as historical control).



	Median Lille
DUR-928	0.10
UL	0.41

1)Our advisor, Dr. Craig McClain from UL, shared anonymized data from his study, in which 15 AH patients with initial MELD scores ranging from 15-30 received either supportive care alone (n=8 moderate AH patients) or supportive care with corticosteroids (n=7 severe AH patients). Two of the UL control patients died by Day 28.
2)One patient in the larsucosterol (also known as "DUR-928") group did not return for the Day 7 or 28 visit. All 19 patients, including this one, treated with larsucosterol in this trial survived the 28-Day follow-up period.
3)Lille scores in the larsucosterol group were significantly lower than that of the UL patients (p=0.01; Wilcoxon's Rank Sum Test).

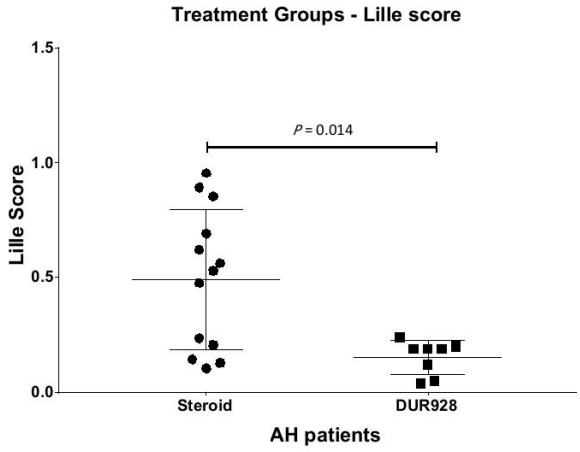
As shown in the table below, all patients in the 30 mg and 90 mg larsucosterol dosing groups were treatment responders based on their Lille scores, regardless of disease severity by DF, MELD, or baseline serum bilirubin levels. 89% of the overall larsucosterol patient population (16 of 18) were treatment responders based on Lille. Patients with severe AH, as defined by DF ≥32 or MELD 21-30, and baseline serum bilirubin above 8 mg/dL, had similarly high response rates to larsucosterol treatment.

AH Patient Category	n[1]	Responders (Lille<0.45)	Lille Median (Quartile)
All Patients[2]	18	89%	0.10 (0.04, 0.20)
³30 mg or 90 mg larsucosterol	14	100%	0.05 (0.04, 0.19)
DF≥32 (SAH)[2, 4]	15	87%	0.19 (0.05, 0.22)
³30 mg or 90 mg larsucosterol	11	100%	0.12 (0.05, 0.19)
MELD 21-30[2]	12	83%	0.19 (0.11, 0.25)
³30 mg or 90 mg larsucosterol	8	100%	0.19 (0.10, 0.19)
Baseline bilirubin >8mg/dl[2]	11	82%	0.10 (0.05, 0.20)
³30 mg or 90 mg larsucosterol	8	100%	0.10 (0.05, 0.19)

1)One patient did not return for Day 7 and 28 visits.
2)Including patients receiving 30 mg, 90 mg and 150 mg of larsucosterol.
3)Excluding patients receiving 150 mg of larsucosterol.
4)DF is calculated using the patient's prothrombin time and serum bilirubin level. DF was introduced in 1978 as a predictor of significant mortality risk for AH patients. A DF≥32 identified AH patients with a 30-Day mortality rate of ≥50%.

The Lille scores of patients treated with larsucosterol in this trial were also significantly lower than several selected published historical studies *(Hepatology 2007, 45:1348-1354; Gut 2011, 60:255-260)*, in which patients had similar baseline bilirubin, albumin, creatinine, prothrombin time and DF scores, and were treated with standard of care with or without corticosteroids. Due to the historical nature of these studies, such comparisons should be interpreted with caution.

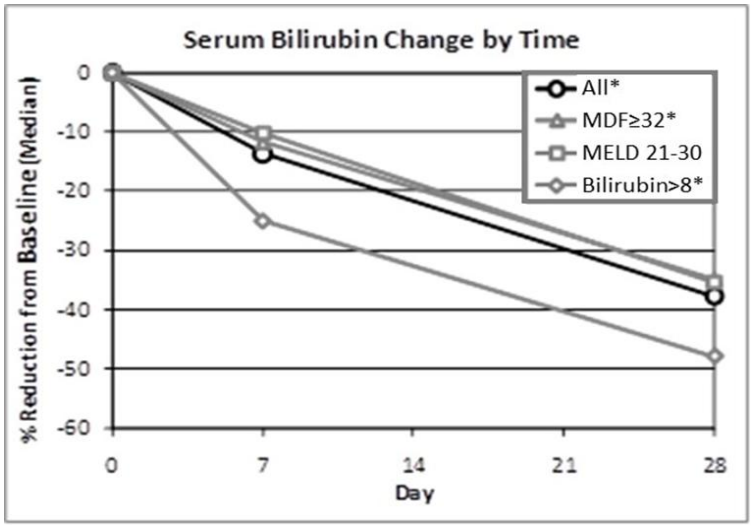
A sub-group analysis was conducted to compare severe AH patients in the 30 mg and 90 mg dosing groups (n=8) with well-matched severe AH patients (n=13) who received corticosteroids for 28 days in a contemporaneous study at UL. Patients shown in the chart below in the UL steroid group had a mean baseline MELD of 24.46 and mean baseline Maddrey's DF score of 62.98. The 8 patients in the larsucosterol group had baseline mean MELD of 24.50 and mean baseline Maddrey's DF score of 61.25. All patients treated with larsucosterol survived the 28-Day follow up period, while 3 of the 13 patients (23%) in the UL steroid group died within the first 28 days.



The steroid group in the above graph includes the 7 severe AH patients treated with steroids from the UL group shown in the MELD vs Lille graph above plus an additional 6 severe AH patients subsequently treated in the UL study.

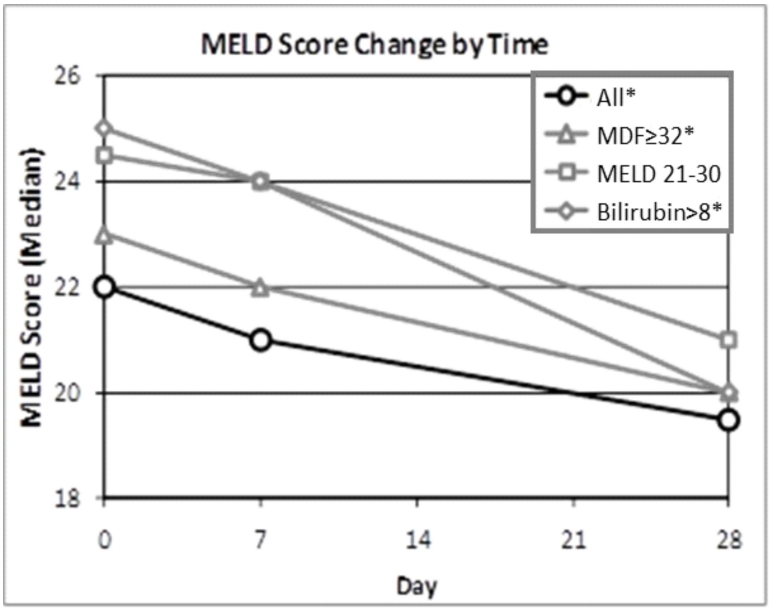
Bilirubin

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 the liver is functioning. Elevated bilirubin levels usually signify liver dysfunction and disease. In this trial (shown in the chart below), patients treated with larsucosterol had a significant early reduction from baseline in bilirubin by Day 7. Patients with more elevated bilirubin at baseline (serum bilirubin >8 mg/dL) had a median reduction from baseline of 25% by Day 7 and 48% by Day 28.



**p<0.05 compared to baseline (Wilcoxon's Signed Rank Test)*

As discussed above, MELD is another commonly used scoring system used to assess the severity and prognosis of AH patients. Patients with MELD scores of 11-20 are classified as having moderate AH and patients with MELD scores of 21-30 are classified as having severe AH. As with Lille scores, the lower the MELD score, the better the prognosis for the AH patient. In this trial (shown in the chart below), the median reduction from baseline in MELD among all larsucosterol treated patients was >2 points and among those with baseline bilirubin levels >8 mg/dL was 5 points by Day 28.



**p<0.05 compared to baseline (Wilcoxon's Signed Rank Test)*

MELD is calculated based on (a) bilirubin, (b) serum creatinine (sCr), and (c) International Normalized Ratio (INR), which is a measure of prothrombin time.

Safety and Pharmacokinetics

In the Phase 2a study of larsucosterol in AH, larsucosterol was well tolerated at all doses tested. There were no drug-related serious adverse events and only three adverse events designated as possibly or probably related to larsucosterol: one occurrence of moderate generalized pruritus, one mild rash and one grade two alkaline phosphatase elevation. There were no discontinuations, early withdrawals or termination of study drug or study participation due to adverse events. All patients treated with larsucosterol survived through the 28-Day follow-up period. Drug exposures were dose proportional and were not affected by the severity of the disease.

In December 2020, we announced that the FDA had granted larsucosterol Fast Track Designation for the treatment of AH. 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.

In January 2021, we announced the dosing of the first patient in our Phase 2b study in patients with severe AH (AHFIRM). AHFIRM is a randomized, double-blind, placebo-controlled, international, multi-center Phase 2b study to evaluate the safety and efficacy of larsucosterol in approximately 300 patients with severe AH. The study is comprised of three arms targeting approximately 100 patients each: (1) Placebo plus supportive care, with or without methylprednisolone capsules at the investigators' discretion; (2) larsucosterol (30 mg); and (3) larsucosterol (90 mg). Patients in the larsucosterol arms receive the same supportive care without steroids. In order to maintain blinding, patients in the two active arms receive matching placebo capsules if the investigator prescribes steroids. Patients receive an intravenous (IV) dose of larsucosterol or placebo (sterile water) on Day 1 and a second identical IV dose on Day 4 if they are still hospitalized. The primary outcome measure will be the 90-Day incidence of mortality or liver transplantation for patients treated with larsucosterol compared to those treated with placebo. Secondary endpoints include the difference in 90-Day mortality between patients treated with larsucosterol compared to those treated with placebo, the difference in 28-Day mortality or liver transplantation for patients treated with larsucosterol compared to those treated with placebo, and the difference in mortality between patients treated with larsucosterol compared to those treated with placebo. We now have over 60 clinical trial sites across the United States, U.K., E.U. and Australia. We currently expect to enroll the last patient in the AHFIRM trial in the second quarter of 2023, which should enable top-line results to be reported in the second half of 2023.

Phase 1 trials of larsucosterol administered through injection have supported the development of larsucosterol in AH. The initial Phase 1 trial in healthy subjects was a single-site, randomized, double-blinded, placebo-controlled, single-ascending-dose study that evaluated the safety, tolerability and PK of intramuscular (IM) injected larsucosterol. The 24-subject study (16 healthy volunteers on larsucosterol and 8 on placebo) of four escalating dose levels resulted in dose proportional systemic exposure of larsucosterol. Larsucosterol was well-tolerated at all dose levels, with no serious treatment-related adverse events reported. We also conducted a multiple-dose study involving 10 healthy subjects, in which participants received IM-injected larsucosterol for five consecutive days (8 subjects on larsucosterol, 2 on placebo) using the next to highest dose from the single dose study. No serious treatment related adverse events were reported, no subjects withdrew from the study, no accumulation in plasma concentrations were observed with repeat dosing, and the pain scores and injection site reactions were minimal. We also conducted a single-ascending dose intravenous (IV) infusion study with 16 healthy subjects and observed no treatment-related serious adverse events. The systemic exposure following IV infusion was dose proportional.

A Phase 1 drug-drug interaction study conducted in healthy subjects demonstrated that neither orally administered nor intravenously injected larsucosterol at doses tested affected the safety and PK of midazolam, a drug metabolized by CYP3A4, which is one of the important enzymes associated with clinically relevant drug-drug interactions.

We also conducted a Phase 1b study with injected larsucosterol in patients with impaired kidney function (stage 3 and 4 chronic kidney disease (CKD)) and matched control subjects (MCS), matched by age, body mass and gender with normal kidney function. This study was a single-site, open-label, single-ascending-dose study in two successive cohorts (first a low dose of 30 mg and then a high dose of 120 mg) evaluating safety and PK of intramuscular injected larsucosterol. The low dose cohort consisted of 6 patients with CKD and 3 MCS; the high dose cohort consisted of 5 CKD patients and 3 MCS. In this trial, larsucosterol was well tolerated among all subjects and the PK parameters between the kidney function impaired patients and the MCS were comparable.

Chronic Liver Disease Program with Orally Administered Larsucosterol

Market Opportunity. 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. Non-alcoholic steatohepatitis (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 treatment of NAFLD or NASH. In addition to these liver diseases, there are a number of orphan liver diseases for which we may seek to develop larsucosterol.

Clinical Program. In 2020, we completed a Phase 1b randomized, multi-center, and open-label clinical study in the United States to evaluate safety, PK and signals of biological activity of larsucosterol in NASH patients with stage 1-3 fibrosis. Larsucosterol (at doses of 50 mg QD, 150 mg QD and 300 mg BID) was administered orally for 28 days with 20 patients or more per dose group for

a total of 65 patients in the trial. Key endpoints included safety and PK, and clinical chemistry/efficacy signals, such as liver enzymes (ALT, AST and GGT), serum lipids (e.g., triglycerides), biomarkers (e.g., CK-18s, inflammatory cytokines), and insulin resistance (i.e., HOMA-IR), as well as liver fat content and liver stiffness by imaging (e.g., MRI-PDFF (as defined below) and FibroScan®).

Both the 50 mg and 600 mg dose groups showed a statistically significant median reduction at Day 28 from baseline of serum alanine aminotransferase ("ALT") levels at -16% and -17%, respectively. The 600 mg dose group also showed statistically significant median reductions at Day 28 from baseline of serum aspartate aminotransferase ("AST") (-18%) and gamma-glutamyl transferase ("GGT") (-8%), and the 50 mg dose group had a statistically significant reduction at Day 28 from baseline in liver stiffness as measured by Fibroscan (-10%).

Patients in the 50 mg or 150 mg dose groups also had statistically significant median reduction at Day 28 from baseline of serum triglycerides (-13% in the 50 mg group) or LDL-C (-11% in the 150 mg group). Patients with elevated baseline triglycerides (≥200 mg/dL; n=16) across all dose groups had a median reduction at Day 28 from baseline of -24% ($p < 0.01$). Furthermore, patients in the 50 mg and 150 mg groups had 22% and 18% median reductions (not statistically significant) of HOMA-IR from baseline respectively after 4 weeks of daily oral dosing of larsucosterol. The 600 mg group did not show a change in HOMA-IR.

At Day 28, 43% of patients in all three dose groups showed ≥ 10% liver fat reduction from baseline as measured by magnetic resonance imaging - proton density fat fraction (MRI-PDFF). In this subgroup, there was a significant reduction from baseline in median liver fat content (-18%, -19%, and -23%, in the 50 mg, 150 mg and 600 mg groups respectively). The reduction of liver fat content was accompanied by a significant median reduction from baseline of serum ALT (-21%, -19%, and -32%, in the 50 mg, 150 mg and 600 mg groups respectively), as well as both CK-18, M30 and M65 in the 50 mg and 600 mg groups.

Larsucosterol was well tolerated at all three doses evaluated. There were no serious adverse events reported during the study, and no discontinuations, early withdrawals or termination of study drug or study participation due to adverse events. PK parameters after repeat dosing were comparable to those after a single dose (from a prior study), indicating no accumulation of the drug after repeat dosing. We are working with a number of disease experts to determine next steps for larsucosterol in NASH.

We have completed multiple Phase 1 trials in healthy subjects with orally administered larsucosterol. These include single-ascending-dose and multiple-ascending-dose studies as well as a food effect study. In all of these studies larsucosterol was well-tolerated at all dose levels, with no serious treatment-related adverse events reported. Dose-related increases in plasma concentrations were observed and no accumulation in plasma concentrations or food effects were observed with repeat dosing.

We also conducted a Phase 1b trial in cirrhotic and non-cirrhotic NASH patients and matched control subjects ("MCS") (matched by age, body mass index and gender with normal liver function) utilizing orally administered larsucosterol. This was an open-label, single-ascending-dose safety and PK study conducted in Australia in two successive dose cohorts (first a low dose of 50 mg and then a high dose of 200 mg). Both cohorts consisted of 10 NASH patients and 6 MCS. Data from this study were presented at the International Liver Congress™ 2017 organized by the European Association for the Study of the Liver (EASL) in Amsterdam in April 2017. All patients and MCS in this study tolerated larsucosterol well. One patient (with a prior history of arrhythmia and an ongoing viral infection) in the high dose cohort experienced a serious adverse event (i.e., shortness of breath), which occurred without unusual biochemical changes and resolved without intervention but was considered possibly treatment related by the physician due to its temporal association with dosing. In both low and high dose cohorts, the PK parameters were comparable between the NASH patients and the MCS. In addition, the systemic exposure following the low and high doses of larsucosterol was dose dependent.

While this study was not designed to assess efficacy, we observed statistically significant reductions from baseline levels of several biomarkers after both doses of larsucosterol. A single oral dose of larsucosterol significantly reduced the levels of both full-length (M65) and cleaved (M30) cytokeratin-18 (CK-18), bilirubin, hsCRP, and IL-18 in these subjects. The mean reduction of full-length CK-18 (a generalized cell death marker) at the measured time point of greatest effect (12 hours after dosing) was 33% in the low dose cohort and 41% in the high dose cohort. The mean decrease of cleaved CK-18 (a cell apoptosis marker) at the measured time point of greatest effect (12 hours after dosing) was 37% in the low dose cohort and 47% in the high dose cohort. The mean reduction of total bilirubin (a liver function marker) at the measured time point of greatest effect (12 hours after dosing) was 27% in the low dose cohort and 31% in the high dose cohort. The mean decrease of high sensitivity C-Reactive Protein (hsCRP) (a marker of inflammation) at the measured time point of greatest effect (24 hours after dosing) was 8% in the low dose cohort and 13% in the high dose cohort. The mean decrease of IL-18 (an inflammatory mediator) at the measured time point of greatest effect (8 hours after dosing) was 4% in the low dose cohort and 8% in the high dose cohort.

We also conducted a Phase 1b open-label, multi-center U.S. study to evaluate the safety, tolerability, and pharmacokinetics (PK) of larsucosterol in subjects with moderate (Child-Pugh B scores, n=10) and severe (Child-Pugh C scores, n=7) hepatic function impairment (HI), and MCS (n=10) with normal hepatic function. Each subject received a single oral dose of 200 mg larsucosterol. Results from this study were presented at the International Liver Conference 2021 (EASL). Larsucosterol 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 larsucosterol 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 larsucosterol in subjects with HI resulted in statistically significant median reductions from baseline of the apoptosis biomarker M30 (cCK-18) at 12 hours post-dose.

Collectively, the biological signals observed in NASH and HI patients plus results from our animal models and cell culture studies suggest potential therapeutic activity of larsucosterol for patients with liver diseases. However, additional studies are required to evaluate the safety and efficacy of larsucosterol, and there is no assurance that these biomarker, clinical chemistry and liver imaging effects will be associated with clinically relevant benefits, or that larsucosterol will demonstrate safety or efficacy in treating liver diseases in our ongoing or future trials.

Approved and Commercial Pharmaceutical Products

1. Full Prescribing Information, including the Boxed Warning, is available at www.posimir.com.
2. DURECT to receive low double-digit to mid-teen royalties on net product sales of POSIMIR plus up to $122 million in additional milestone payments.
3. DURECT to receive earn-outs or royalties based on net sales of PERSERIS and Methydur. PERSERIS prescribing information, including BOXED WARNING and Medication Guide visit www.perseris.com.

POSIMIR® (bupivacaine solution)

POSIMIR (bupivacaine solution) for infiltration use is a novel and proprietary product that combines the strength of 660 mg of bupivacaine base with the innovative SABER® platform technology, enabling continuous sustained delivery of a non-opioid local analgesic over three days in adults, which we believe coincides with the time period of the greatest need for post-surgical pain control in most patients. POSIMIR contains more bupivacaine than any other approved single-dose sustained-release bupivacaine product. At the end of surgery, POSIMIR is administered into the subacromial space under direct arthroscopic visualization, where it continuously releases bupivacaine for 72 hours or more.

In February 2021, the FDA approved POSIMIR for infiltration use 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.

In December 2021, we entered into the Innocoll Agreement with Innocoll. Pursuant to the Innocoll Agreement, we granted to Innocoll an exclusive, royalty-bearing, sublicensable right and license to develop, manufacture and commercialize POSIMIR in the United States. The Innocoll Agreement provides for the assignment of our supply agreement with a contract manufacturing organization to Innocoll and also provides Innocoll with the right, within the United States, to expand the approved indications of POSIMIR. We retain, outside the United States, all of the global rights to POSIMIR. Innocoll paid us an initial non-refundable, upfront fee of $4.0 million as well as a fee in the amount of $1.3 million primarily to cover the manufacturing supplies and excipients and certain equipment transferred to Innocoll pursuant to the terms of the Innocoll Agreement, and certain recently incurred DURECT expenses the parties negotiated for Innocoll to reimburse. In the fourth quarter of 2021, we recognized $4.1 million as collaborative research and development and other revenue, $1.1 million as product revenue, and a reduction of $0.1 million in net equipment. At December 31, 2021, we included $5.3 million due from Innocoll in accounts receivable on our balance sheet; these funds were received in January 2022. In August 2022, we were issued a new patent by the U.S. Patent and Trademark Office, extending U.S. patent coverage of POSIMIR to at least 2041, resulting in an $8.0 million milestone payment by Innocoll to the Company. In September 2022, Innocoll launched POSIMIR in the U.S., triggering a $2.0 million milestone payment to the Company for the first commercial sale of POSIMIR. As the commercial launch of POSIMIR progresses, we will also earn low double-digit to mid-teen royalties on net product sales of POSIMIR in the U.S. We may earn additional milestone payments up to $122.0 million in the aggregate, depending on the achievement of certain commercial, regulatory and intellectual property milestone payments with respect

to POSIMIR. Pursuant to the terms of the Innocoll Agreement, except as otherwise expressly provided in the Innocoll Agreement, Innocoll is responsible for expenses relating to the manufacturing, development and commercialization of POSIMIR in the United States.

PERSERIS™(risperidone)

In September 2017, we entered into an agreement with Indivior, under which we assigned to Indivior certain patents that may provide further intellectual property protection for PERSERIS, Indivior's extended-release injectable suspension for the treatment of schizophrenia in adults. In consideration for such assignment, Indivior made non-refundable upfront and milestone payments to DURECT totaling $17.5 million. Additionally, under the terms of the agreement with Indivior, DURECT receives quarterly earn-out payments that are based on a single-digit percentage of U.S. net sales of PERSERIS into 2026. Indivior commercially launched PERSERIS in the U.S. in February 2019.

ORADUR™-ADHD Program

We developed a proprietary drug product for the treatment of ADHD called Methydur in collaboration with Orient Pharma, a diversified multinational pharmaceutical, healthcare and consumer products company with headquarters in Taiwan. We have licensed worldwide Methydur rights to OP and they launched Methydur commercially in Taiwan in September 2020. OP may seek commercialization partners in other countries throughout the world, including China and the U.S. We receive a single-digit royalty on sales of Methydur by OP or its commercialization partners as well as potential milestones and sub-license fees.

Drug Delivery Technologies and Programs

Our drug delivery technologies are designed to deliver the right drug to the right place, in the right amount and at the right time to treat a variety of chronic, acute and episodic diseases and conditions. We aim to improve therapy for a given disease or patient population by controlling the rate and duration of drug administration. In addition, if advantageous for the therapy, our technologies can target the delivery of the drug to its intended site of action.

Our technologies are suitable for providing long-term drug therapy because they can often store highly concentrated, stabilized drugs in a small volume and protect the drug from degradation by the body. This, in combination with the ability to continuously deliver desired doses of a drug, can extend the therapeutic value of a wide variety of drugs, including, in some cases, those which would otherwise be ineffective, too unstable, too potent or cause adverse side effects. In some cases, delivering the drug directly to the intended site of action can improve efficacy while minimizing unwanted side effects elsewhere in the body, which may limit the long-term use of many drugs. Our technologies may thus provide better therapy for chronic diseases or conditions, or for certain acute conditions where longer drug dosing is required or advantageous, by replacing multiple injection therapy or oral dosing, improving drug efficacy, reducing side effects and ensuring dosing compliance. Our technology may thereby improve patients' quality of life by eliminating more repetitive treatments, reducing dependence on caregivers and allowing patients to lead more independent lives.

We currently focus our drug delivery technology efforts around our SABER and CLOUD Bioerodible Injectable Depot Systems. SABER uses a high viscosity base component, such as sucrose acetate isobutyrate (SAIB), to provide controlled release of a drug. When the high viscosity SAIB is formulated with drug, biocompatible excipients and other additives, the resulting formulation is easily injectable with standard syringes and needles. After injection of a SABER formulation, the excipients diffuse away over time, leaving a viscous depot which provides controlled sustained release of drug. CLOUD is a class of bioerodible injectable depot technology which generally does not contain SAIB but includes various other release rate modifying excipients and/or bioerodible polymers to achieve the delivery of drugs for periods of days to months from a single injection.

The SABER technology is the basis of POSIMIR (described above). The SABER technology is also utilized in certain feasibility programs.

Product Revenues

We also currently generate product revenue from the sale of two product lines:

- ALZET® osmotic pumps which are used for animal research; and
- certain key excipients that are included in Methydur and one excipient that is included in POSIMIR and in a marketed animal health product.

Because we consider our core business to be developing and commercializing pharmaceuticals, we do not intend to significantly increase our investments in or efforts to sell or market any of our existing product lines. However, we expect that we will continue to make efforts to increase our revenues related to collaborative research and development by extending and expanding our current collaborations as well as entering into additional research and development agreements with third-party collaborators to develop product candidates based on our drug delivery technologies.

Operating Results

Since our inception in 1998, we have generally had a history of operating losses. At September 30, 2022, we had an accumulated deficit of $550.9 million. Our net losses were $2.5 million and $24.9 million for the three and nine months ended

September 30, 2022 compared with net losses of $10.0 million and $29.3 million for the corresponding periods in 2021. These losses have resulted primarily from costs incurred to research and develop our product candidates and to a lesser extent, from selling, general and administrative costs associated with our operations and product sales. We expect our research and development expenses in the near future to increase compared to the third quarter of 2022 as we continue to incur research and development expenses related to larsucosterol. We expect our selling, general and administrative expenses in the near future to be comparable to the third quarter of 2022. However, we expect to incur continuing losses and negative cash flows from operations for the foreseeable future.

Critical Accounting Policies and Estimates

The preparation of financial statements in conformity with U.S. generally accepted accounting principles requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the dates of the financial statements and the reported amounts of revenues and expenses during the reporting periods. The most significant estimates and assumptions relate to revenue recognition, prepaid and accrued contract research expenses, and stock-based compensation. Actual amounts could differ significantly from these estimates. There have been no material changes to our other critical accounting policies and estimates as compared to the disclosures in our annual report on Form 10-K for the year ended December 31, 2021.

Results of Operation

Three and nine months ended September 30, 2022 and 2021

Collaborative research and development and other revenue

We recognize revenues from collaborative research and development activities and service contracts. Collaborative research and development and other revenue primarily represents reimbursement of qualified expenses related to collaborative agreements with various third parties to research, develop and commercialize potential products using our drug delivery technologies, and revenue from the recognition of upfront fees and milestone payments in connection with our collaborative or license agreements.

We expect our collaborative research and development and other revenues to fluctuate in future periods pending our efforts to enter into potential new collaborations, our existing third-party collaborators' commitment to and progress in the research and development programs, and any royalty or earn-out revenue recognized from collaborators or counterparties.

The collaborative research and development and other revenues associated with our major collaborators or counterparties were $10.6 million and $11.7 million for the three and nine months ended September 30, 2022 compared with $443,000 and $1.8 million for the corresponding periods in 2021. The collaborative research and development and other revenues in the three and nine months ended September 30, 2022 included $8.0 million of patent milestone revenue and $2.0 million of first commercial sale milestone revenue compared with zero in the corresponding periods in 2021. In addition, the collaborative research and development and other revenues included (a) amounts related to earn-out revenue from Indivior UK Limited (Indivior) with respect to PERSERIS net sales; (b) feasibility programs and research and development activities funded by our collaborators, (c) royalty revenue from Orient Pharma with respect to Methydur net sales and (d) royalty revenue from Innocoll with respect to POSIMIR net sales.

Product revenue

A portion of our revenues is derived from product sales, which include our ALZET mini pump product line, and certain excipients that are included in Methydur and in an animal health product. Net product revenues were $1.4 million and $4.3 million for the three and nine months ended September 30, 2022 compared with $1.7 million and $4.9 million for the corresponding periods in 2021. The decreases in the three and nine months ended September 30, 2022 were primarily attributable to lower revenue from our ALZET mini pump product line as a result of lower units sold, partially offset by higher revenue from certain excipients that are included in Methydur and in an animal health product compared to the corresponding periods in 2021.

Cost of product revenues

Cost of product revenues were $345,000 and $1.1 million for the three and nine months ended September 30, 2022 compared with $364,000 and $1.1 million for the corresponding periods in 2021. Cost of product revenues in the three months ended September 30, 2022 decreased slightly primarily due to lower units sold from our ALZET product line, partially offset by higher costs of goods associated with certain excipients that are included in Methydur and in an animal health product, compared to the corresponding periods in 2021. Stock-based compensation expense recognized related to cost of product revenues was $5,000 and $15,000 for the three and nine months ended September 30, 2022 compared to $6,000 and $17,000 for the corresponding periods in 2021.

As of September 30, 2022, we had 10 manufacturing employees compared with 10 as of September 30, 2021. We expect the number of employees involved in manufacturing will remain comparable in the near future.

Research and development

Research and development expenses are primarily comprised of salaries, benefits, stock-based compensation and other compensation cost associated with research and development personnel, overhead and facility costs, preclinical and non-clinical development costs, clinical trial and related clinical manufacturing costs, contract services, and other outside costs.

Research and development expenses were $9.9 million and $26.9 million for the three and nine months ended September 30, 2022 compared to $8.0 million and $23.4 million for the corresponding periods in 2021. We incurred higher research and development costs associated with larsucosterol and the depot injectable programs, partially offset by lower research and development costs associated with POSIMIR and other research programs in the three and nine months ended September 30, 2022 compared to the corresponding periods in 2021, as more fully discussed below. Stock-based compensation expense recognized related to research and development personnel was $292,000 and $918,000 for the three and nine months ended September 30, 2022 compared to $317,000 and $952,000 for the corresponding periods in 2021. As of September 30, 2022, we had 43 research and development employees compared with 46 as of September 30, 2021. We expect research and development expenses in the near future to increase compared to the third quarter of 2022 as we expect to incur higher research and development expenses for larsucosterol.

	Three months ended September 30,		Nine months ended September 30,	
	2022	2021	2022	2021
Larsucosterol	$ 9,321	$ 6,879	$ 24,683	$ 18,350
Depot injectable programs	367	341	1,173	1,044
POSIMIR	27	619	517	3,078
Others	166	184	536	959
Total research and development expenses	$ 9,881	$ 8,023	$ 26,909	$ 23,431

Larsucosterol

Our research and development expenses for larsucosterol were $9.3 million and $24.7 million in the three and nine months ended September 30, 2022 compared to $6.9 million and $18.4 million for the corresponding periods in 2021. The increases in the three and nine months ended September 30, 2022 were primarily due to higher clinical trial related expenses, higher contract manufacturing expenses and higher employee-related costs for larsucosterol compared with the corresponding periods in 2021.

We continue to assess the impact of the COVID-19 outbreak on our business, including our larsucosterol Phase 2b trial in alcohol-associated hepatitis; COVID-19 may affect our ability to initiate and/or complete recruitment and data analysis for our clinical trials, including larsucosterol trials, in our planned timeframe.

Depot injectable programs

Our research and development expenses for depot injectable programs were $367,000 and $1.2 million in the three and nine months ended September 30, 2022 compared to $341,000 and $1.0 million for the corresponding periods in 2021. The increase in the three months ended September 30, 2022 was primarily due to higher employee-related costs and higher outside expenses for these programs compared with the corresponding period in 2021. The increase in the nine months ended September 30, 2022 was primarily due to higher employee-related costs, partially offset by lower outside expenses for these programs compared with the corresponding period in 2021.

POSIMIR

Our research and development expenses for POSIMIR were $27,000 and $517,000 in the three and nine months ended September 30, 2022 compared to $619,000 and $3.1 million for the corresponding periods in 2021. The decrease in the three months ended September 30, 2022 was primarily due to lower manufacturing supplies and lower employee related costs for this program compared with the corresponding period in 2021. The decrease in the nine months ended September 30, 2022 was primarily due to lower consulting expenses and employee-related costs for this program compared with the corresponding period in 2021.

Other DURECT research programs

Our research and development expenses for all other programs were $166,000 and $536,000 in the three and nine months ended September 30, 2022 compared to $184,000 and $959,000 for the corresponding periods in 2021. The decreases in the three and nine months ended September 30, 2022 was primarily due to lower employee-related costs associated with these programs compared with the corresponding periods in 2021.

We cannot reasonably estimate the timing and costs of our research and development programs due to the risks and uncertainties associated with developing pharmaceuticals as outlined in the “Risk Factors” section of this report. The duration of development of our research and development programs may span as many as ten years or more, and estimation of completion dates or costs to complete are highly speculative and subjective due to the numerous risks and uncertainties associated with developing pharmaceutical products, including significant and changing government regulation, the uncertainties of future preclinical and clinical study results, uncertainties related to COVID-19, the uncertainties with our collaborators’ commitment to and progress in the programs and the uncertainties associated with process development and manufacturing as well as sales and marketing. In addition, with respect to our development programs subject to third-party collaborations, the timing and expenditures to complete the programs are subject to the control of our collaborators. Therefore, we cannot reasonably estimate the timing and costs of the efforts necessary to complete the research and development programs. For additional information regarding these risks and uncertainties, see “Risk Factors” below.

Selling, general and administrative. Selling, general and administrative expenses are primarily comprised of salaries, benefits, stock-based compensation and other compensation costs associated with finance, legal, business development, sales and marketing and other administrative personnel, overhead and facility costs, and other general and administrative costs.

Selling, general and administrative expenses were $3.9 million and $11.6 million in the three and nine months ended September 30, 2022 compared to $3.2 million and $9.9 million for the corresponding periods in 2021. The increases in the three and nine months ended September 30, 2022 were primarily due to higher patent expenses as well as higher employee expenses compared to the corresponding periods in 2021. Stock-based compensation expense recognized related to selling, general and administrative personnel was $281,000 and $941,000 for the three and nine months ended September 30, 2022 compared to $330,000 and $1.1 million for the corresponding periods in 2021.

We had 26 selling, general and administrative employees as of September 30, 2022 compared with 23 as of September 30, 2021. We expect selling, general and administrative expenses in the near future to be comparable to the third quarter of 2022.

Other income (expense). Interest and other income was $284,000 and $465,000 for the three and nine months ended September 30, 2022 compared to $34,000 and $110,000 for the corresponding periods in 2021. The increases in the three and nine months ended September 30, 2022 were primarily due to higher interest rates associated with our cash and investments compared with the corresponding periods in 2021.

Interest and other expense was $623,000 and $1.7 million for the three and nine months ended September 30, 2022 compared to $553,000 and $1.6 million for the corresponding periods in 2021. The increases in the three and nine months ended September 30, 2022 were primarily due to higher interest rates on our term loan compared with the corresponding periods in 2021.

Liquidity and Capital Resources

We had cash, cash equivalents and investments totaling $52.0 million at September 30, 2022 compared to cash, cash equivalents, cash held in escrow and investments of $70.0 million at December 31, 2021. These balances include $150,000 of interest-bearing marketable securities classified as restricted investments on our balance sheets as of September 30, 2022 and December 31, 2021. The decrease in cash, cash equivalents and investments was primarily due to cash used in ongoing operating activities and interest payments, partially offset by payments received from collaboration partners and customers. At December 31, 2021, we included $5.3 million due from Innocoll in accounts receivable on our balance sheet; these funds were received in January 2022.

We used $17.9 million of cash in operating activities for the nine months ended September 30, 2022 compared to $26.2 million for the corresponding period in 2021. The cash used for operations was primarily to fund operations as well as our working capital requirements, partially offset by the changes in accounts receivable, prepaid expenses and other assets, and accrued and other liabilities.

We generated $18.4 million of cash in investing activities for the nine months ended September 30, 2022 compared to $9.9 million for the corresponding period in 2021. The increase in cash provided by investing activities was primarily due to a decrease in net purchases of available-for-sale securities partially offset by a decrease in proceeds from maturities of available-sale-securities for the nine months ended September 30, 2022 compared with the corresponding period in 2021. In addition, we received $15 million of cash from sale of the LACTEL product line in the nine months ended September 30, 2021.

We received $59,000 of cash from financing activities for the nine months ended September 30, 2022 compared to $50.4 million for the corresponding period in 2021. The decrease in cash received from financing activities was primarily due to lower net proceeds from shares sold under our shelf registration statement as well as lower proceeds from the exercise of stock options in the nine months ended September 30, 2022 compared with the corresponding period in 2021. In February 2021, we completed an underwritten public offering of 20,364,582 shares of our common stock at a price of $2.2386 per share pursuant to an underwriting agreement with Cantor Fitzgerald & Co., raising total gross proceeds of approximately $45.6 million before deducting estimated offering expenses. Total stock issuance costs related to this financing were approximately $195,000, resulting in net proceeds of approximately $45.4 million. In the nine months ended September 30, 2021, we also raised net proceeds (net of commissions) of approximately $2.4 million from the sale of 950,009 shares of our common stock in the open market at a weighted average price of $2.60 per share pursuant to the 2018 Registration Statement (as defined below) and 2015 Sales Agreement (as defined below).

We anticipate that cash used in operating activities in the near future will increase compared to the third quarter of 2022 as we received an $8.0 million milestone payment from Innocoll during the three months ended September 30, 2022 and we continue to incur research and development expenses related to larsucosterol in the near future.

In July 2021, we filed a shelf registration statement on Form S-3 with the SEC (the "2021 Registration Statement") (File No. 333-258333), which upon being declared effective in August 2021, terminated our registration statement filed in August 2018 (the "2018 Registration Statement") (File No. 333-226518) and allowed us to offer up to $250.0 million of securities from time to time in one or more public offerings, inclusive of up to $75.0 million of shares of our common stock which we may sell, subject to certain limitations, pursuant to a sales agreement dated July 30, 2021 with Cantor Fitzgerald (the "2021 Sales Agreement"). The 2021 Sales Agreement replaced a prior sales agreement dated November 3, 2015 with Cantor Fitzgerald & Co. (the "2015 Sales Agreement").

As of November 1, 2022, we had up to $250.0 million of our securities available for sale under the 2021 Registration Statement, of which $75.0 million of our common stock are available pursuant to the 2021 Sales Agreement.

Any material sales in the public market of our common stock, under the 2021 Sales Agreement or otherwise under the 2021 Registration Statement, could adversely affect prevailing market prices for our common stock.

During the nine months ended September 30, 2022, there were no significant changes in our commercial commitments and contractual obligations as compared with the information presented in our Annual Report on Form 10-K for the year ended December 31, 2021.

The COVID-19 pandemic is continuing to impact our business in several ways. COVID-19 has had a negative impact on orders for our ALZET product line as many ALZET customers reduced their activities during the pandemic. For larsucosterol, we may continue to experience delays in patient enrollment in the Phase 2b AHFIRM clinical trial or disruptions in supplies of larsucosterol or other items required for clinical trials. Delays and potential disruptions would increase the overall costs of development of larsucosterol. We are actively monitoring the impact of COVID-19 and the possible effects on our financial condition, liquidity, operations, clinical trials, suppliers, industry and workforce. However, the full extent, consequences, and duration of COVID-19 and the resulting impact on the Company cannot currently be predicted. We will continue to evaluate the impact that these events could have on our operations, financial position, and the results of operations and cash flows. Additional volatility in capital markets and/or clinical trial delays resulting from the impacts of COVID-19 may also limit our ability to raise capital on acceptable terms, if at all.

We believe that our existing cash, cash equivalents and investments will be sufficient to fund our planned operations, existing debt and contractual commitments and planned capital expenditures through at least the next 12 months from September 30, 2022. We may consume available resources more rapidly than currently anticipated, resulting in the need for additional funding. Over the next twelve months, we anticipate a limited increase in revenues primarily from the launch of POSIMIR by Innocoll. However, we expect to incur continuing losses and negative cash flows from operations for the foreseeable future.

Depending on whether we enter into additional collaborative agreements in the near term and the extent to which we earn revenues from our collaborative agreements, we may decide to raise additional capital through a variety of sources in the short-term and in the long-term, including:

- the public equity markets;
- private equity financings;
- collaborative arrangements; and/or
- public or private debt.

There can be no assurance that we will enter into additional collaborative agreements or maintain existing collaborative agreements in the near term, will earn collaborative revenues or that additional capital will be available on favorable terms, if at all. If adequate funds are not available, we may be required to significantly reduce or refocus our operations or to obtain funds through arrangements that may require us to relinquish rights to certain of our products, technologies or potential markets, either of which could have a material adverse effect on our business, financial condition and results of operations. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of such securities would result in ownership dilution to our existing stockholders (assuming convertible debt securities were converted into shares).

Our cash and investments policy emphasizes liquidity and preservation of principal over other portfolio considerations. We select investments that maximize interest income to the extent possible given these two constraints. We satisfy liquidity requirements by investing excess cash in securities with different maturities to match projected cash needs and limit concentration of credit risk by diversifying our investments among a variety of high credit-quality issuers.

We are experiencing certain operational and other challenges as a result of COVID-19, which could delay or halt our research and development programs or clinical programs. See Item 1A - Risk Factors for further discussion of the current and expected impact on our business and programs.

Available information

Our corporate website address is www.durect.com. We use the investor relations page of our website for purposes of compliance with Regulation FD and as a routine channel for distribution of important information, including news releases, analyst presentations, financial information and corporate governance practices. Our filings with the SEC are posted on our website and

available free of charge as soon as reasonably practical after they are electronically filed with, or furnished to, the SEC. The SEC's website, www.sec.gov, contains reports, proxy statements and other information regarding issuers that file electronically with the SEC. The content on any website referred to in this Quarterly Report on Form 10-Q is not incorporated by reference in this Form 10-Q unless expressly noted. Further, the Company's references to website URLs are intended to be inactive textual references only.

Item 3. Quantitative and Qualitative Disclosures about Market Risk

As of September 30, 2022, our exposure to market risk has not changed materially since December 31, 2021. For more information on financial market risks related to changes in interest rates, reference is made to Item 7A. Quantitative and Qualitative Disclosures About Market Risk contained in Part II of our Annual Report on Form 10-K for the fiscal year ended December 31, 2021, filed with the SEC on March 8, 2022.

Item 4. Controls and Procedures

Evaluation of Disclosure Controls and Procedures: The Company's principal executive and principal financial officers reviewed and evaluated the Company's disclosure controls and procedures (as defined in Exchange Act Rule 13a-15(e)) as of the end of the period covered by this Quarterly Report on Form 10-Q. Based on that evaluation, the Company's principal executive and principal financial officers concluded that the Company's disclosure controls and procedures are effective at ensuring that information required to be disclosed by the Company in reports that the Company files or submits under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in SEC rules and forms, and is accumulated and communicated to management, including the Company's principal executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosure.

Changes in Internal Control Over Financial Reporting: There were no significant changes in the Company's internal control over financial reporting (as defined in Exchange Act Rule 13a-15(f)) during the Company's most recently completed fiscal quarter that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting.

PART II—OTHER INFORMATION

Item 1. Legal Proceedings

We are not a party to any material legal proceedings.

Item 1A. Risk Factors.

In addition to the other information in this Quarterly Report on Form 10-Q, a number of factors may affect our business and prospects. These factors include but are not limited to the following, which you should consider carefully in evaluating our business and prospects. If any of the following risks actually occur, our business, financial condition, results of operations and growth prospects may be materially and adversely affected.

Those risk factors below denoted with a "*" are newly added or have been materially updated from our Annual Report on Form 10-K filed with the Securities and Exchange Commission, or the SEC, on March 8, 2022.

Summary

•We are dependent on the success of larsucosterol (also called DUR-928) and the path to regulatory approval is uncertain; we cannot be certain that it will receive regulatory approval or be commercialized

•The FDA's Fast Track Designation of larsucosterol in AH may not lead to a faster development or regulatory review or approval

•Safety data and indications of activity from completed larsucosterol clinical trials may not predict safety, activity or efficacy in future trials

•Open-label trials of larsucosterol in NASH and AH have inherent limitations

•Ongoing and future clinical trials for larsucosterol may be delayed and may not demonstrate efficacy or safety

•We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates

•Key components of larsucosterol are provided by a limited number of suppliers, and supply shortages or loss of these suppliers could result in delays or interruptions in supply or increased costs

•The COVID-19 pandemic has impacted and may adversely impact our business for the foreseeable future, including posing challenges to conducting clinical trials

•We have a significant amount of debt. Compliance with repayment obligations and other covenants may be difficult; failure to fulfill our obligations may cause the repayment obligations to accelerate

•We will require and may have difficulty or be unsuccessful in raising needed capital in the future

•We do not control the commercialization of POSIMIR, PERSERIS or Methydur

•For certain of our product candidates, we depend to a large extent on third-party collaborators, and we have limited or no control over their development, sales, distribution, disclosure, regulatory strategy or potential commercialization

•Cancellation of third-party collaborations may adversely affect potential economic benefits

•If we do not enter into new collaboration agreements, our revenues and/or cash flows will be reduced relative to prior periods

•Our cash flows are likely to differ from our reported revenues and earnings

•Our business strategy includes entering into additional collaborative agreements to support development, clinical trials, manufacturing and commercialization of product candidates. We may not be able to successfully negotiate or enter into acceptable collaboration agreements

•Failure to comply with governmental regulations could materially harm our business

•We have a history of operating losses, expect to continue to have losses and may never achieve or maintain profitability and we may not successfully manage our company through varying business cycles including the COVID-19 pandemic

•We may develop our own sales force and commercial group to market future products, but we have limited sales and marketing experience and may not be able to do so effectively

•Write-offs related to impairment of goodwill, long-lived assets, inventories and other non-cash charges may adversely impact profitability and cause cash flows to differ from reported revenues

•Global credit and financial market conditions could negatively impact the value of our investments

•We depend upon key personnel who may terminate their employment with us at any time, and we may not be able to attract and retain sufficient qualified personnel on a timely basis, if at all

•Cyber-attacks or other failures in telecommunications or information technology systems could result in information theft, data corruption and significant disruption of our business operations

•Our corporate headquarters, certain manufacturing facilities and personnel are located in a seismically active area near wildfire zones; our business also involves environmental risks and risks related to handling regulated substances

•As a non-accelerated filer, we are not required to comply with the auditor attestation requirements of the Sarbanes-Oxley Act and, consequently, some investors may find our common stock less attractive

•If we are unable to protect, maintain or enforce our intellectual property rights or secure rights to third-party intellectual property, we may lose valuable assets, lose market share or incur costly litigation or our third-party collaborators may choose to terminate their agreements with us, which may depend on our intellectual property

•We may be sued by third parties claiming that our products or product candidates infringe on their IP rights, particularly because there is substantial uncertainty about the validity and breadth of biopharmaceutical patents

•Competitive products or technologies could impair our ability to establish, maintain or grow our business

•Our relationships with physicians, patients and third-party payers are subject to anti-kickback, fraud and abuse, privacy and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings

•We could be exposed to significant product liability claims and we are subject to healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages and reputational harm

•Healthcare reform measures could hinder or prevent our product candidates' commercial success

•Market acceptance of our products or product candidates is uncertain, and failure to achieve market acceptance or adequate reimbursement from third-party payers will harm our future revenues and profitability

•Inability to train physicians to use our products may prevent market acceptance of our products

•We may be adversely affected by the effects of inflation

•Risks related to actions on trade by the U.S. and foreign governments, new accounting pronouncements and legislative actions could adversely affect the Company's results of operations and financial condition

•Our stock price currently does not meet the minimum bid price for continued listing on Nasdaq and effecting a reverse stock split, if determined as necessary by our board of directors in its discretion, may not achieve one or more of our objectives, including retaining our Nasdaq listing

•Our operating history makes evaluating our stock difficult, the price of our stock may be volatile

•Investors may experience substantial dilution of their investment

•Our ability to use net operating losses and other tax attributes is uncertain and may be limited

•We have broad discretion over the use of our cash and investments, which may not always yield a favorable return

•Our certificate of incorporation, bylaws and Delaware law could discourage an acquisition of us

•Having Delaware as the exclusive forum for substantially all disputes between us and our stockholders could limit our stockholders' ability to obtain a favorable judicial forum for disputes

•Because the Company is a "smaller reporting company," we may take advantage of certain scaled disclosures available to us, resulting in holders of our securities receiving less Company information than they would receive from a public company that is not a smaller reporting company

Risks Related To Our Business

We are dependent on the success of larsucosterol and the path to regulatory approval is uncertain; we cannot be certain that it will receive regulatory approval or be commercialized

Our business depends substantially on the successful development of larsucosterol, which has completed multiple clinical trials, including a Phase 1b clinical trial in NASH and a Phase 2a clinical trial in AH, and is currently enrolling patients for a Phase 2b clinical trial (AHFIRM) in patients with severe AH. In AH and NASH, there are no currently approved drugs. Ongoing and future clinical trials will need to establish clinically and statistically significant proof of efficacy, and sufficient evidence of safety to support filing for regulatory approval and/or additional clinical trials and ultimately regulatory approval. Larsucosterol will require additional

development, including completion of ongoing clinical trials and potentially additional clinical trials as well as potentially further preclinical studies, and other non-clinical parameters, to obtain regulatory clearances before it can be commercialized. We will have to interact with the FDA and other regulatory agencies regarding important aspects of the clinical development program, potentially including the size and design of clinical trials, the specific primary and secondary endpoints for the clinical trials, inclusion and exclusion criteria, stopping rules, duration of follow up, size of the safety databases, statistical analysis plans and other matters. Positive results obtained during early development do not necessarily mean later development will succeed or that regulatory clearances or approvals will be obtained. Changes to any of these aspects of our clinical trial design could result in the requirement for additional trials or delay development and approval of larsucosterol. Our drug development efforts may not lead to commercial drugs, for several reasons such as if larsucosterol fails to be shown to be safe and effective or if we do not have adequate financial or other resources to advance larsucosterol through clinical development and the approval processes. We consider larsucosterol to be our lead and most important asset. If larsucosterol fails to demonstrate safety or efficacy at any time or during any phase of development, we would experience potentially significant delays in, or be required to abandon, development of larsucosterol, which would materially harm our business. Even if the Phase 2b AHFIRM trial successfully demonstrates a reduction in mortality or liver transplantation over placebo plus standard of care, (1) additional clinical trial(s) may be required to support an NDA filing and ultimately to support approval by FDA and/or other regulatory bodies; and (2) accelerated regulatory pathways (such as an FDA priority review designation) may not be available.

We do not anticipate that larsucosterol will be eligible to receive regulatory approval from the FDA or comparable foreign authorities and begin commercialization for a number of years, if ever. This uncertainty may make it difficult to predict the timing or expense required to obtain regulatory approval for larsucosterol. We also may need to revise our clinical development plans after trials have commenced or have been completed, which could add to the time and expense associated with the clinical development of larsucosterol. If we are unable to reach an agreement with the FDA or other regulatory agencies regarding clinical development plans for larsucosterol, we may curtail or limit our development activities for this product candidate. Even if we ultimately receive regulatory approval for larsucosterol, we or our potential future partners, if any, may be unable to commercialize it successfully for a variety of reasons. These include, for example, the availability of alternative, potentially superior or less expensive treatments, lack of cost-effectiveness, the lack of favorable access and/or commercial pricing, the cost or technical challenges of manufacturing the product on a commercial scale and competition with other treatments. The success of larsucosterol may also be limited by the prevalence and severity of any adverse side effects, including mortality. If we fail to obtain regulatory approval and successfully commercialize larsucosterol, we may be unable to raise sufficient capital or generate sufficient revenues to attain or maintain profitability, and our financial condition and stock price may decline.

The FDA's Fast Track Designation of larsucosterol may not lead to a faster development or regulatory review or approval

The FDA grants Fast Track Designation to therapies that are considered capable of addressing unmet medical needs and possess the potential to treat serious or life-threatening disease conditions in order to facilitate its development and expedite the review procedure. Even though larsucosterol has received Fast Track Designation for the treatment of AH, we may not experience a faster development process, review or approval compared to conventional FDA procedures, or receive FDA approval at all, in that indication or any other. A Fast Track Designation does not change the standards for approval. The FDA may also withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program.

In addition, the statutes and regulations that define the timelines and criteria for approval of drugs and biologics are subject to change by Congress and the responsible administrative agencies. For example, the Prescription Drug User Fee Act ("PDUFA") authorizes the FDA to collect fees and use them for the review of human drug applications and defines the review time targets for such applications. The current legislative authority for PDUFA will expire in September 2027. New legislation will then be required for the FDA to continue collecting prescription drug user fees in future fiscal years and for manufacturers to have clarity regarding the time the FDA will spend in review before granting regulatory approval. If PDUFA reauthorization is not completed in the future, the review and approval times for new drugs like larsucosterol could be significantly longer than currently expected, which could delay potential marketing approval and launch.

Safety data and indications of activity from completed Phase 1 and 2 clinical trials of larsucosterol may not predict safety, activity or therapeutic efficacy in future trials

Although Phase 1 and Phase 2 clinical trials of larsucosterol have shown positive initial data in AH patients, including reductions in bilirubin and MELD scores from baseline and promising Lille scores, and demonstrated in NASH patients that larsucosterol may lead to the reduction from baseline in liver enzymes, liver stiffness and serum lipids as well as certain biomarkers, such initial results, indications of activity and biomarker changes as well as favorable tolerability may ultimately not be correlated with treatment or improvement in the associated disease, and there is a risk that larsucosterol may not demonstrate therapeutic efficacy in larger placebo-controlled trials such as AHFIRM, despite encouraging initial data and improvements in biomarker levels in smaller, early trials. The failure of larsucosterol to show efficacy in one indication may negatively affect its perceived value in other indications, and the emergence of safety signals in ongoing or future clinical trials would significantly harm our business.

Open-label trials of larsucosterol in NASH and AH have inherent limitations

The most recently completed NASH and AH trials of larsucosterol were open-label trials with no control groups. Open label trials have inherent risk of bias given that the patients and physicians know that the patients received active study drug, which can lead to placebo effects. Trials without control groups have an inherent risk in that the comparisons used to determine the study drug's

effect and side effect profile are based on comparisons with baseline (pre-treatment) levels (for blood chemistry and biomarker endpoints) and/or with historical controls, which may not have been conducted under similar enough conditions to make accurate comparisons and/or draw accurate conclusions from those comparisons. Additionally, larger placebo-controlled clinical trials are required to evaluate the safety and efficacy of larsucosterol to treat any indication, including AH and NASH. There can be no assurance that ongoing or future studies will demonstrate the safety or efficacy of larsucosterol in a statistically significant or clinically meaningful manner.

Ongoing and future clinical trials for larsucosterol may be delayed and may not demonstrate efficacy or safety

The Phase 2b AHFIRM trial of larsucosterol in patients with AH is subject to potential delays resulting from the COVID-19 pandemic as well as timing of entering contracts with clinical sites and contract research organizations ("CROs"), obtaining institutional review board approvals and delays in other activities that need to be put in place prior to clinical trial initiation at each clinical trial site. Given uncertainty of COVID-19-related impacts on clinical trial sites in the U.S., U.K., E.U. and Australia, the timing of availability of top-line data from this trial cannot be predicted with certainty. There can be no assurance that the trial will enroll as anticipated if at all, and delays in enrollment could add to the costs and expenses of this trial and harm our business. There can also be no assurance that biological activity demonstrated in previous animal disease models or earlier clinical trials of larsucosterol will also be seen in ongoing trials or future clinical trials, or that any clinically relevant biological activity will be observed, or that enrollment rates will be favorable or that these additional trials will not identify safety issues. Failure of the AHFIRM trial to achieve desired results in its anticipated timeframe would negatively impact our business and ability to raise additional capital.

We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates

We may experience delays in completing our preclinical studies and initiating or completing clinical trials, and we may experience numerous unfavorable events during, or as a result of, any future clinical trials that we may conduct that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- regulators, institutional review boards ("IRBs"), or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at one or more prospective trial sites;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective CROs the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites. We may be forced to accept unfavorable contract provisions in such agreements based on country, territory or local laws or requirements of institutions or IRBs where important clinical investigators practice;
- clinical trials of our product candidates may produce negative or inconclusive results, clinical trial subjects receiving placebo or standard of care may experience better than expected outcomes, and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials or we may decide to abandon product development programs;
- non-compliance by clinical trial sites or clinical investigators with the study protocol or applicable laws;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, or participants may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- we may elect to, or regulators or IRBs or ethics committees may require us or our investigators to, suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; and
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or IRBs or ethics committees to suspend or terminate the trials, or reports may arise from preclinical or clinical testing of other therapies that raise safety or efficacy concerns about our product candidates.

We could encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions at which such trials are being conducted, by the Data Safety Monitoring Board for such trial or by the FDA or other regulatory authorities. Such authorities may impose such a suspension or termination or clinical hold due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site

by the FDA or other regulatory authorities, changes in clinical trial design, safety issues or adverse side effects, failure to demonstrate a benefit from using a product, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Further, the FDA may disagree with our clinical trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials.

Our product development costs will also increase if we experience delays in testing or regulatory approvals. We do not know whether any of our future clinical trials will begin as planned, or whether any of our current or future clinical trials will need to be restructured or will be completed on schedule, if at all. Significant preclinical study or clinical trial delays, including those caused by the COVID-19 pandemic, also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations. Any delays in our ongoing or future preclinical or clinical development programs may harm our business, financial condition and prospects significantly.

Key components of larsucosterol are provided by a limited number of suppliers, and supply shortages or loss of these suppliers could result in delays or interruptions in supply or increased costs

While we have entered into contract manufacturing agreements with multiple vendors for larsucosterol, we currently have a third-party sole supplier for GMP supplies of larsucosterol. This third party is our sole source for the drug product required for development and commercialization of this drug candidate.

The reliance on a sole or limited number of suppliers could result in:

•an inability to obtain an adequate supply of larsucosterol;

•delays associated with finding and contracting with a new supplier (if we can find one capable of replacing the old supplier and negotiate commercially reasonable terms) and then transferring the know-how and technology required to perform the services to the new supplier; and

•reduced control over pricing, quality and delivery time.

There can be no assurance that we will receive sufficient quantities of larsucosterol to commence and conduct the non-clinical trials, clinical trials and CMC activities we are planning, and delays in supply could delay development of larsucosterol. In addition, certain of our third-party manufacturers and suppliers may be experiencing delays as a result of the COVID-19 pandemic or have otherwise encountered delays in providing their goods and services. As a result, we may not be able to manufacture our product candidates for our clinical trials and conduct other research and development operations and maintain current clinical and pre-clinical timelines. In addition, if additional third parties in our supply chain are adversely impacted by restrictions resulting from the pandemic, including staffing shortages, raw material shortages, production slowdowns and/or disruptions in delivery systems, our supply chain may be disrupted in other ways, further limiting our ability to manufacture our product candidates for our clinical trials and conduct our research and development operations.

We have supply agreements in place for certain components of our products and product candidates, but do not have in place long term supply agreements with respect to all of the components of any of our products or product candidates. Therefore, the supply of a particular component could be terminated without DURECT's consent at any time without penalty to the supplier. In addition, we may not be able to procure required components or drugs from third-party suppliers at a commercially reasonable quantity, quality, cost and timing. In addition, certain of our suppliers may be experiencing delays as a result of the COVID-19 pandemic or have otherwise encountered delays in providing their services. Any interruption in the supply of single source components (including active pharmaceutical ingredients, excipients, or components like vials, stoppers, filters and the like), products or product candidates, could cause us to seek alternative sources of supply or attempt to manufacture these items internally if feasible. Furthermore, in some cases, we are relying on our third-party collaborators to procure supply of necessary components. If the supply of any components for our products or product candidates is interrupted, components from alternative suppliers may not be available in sufficient volumes or at acceptable quality levels within required timeframes, if at all, to meet our needs or those of our third-party collaborators. This could delay our ability to obtain commercial product supplies or complete development and obtain approval for commercialization and marketing of our product candidates, causing us to lose sales, incur additional costs, delay new product introductions and could harm our reputation and make access to capital more difficult, expensive or impossible. The COVID-19 pandemic has affected and is likely to continue to affect the manufacturing and shipment of goods globally. Many countries have imposed or are imposing certain restrictions on the movement of people and goods and may continue to lift and reimpose such restrictions as needed. Any delay in production or delivery of the components and drug substances used in our products or product candidates for any reason, including due to an extended closure of our suppliers' plants as a result of efforts to limit the spread of COVID-19, could adversely impact our business and hinder our growth.

The COVID-19 pandemic has impacted and may adversely impact our business for the foreseeable future, including posing challenges to conducting clinical trials

The global COVID-19 pandemic has disrupted our operations and delayed our clinical trials. In particular, the COVID-19 pandemic delayed the initiation of our AHFIRM Phase 2b clinical trial to evaluate the safety and efficacy of larsucosterol in severe AH patients, and it has delayed and may in the future delay the pace of enrollment in this trial and other clinical trials. As a result of the COVID-19 pandemic, there have been and may continue to be longer lead times required for acquiring components and supplies used in manufacturing of larsucosterol, and there have been periods of reduced demand for our ALZET products, which are used in scientific and pre-clinical research. In addition, COVID-19 may have an adverse impact on the economies and financial markets of many countries, resulting in a severe and prolonged global economic downturn that could continue to affect demand for our ALZET product line and impact our operating results. The COVID-19 pandemic may also adversely impact our ability to raise additional capital to provide sufficient funding to continue our product development efforts, including clinical trials. COVID-19 initially had an adverse impact on the capital markets and could again, which would make it more difficult for companies such as ours to access capital. The extent to which the pandemic impacts our operations will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration and severity of the pandemic, the impact of new variants of the virus, and the actions that may be required to contain the COVID-19 virus or treat its impact. As a result of the COVID-19 pandemic, we may continue to experience disruptions that could severely impact our business, preclinical studies and clinical trials including:

- delays or difficulties in enrolling patients in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by federal, state or local governments, employers and others or interruption of clinical trial subject visits and study procedures, which may impact the integrity of subject data and clinical study endpoints, the ability to collect, ship and analyze biological samples from clinical trial patients due to concerns about potential contamination of samples and/or exposure of clinical staff to patients with COVID-19;
- interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines;
- disruption or delays in manufacturing of clinical and commercial supplies due to issues experienced by our contract manufacturing organizations and/or shortages and delays in obtaining raw materials and supplies required in the manufacturing processes;
- interruption of or delays in receiving supplies of our products and product candidates from our contract manufacturing organizations due to staffing shortages, production slowdowns or stoppages, prioritization of pandemic-related activities over ours and disruptions in delivery systems;
- interruptions in preclinical studies due to restricted or limited operations at laboratory facilities;
- limitations on employee resources that would otherwise be focused on the conduct of our preclinical studies, clinical trials, and manufacturing activities including because of sickness of employees or their families or the desire of employees to avoid contact with groups of people; and
- material delays and complications with respect to our research and development programs.

Delays or difficulties in the enrollment of subjects in clinical trials may increase our overall development expenses and delay clinical trial data and receipt of necessary regulatory approvals

Successful and timely completion of clinical trials will require that we enroll a sufficient number of subjects and/or patients within a reasonable period of time. Enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, our ability to recruit clinical sites and the ability of clinical sites to successfully recruit subjects to participate in clinical trials. Initiation of and enrollment in many clinical trials has been and is being adversely affected by COVID-19, which has at times caused some institutions to stop enrolling patients, has created a large number of clinical trial proposals for potential clinical trial sites to review and consider, and has caused many individuals to avoid contact with hospitals or other healthcare providers. Additionally, some of the patients in our clinical trials, including AH patients, are hospitalized and concerns about exposure to COVID-19 limit clinical trial staff's access to patients, the frequency of interactions between patients and staff, the ability to obtain blood draws and other biological sample collection, and may limit the ability to ship samples to outside laboratories for analysis. In areas heavily impacted by COVID-19, there may be limited hospital staff available for clinical trial

activities due to staff becoming infected or due to de-prioritization of clinical trial activities. Trials may be subject to delays as a result of patient enrollment taking longer than anticipated or patient withdrawal. We may not be able to initiate or continue clinical trials for larsucosterol if we are unable to sign and maintain sufficient clinical sites, locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or other regulatory authorities or if we are unable to collect and analyze biological samples required for trial endpoints. It is possible that the inclusion and exclusion criteria for patients to be enrolled in these trials or COVID-19-related issues may make the trials more difficult to conduct or may significantly extend the time required for enrollment and the cost of these trials.

We cannot predict how successful we will be at enrolling patients in our clinical trials. Enrollment is affected by many factors including:

- the eligibility criteria for the trial in question;
- the prevalence and incidence of the conditions being studied;
- COVID-19-related challenges with patient access, hospital prioritization, clinical trial staff availability, ability to collect, ship and analyze patients' biological samples, availability of personal protective equipment, swabs, reagents and other materials and supplies;
- the perceived risks and benefits of our product candidates;
- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs or therapeutic biologics that may be approved for the indications we are investigating;
- the efforts to facilitate timely enrollment in clinical trials;
- competition for clinical sites and patients from other clinical trials;
- the willingness of potential clinical trial patients to provide informed consent to participate in the trial;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective patients.

Our inability to sign up and maintain sufficient clinical trial sites and/or enroll a sufficient number of patients for clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in these clinical trials may result in increased development costs for our drug candidates or delays in regulatory filings and approvals, which would cause the value of our company to decline and limit our ability to obtain additional financing.

The FDA or other regulatory agencies may require more information or clinical studies for all of our product candidates, and our product candidates may never be approved

The failure to adequately demonstrate the safety and effectiveness of a pharmaceutical product candidate under development to the satisfaction of FDA and other regulatory agencies will result in delays to the regulatory approval or non-approvability of our product candidates, and could materially harm our business. Clinical trials may not demonstrate the sufficient levels of safety and efficacy necessary to obtain the requisite regulatory approvals for our product candidates, or may require such significant numbers of patients or additional costs to make it impractical to satisfy the regulatory agency's requirements, and thus our product candidates may not be approved for marketing. During the review process, the FDA or other regulatory agencies may request additional information regarding the efficacy or safety of our product candidates, and providing such additional information could require significant additional work and expense, and take a significant amount of time, resulting in a material delay of approval or the failure to obtain approval or lead the company to abandon the development of that product candidate. During the review process, the FDA, or other regulatory agencies, may also request more information regarding the chemistry, manufacturing or controls related to our product candidates, and answering such questions could require significant additional work and expense, and take a significant amount of time, resulting in a material delay of approval or the failure to obtain approval or abandonment of the product candidate. Additionally, even if our product candidates receive FDA or other regulatory agency approval, the regulatory agency may require that we conduct additional clinical or non-clinical studies after such approval, place limitations on the use of our products in applicable labels, require marketing under a REMS program, include commercially unattractive language in the approved product label, delay approval to market our products or limit the indicated use of our products, which may harm our business and results of operations.

We have a significant amount of debt. Compliance with repayment obligations and other covenants may be difficult, and failure to fulfill our obligations under the applicable loan agreements may cause our repayment obligations to accelerate

In July 2016, we entered into a Loan and Security Agreement (as amended, the "Loan Agreement") with Oxford Finance LLC ("Oxford Finance"), pursuant to which Oxford Finance provided a $20 million secured single-draw term loan to us with an initial maturity date of August 1, 2020. The term loan was fully drawn at close and the proceeds may be used for working capital and general

business requirements. The term loan repayment schedule provided initially for interest only payments for the first 18 months, followed by consecutive monthly payments of principal and interest in arrears starting on March 1, 2018 and continuing through the maturity date of August 1, 2020. Following five amendments, we make interest only payments under the amended Loan Agreement until June 1, 2023 and the final maturity date of the loan is September 1, 2025. The Loan Agreement provides for a floating interest rate (7.95% initially and 9.86% as of September 30, 2022) based on an index rate plus a spread and an additional payment equal to 10% of the principal amount of the term loan, which is due when the term loan becomes due or upon the prepayment of the facility. Any increases in prevailing interest rates could increase our expenses under the Loan Agreement. If we elect to prepay the loan, there is also a prepayment fee between 0.75% and 2.5% of the principal amount of the term loan depending on the timing of prepayment. Our debt repayment obligations under the Loan Agreement, as amended, may prove a burden to the Company as they become due, particularly following the expiration of the interest-only period. Increased payment requirements that would start after June 2023 would increase our cash expenditures and require us to raise additional capital or renegotiate or refinance the Loan Agreement. There can be no assurance that additional capital will be available on acceptable terms, if at all, or that we would be able to successfully renegotiate or refinance the Loan Agreement on acceptable terms, if at all. If our debt repayments increase, we may be required to scale back development programs or other operations, which could have an adverse effect on our business.

The Loan Agreement contains customary events of default, including, among other things, our failure to fulfill certain of our obligations under the Loan Agreement and the occurrence of a material adverse change in our business, operations or condition (financial or otherwise), a material impairment of the prospect of repayment of any portion of the loan, the failure to deliver an unqualified audit report and board approved financial projections within time periods set forth in the Loan Agreement, or a material impairment in the perfection or priority of lender's lien in the collateral or in the value of such collateral. In the event of default by us under the Loan Agreement, the lender would be entitled to exercise its remedies thereunder, including the right to accelerate the debt, upon which we may be required to repay all amounts then outstanding under the Loan Agreement, which could harm our business, operations and financial condition.

In addition, the term loan is secured by substantially all of our assets, except that the collateral does not include any equity interests in the Company, any intellectual property (including all licensing, collaboration and similar agreements relating thereto), and certain other excluded assets. The Loan Agreement contains customary representations, warranties and covenants by us, which covenants limit our ability to convey, sell, lease, transfer, assign or otherwise dispose of certain of our assets; engage in any business other than the businesses currently engaged in by us or reasonably related thereto; liquidate or dissolve; make certain management changes; undergo certain change of control events; create, incur, assume, or be liable with respect to certain indebtedness; grant certain liens; pay dividends and make certain other restricted payments; make certain investments; make payments on any subordinated debt; and enter into transactions with any of our affiliates outside of the ordinary course of business or permit our subsidiaries to do the same. Complying with these covenants may make it more difficult for us to successfully execute our business strategy.

We will require and may have difficulty or be unsuccessful in raising needed capital in the future

Our business currently does not generate sufficient revenues to meet our capital requirements and we do not expect that it will do so in the near future. We have expended and will continue to expend substantial funds to conduct the research, development, manufacturing and clinical testing of our product candidates, funding and establishing additional clinical- and commercial-scale manufacturing arrangements and facilities, and to provide for the pre-commercial and commercial activities associated with the marketing, sales and distribution of our products and product candidates. We will require additional funds for these purposes. Additional funds may not be available on acceptable terms, if at all, and such availability will depend on a number of factors, some of which are outside of our control, including general capital markets conditions and investors' view of our prospects and valuation. If adequate funds are unavailable from operations or additional sources of financing or if our collaboration partners fail to pay us milestone payments, or we are unable to obtain adequate financing on a timely basis or to enter into agreements with collaboration partners, we may have to delay, reduce the scope of or eliminate one or more of the above-mentioned activities which would materially harm our business, financial condition and results of operations.

We believe that our cash, cash equivalents and investments and anticipated revenues will be adequate to satisfy our capital needs for at least the next 12 months from September 30, 2022. However, our independent auditors may not agree with this assessment, and our actual capital requirements will depend on many factors, including:

- continued progress and cost of our research and development programs;
- progress with preclinical studies and clinical trials;
- the time and costs involved in obtaining regulatory approvals, if any;
- costs involved in establishing manufacturing capabilities for pre-clinical, non-clinical, clinical and commercial quantities of our products and product candidates;
- success in entering into collaboration agreements and achieving milestones under such agreements;
- the continuation of our collaborative agreements that provide financial funding for certain of our activities;
- regulatory actions with respect to our and our collaborators' products and product candidates;
- costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing intellectual property rights;
- costs of developing sales, marketing and distribution channels and our ability and that of our collaborators to sell our products, products we have a financial interest in and eventually, product candidates;
- competing technological and market developments;
- market acceptance of our products, products we have a financial interest in and, eventually, product candidates;
- any failure to comply with the covenants in our debt instruments that results in acceleration of repayment obligations;
- impacts of the COVID-19 pandemic;
- costs for recruiting and retaining employees and consultants; and
- unexpected legal, accounting and other costs and liabilities related to our business.

We may consume available resources more rapidly than currently anticipated, resulting in the need for additional funding. We may seek to raise additional funds through equity or debt financings, convertible debt financings, collaborative arrangements with corporate collaborators or other sources, which, in each case, may be dilutive to existing stockholders and may cause the price of our common stock to decline. In addition, in the event that additional funds are obtained through arrangements with collaborators or other sources, we may have to relinquish rights to some of our technologies, products or product candidates that we would otherwise seek to develop or commercialize ourselves. If adequate funds are not available, we may be required to significantly reduce or refocus our product development efforts and other activities, resulting in delays in generating future revenue.

We do not control the commercialization of POSIMIR, PERSERIS or Methydur

We rely on Innocoll for the commercialization of POSIMIR. The current approved labeling for POSIMIR is limited, and Innocoll is responsible for completing post-marketing non-clinical studies and any additional studies required by FDA, and negative results from these studies could adversely affect commercialization of POSIMIR. Innocoll is also responsible for manufacturing POSIMIR. If Innocoll does not successfully grow POSIMIR sales, the royalty payments we receive under our agreement with them will be limited and we may not receive additional milestone payments from them. We rely on Indivior for the commercialization of PERSERIS. There can be no assurance that PERSERIS sales will maintain current levels or grow materially. If Indivior does not successfully grow PERSERIS sales, future earn-out payments we receive under our agreement with them will be limited. We rely on Orient Pharma for the commercialization of Methydur. If Orient Pharma does not successfully grow Methydur sales, the royalty payments we receive under our agreement with them will be limited. The sales of each of these products may be negatively impacted by the COVID-19 pandemic.

For certain of our product candidates, we depend to a large extent on third-party collaborators, and we have limited or no control over their development, sales, distribution and disclosure for those product candidates

Our performance for certain of our product candidates depends to a large extent on the ability of our third-party collaborators to successfully develop and obtain regulatory approvals. We have entered into agreements with Innocoll, Indivior and Orient Pharma under which we granted such third parties the right to develop, apply for regulatory approval for, market, promote or distribute certain products or product candidates, subject to payments to us in the form of product royalties, earn-out and other payments. We have limited or no control over the expertise or resources that any collaborator may devote to the development, clinical trial strategy, regulatory approval, marketing or sale of these product candidates, or the timing of their activities. Any of our present or future collaborators may not perform their obligations as expected. These collaborators may breach or terminate their agreement with us or otherwise fail to conduct their collaborative activities successfully and in a timely manner. Enforcing any of these agreements in the event of a breach by the other party could require the expenditure of significant resources and consume a significant amount of

management time and attention. Our collaborators may also conduct their activities in a manner that is different from the manner we would recommend or would have chosen, had we been developing such product candidates ourselves. Further, our collaborators may elect not to develop or commercialize product candidates arising out of our collaborative arrangements or not devote sufficient resources to the development, clinical trials, regulatory approval, manufacture, marketing or sale of these product candidates. If any of these events occur, we may not recognize revenue from the commercialization of our product candidates based on such collaborations. In addition, these third parties may have similar or competitive products to the ones which are the subject of their collaborations with us, or relationships with our competitors, which may reduce their interest in developing or selling our products or product candidates. We may not be able to control public disclosures made by some of our third-party collaborators, which could negatively impact our stock price.

Cancellation of third-party collaborations may adversely affect potential economic benefits

Third-party collaboration agreements typically allow the third party to terminate the agreement (or a specific program within an agreement) at will by providing notice. Termination can result from failure of the collaboration to achieve anticipated milestones, from changes in strategy of the other party or for other reasons. In these cases, the product rights revert to us or certain rights of the partner to use our proprietary technology are terminated. If there have been payments under such agreements that are being recognized over time, termination of such agreements (or programs) can lead to a near-term increase in our reported revenues resulting from the immediate recognition of the balance of such payments. Termination deprives us of potential future economic benefits under such agreements, and may make it more difficult, unattractive or impossible to enter into agreements with other third parties for use of the assets and/or technologies that were subject to the terminated agreement. For example, termination of our agreements with Innocoll or Orient Pharma could have negative effects on the Company.

If we do not enter into new collaboration agreements, our revenues and/or cash flows will be reduced relative to prior periods

Our revenues have been based to a significant extent on collaborative arrangements with third parties, pursuant to which we receive payments based on our performance of research and development activities set forth in these agreements. For example, approximately 58% of our total revenues in 2019 were derived from our collaboration agreement with Gilead. In June 2020, Gilead notified us that they were terminating this collaboration, resulting in accelerated recognition of $22.7 million in deferred revenue related to a nonrefundable upfront license fee and a milestone payment totaling $35.0 million that had previously been received. In addition, we have seen periodic fluctuations in revenues associated with our other collaboration agreements, which reflect the current development stage of the product candidates subject to those agreements, and our collaborator's needs for our services. Long-term growth of our collaboration revenues requires us to enter into new collaboration agreements, and there can be no assurance that we will do so. Even if we enter into new collaboration agreements, we may not be able to fulfill our obligations or attain milestones set forth in any specific agreement, which could cause our revenues and/or cash flows to fluctuate or be less than anticipated and may expose us to liability for contractual breach. In addition, these agreements may require us to devote significant time and resources to communicating with and managing our relationships with such collaborators and resolving possible issues of contractual interpretation which may detract from time our management would otherwise devote to managing our operations. Such agreements are generally complex and contain provisions that could give rise to legal disputes, including potential disputes concerning ownership of intellectual property. Such disputes can delay or prevent the development of potential new product candidates, or can lead to lengthy, expensive litigation or arbitration. In general, our collaboration agreements, may be terminated by the other party at will or upon specified conditions including, for example, if we fail to satisfy specified performance milestones or if we breach the terms of the agreement. Acquisitions of our collaborators or strategic changes or re-organizations or re-prioritizations of our collaborators can lead to turnover of program staff, a review of development programs and strategies by the acquirer, and other events that can disrupt a program, resulting in program delays or discontinuations.

If we do not enter into new collaboration agreements, our anticipated revenues and/or cash flows will be reduced relative to periods of increased research and development revenues, such as occurred in 2020.

Our cash flows are likely to differ from our reported revenues and earnings

Our revenues and earnings will likely differ from our cash flows from revenue-generating activities. Upfront payments received upon execution of collaborative agreements may be recorded as deferred revenue, in which case they are generally recognized over the period of our performance obligations with the third-party collaborator pursuant to the applicable agreement. The period of performance obligations may also be revised on a prospective basis. As of September 30, 2022, we had $812,000 of deferred revenue which will be recognized in future periods and may cause our reported revenues to be greater than cash flows from our ongoing revenue-generating activities. Assumptions related to revenue recognition of deferred revenue are reviewed in each accounting period and changes are recorded in the current period. In certain circumstances, changes in assumptions related to the timing and amount of work required to complete a performance obligation tied to deferred revenue can result in negative revenue for an accounting period or the accelerated recognition of non-cash revenue.

Our business strategy includes relying on third parties to support development, clinical testing, manufacturing and commercialization of our products and product candidates.

Our current business strategy includes reliance on third-party CROs, consultants, service providers and suppliers to provide critical services to support development, clinical testing, and manufacturing of our products and product candidates, including, but not

limited to larsucosterol and others. For example, we currently depend on third-party vendors to manage and monitor most of our clinical trials. We rely on third parties to manufacture or perform manufacturing steps relating to our products, product candidates and components. We anticipate that we will continue to rely on these and other third-party contractors to support development, clinical testing, and manufacturing of our products and product candidates. Third parties may not execute their responsibilities and tasks competently in compliance with their contractual obligations to us, applicable laws and regulations or in a timely or cost-effective fashion. Failure of these contractors to provide the required services in a competent or timely manner or on reasonable commercial terms could materially delay the development and approval of our product candidates or commercialization of our products, increase our expenses and materially harm our business, financial condition, results of operations and access to capital.

Failure to comply with governmental regulations could materially harm our business

Developing, manufacturing, marketing or promoting a drug is subject to very strict regulations and controls. Furthermore, clearance or approval may entail ongoing requirements for post-marketing studies or surveillance. The manufacture and marketing of drugs are subject to continuing FDA and foreign regulatory review and requirements that we update our regulatory filings. Later discovery of previously unknown problems with a product, manufacturer or facility, or our failure to update regulatory files, may result in restrictions, including withdrawal of the product from the market. Any of the following or other similar events, if they were to occur, could delay or preclude us from further developing, marketing or realizing full commercial value of our products or product candidates, which in turn would materially harm our business, financial condition and results of operations:

- failure to obtain or maintain requisite governmental approvals;
- failure to meet good manufacturing practice ("GMP"), good laboratory practice and/or other governmental requirements for drug development;
- failure to obtain approvals for commercially valuable intended uses of our products and product candidates; or
- FDA required product withdrawals, clinical holds or warnings arising from identification of serious adverse side effects in our products and product candidates.

Manufacturers of drugs must comply with the applicable FDA GMP regulations, which include production design controls, testing, quality control and quality assurance requirements as well as the corresponding maintenance of records and documentation. Compliance with current GMP regulations is difficult and costly. Manufacturing facilities are subject to ongoing periodic inspection by the FDA and corresponding state and in some cases, foreign agencies, including unannounced inspections, and must be licensed before they can be used for the commercial manufacture of our products and product candidates. We and/or our present or future suppliers and distributors may be unable to comply with the applicable GMP regulations and other FDA and/or foreign regulatory requirements. If we, our third-party collaborators or our respective suppliers do not achieve compliance for our products or product candidates we or they manufacture, the FDA or foreign equivalents may refuse or withdraw marketing clearance or approvals, put our or our partner's clinical trial on hold, withdraw or reject an investigational NDA or require product recall, which may cause interruptions or delays in the development, manufacture and sale of our products and product candidates.

We have a history of operating losses, expect to continue to have losses and may never achieve or maintain profitability and we may not successfully manage our company through varying business cycles

We have incurred significant operating losses since our inception in 1998 and, as of September 30, 2022, had an accumulated deficit of approximately $550.9 million. We expect to continue to incur significant operating losses over the next several years as we continue to incur significant costs for research and development, clinical trials, manufacturing, sales, and general and administrative functions. Our ability to achieve profitability depends upon our ability, alone or with others, to successfully complete the development of our proposed product candidates, obtain the required regulatory clearances, manufacture and market our proposed product candidates and successfully commercialize our approved products. Development of pharmaceutical product candidates is costly and requires significant investment. In addition, we may choose to license from third parties either rights to particular drugs or other appropriate technology and/or intellectual property rights for use in our products and product candidates. The license fees as well as the operating costs of using or developing these technologies or rights would increase the costs of our products and product candidates as well as our operating costs generally.

Our current revenues are from milestones and royalties from Innocoll related to POSIMIR, the ALZET product line, from certain excipient sales, from earn-out payments from Indivior related to sales of PERSERIS, from royalty payments from Orient Pharma related to sales of Methydur in Taiwan, and from payments under collaborative research and development agreements with third parties. We expect our revenues to decrease in the near future, and we do not expect that collaborative research and development revenues will exceed our operating expenses in the near future. We do not anticipate meaningful revenues to derive from the commercialization and marketing of our products and product candidates in the near future, do not expect to receive additional milestone payments in the near term or meaningful royalties from POSIMIR until the product achieves meaningful sales (if ever) and therefore do not expect to generate sufficient revenues to cover expenses or achieve profitability in the near future.

Our success will depend on properly sizing our Company through growth and contraction cycles caused in part by changing business conditions, which places a significant strain on our management and on our administrative, operational and financial resources. For example, in connection with the COVID-19 pandemic, we required most of our personnel, including all of our administrative employees, to work remotely, restricted on-site staff to only those personnel who must perform activities that must be

completed on-site, implemented social distancing on-site, and closed certain of our offices temporarily. Our increased reliance on personnel working from home may negatively impact productivity, or disrupt, delay, or otherwise adversely impact our business. In addition, this could increase our cyber security risk, create data accessibility concerns, and make us more susceptible to communication disruptions, any of which could adversely impact our business operations or delay necessary interactions with the FDA, manufacturing sites, research or clinical trial sites. To manage through such cycles, we may expand or contract our facilities, our operational, financial and management systems and our personnel. If we are unable to manage growth and contractions effectively, our business would be harmed.

Changes in tax law could adversely affect our business and financial condition

The rules dealing with U.S. federal, state, and local income taxation are constantly under review by persons involved in the legislative process and by the IRS and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. For example, on March 11, 2021, President Biden signed into law the "American Rescue Plan Act", which included extenders to the refundable employee retention credit under the Coronavirus Aid, Relief, and Economic Security (CARES) Act and limitations to executive compensation effective for tax years beginning after 2026. Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations.

We may develop our own sales force and commercial group to market future products but we have limited sales and marketing experience and may not be able to do so effectively

We have a small sales and marketing group focused on our ALZET product line. We may choose to develop our own sales force and commercial group to market larsucosterol, if approved, or other products that we may develop in the future. Developing a sales force and commercial group would require substantial expenditures and the hiring of qualified personnel. We have limited sales and marketing experience, and may not be able to effectively recruit, train or retain sales and marketing personnel. If we are not able to put in place an appropriate sales force and commercial group for our products in development and provide that commercial team with sufficient financial and other resources, we may not be able to effectively launch or commercialize these or any other products. We may not be able to effectively sell our products and product candidates, if approved, and our failure to do so could limit or materially harm our business.

We and our third-party collaborators may not sell our product candidates effectively

We and our third-party collaborators (including Innocoll, Indivior and Orient Pharma) compete with many other companies that currently have extensive and well-funded marketing and sales operations. Our marketing and sales efforts and those of our third-party collaborators may be unable to compete successfully against these other companies. We and our third-party collaborators, where applicable, may be unable to establish a sufficient sales and marketing organization on a timely basis, if at all. We and our third-party collaborators, where applicable, may be unable to engage qualified distributors. Even if engaged, these collaborators and distributors may:

- fail to adequately market our products or product candidates;
- fail to satisfy financial or contractual obligations to us;
- cease operations, terminate our collaboration or re-allocate resources away from our products or product candidates with little or no notice to us;
- offer, design, manufacture or promote competing product lines;
- fail to maintain adequate inventory and thereby restrict use of our products or product candidates; or
- build up inventory in excess of demand thereby limiting future purchases of our products of product candidates resulting in significant quarter-to-quarter variability in our sales.

The failure of us or our third-party collaborators to effectively develop, gain regulatory approval for, sell, manufacture and market our products and product candidates will hurt our business, prospects, financial results and may impact our access to capital.

Write-offs related to impairment of goodwill, long-lived assets, inventories and other non-cash charges may adversely impact profitability and cause cash flows to differ from reported revenues

We may incur significant non-cash charges related to impairment write-downs of our long-lived assets, including goodwill. We are required to perform periodic impairment reviews of our goodwill at least annually. The carrying value of goodwill on our balance sheet was $6.2 million at September 30, 2022. To the extent these reviews conclude that the expected future cash flows generated from our business activities are not sufficient to recover the cost of our long-lived assets, we will be required to measure and record an impairment charge to write-down these assets to their realizable values. We completed our last review during the fourth quarter of 2021 and determined that goodwill was not impaired as of December 31, 2021. However, there can be no assurance that upon completion of subsequent reviews a material impairment charge will not be recorded. If future periodic reviews determine that our assets are impaired and a write-down is required, it will adversely impact or delay our profitability.

Inventories, in part, include certain excipients that are sold to customers and included in products and product candidates in development. These inventories are capitalized based on management's judgment of probable sale prior to their expiration date which in turn is primarily based on management's internal estimates. The valuation of inventory requires us to estimate the value of inventory that may become expired prior to use. We may be required to expense previously capitalized inventory costs upon a change in our judgment, due to, among other potential factors, a denial or delay of approval of a product by the necessary regulatory bodies, changes in product development timelines, or other information that suggests that the inventory will not be saleable.

Global credit and financial market conditions could negatively impact the value of our investments

Our cash and cash equivalents are maintained in highly liquid investments with remaining maturities of 90 days or less at the time of purchase. Our short-term investments consist primarily of readily marketable debt securities with original maturities of greater than 90 days from the date of purchase but remaining maturities of less than one year from the balance sheet date. Our long-term investments consist primarily of readily marketable debt securities with maturities of one year or beyond from the balance sheet date. While, as of the date of this filing, we are not aware of any downgrades, material losses, or other significant deterioration in the fair value of our cash equivalents, short-term investments or long-term investments since September 30, 2022, no assurance can be given that deterioration in conditions of the global credit and financial markets would not negatively impact our current portfolio of cash equivalents, short-term investments or long-term investments or our ability to meet our financing objectives.

We depend upon key personnel who may terminate their employment with us at any time, and we may not be able to attract and retain sufficient qualified personnel on a timely basis, if at all

Our success will depend to a significant degree upon the continued services of key management, technical and scientific personnel. In addition, our success will depend on our ability to attract and retain other highly skilled personnel, particularly as we develop and expand our Epigenetic Regulator Program. Competition for qualified personnel is intense, and the process of hiring and integrating such qualified personnel is often lengthy. The market for qualified personnel in the San Francisco Bay Area is very competitive and we may be unable to recruit such personnel on a timely basis, if at all. Our management and other employees may voluntarily terminate their employment with us at any time. Further, in 2021 and into 2022, the labor market in the U.S. experienced a significant increase in workers leaving their positions (often referred to as the "Great Resignation"), which made the market to replace these individuals competitive and resulted in significant wage inflation in response to labor shortages. During the Great Resignation we faced and may continue to face increased challenges of employee attraction and retention. The loss of the services of key personnel, or the inability to attract and retain additional qualified personnel, could result in delays to product development or approval, loss of sales and diversion of management resources as well as difficulties or inability to raise sufficient capital to fund the Company's operations.

Cyber-attacks or other failures in telecommunications or information technology systems could result in information theft, data corruption and significant disruption of our business operations

We utilize information technology, systems and networks to process, transmit and store electronic information in connection with our business activities. As use of digital technologies has increased, cyber incidents, including deliberate attacks and attempts to gain unauthorized access to computer systems and networks, have increased in frequency and sophistication. These threats pose a risk to the security of our systems and networks and the confidentiality, availability and integrity of our data, and may cause a disruption in our operations, harm our reputation, cause us to pay to retrieve our data if it becomes infected or otherwise subject to ransomware, and increase our stock trading risk. There can be no assurance that we will be successful in preventing cyber-attacks or successfully mitigating their effects. Similarly, there can be no assurance that our third-party collaborators, distributors and other contractors and consultants will be successful in protecting our clinical and other data that is stored on their systems. Any cyber-attack or destruction or loss of data could have a material adverse effect on our business and prospects. In addition, we may suffer reputational harm or face litigation or adverse regulatory action as a result of cyber-attacks or other data security breaches and may incur significant additional expense to implement further data protection measures.

Our corporate headquarters, certain manufacturing facilities and personnel are located in a seismically active area near wildfire zones

Our corporate headquarters, certain manufacturing facilities and personnel are located in a geographical area that is known to be seismically active and prone to earthquakes, as well as wildfires and related power outages or power shortages. Should such a natural disaster or power outage or power shortage occur, our ability to conduct our business could be severely restricted, and our business and assets, including the results of our research, development and manufacturing efforts, could be harmed or destroyed.

Our business involves environmental risks and risks related to handling regulated substances

In connection with our research and development activities and our manufacture of materials, products and product candidates, we are subject to federal, state and local laws, rules, regulations and policies governing the use, generation, manufacture, storage, air emission, effluent discharge, handling and disposal of certain materials, biological specimens and wastes. Although we believe that we have complied with the applicable laws, regulations and policies in all material respects and have not been required to correct any material noncompliance, we may be required to incur significant costs to comply with environmental and health and safety regulations in the future. Our research and development involves the use, generation and disposal of hazardous materials, including but not limited to certain hazardous chemicals, solvents, agents and biohazardous materials. Although we believe that our safety procedures for storing, handling and disposing of such materials comply with the standards prescribed by state and federal regulations, we cannot completely eliminate the risk of accidental contamination or injury from these materials. We currently contract with third parties to dispose of these substances generated by us, and we rely on these third parties to properly dispose of these substances in compliance with applicable laws and regulations. If these third parties do not properly dispose of these substances in compliance with applicable laws and regulations, we may be subject to legal action by governmental agencies or private parties for improper disposal of these substances. The costs of defending such actions and the potential liability resulting from such actions are often very large. In the event we are subject to such legal action or we otherwise fail to comply with applicable laws and regulations governing the use, generation and disposal of hazardous materials and chemicals, we could be held liable for any damages that result, and any such liability could exceed our resources.

As a non-accelerated filer, we are not required to comply with the auditor attestation requirements of the Sarbanes-Oxley Act and, consequently, some investors may find our common stock less attractive

We are a non-accelerated filer as defined by Rule 12b-2 of the Exchange Act, and as such, are not required to provide an auditor attestation of management's assessment of internal control over financial reporting, which is generally required for SEC reporting companies under Section 404(b) of the Sarbanes-Oxley Act. Therefore, our internal controls over financial reporting will not receive the level of review provided by the process relating to the auditor attestation included in annual reports of issuers that are subject to the auditor attestation requirements. Because we are not required to have our auditors provide an attestation of our management's assessment of internal control over financial reporting, a material weakness in internal control may remain undetected for a longer period. In addition, if investors may find our common stock less attractive because we are not required to comply with the auditor attestation requirements. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and the trading price for our common stock as well as our ability to raise capital may be negatively affected.

Risks Related to Our Intellectual Property

If we are unable to protect, maintain or enforce our intellectual property rights or secure rights to third-party intellectual property, we may lose valuable assets, lose market share or incur costly litigation or our third-party collaborators may choose to terminate their agreements with us

Our ability to commercially exploit our products will depend significantly on our ability to obtain and maintain patents, maintain trade secret protection and operate without infringing the proprietary rights of others.

As of November 1, 2022, we owned or exclusively in-licensed over 25 unexpired issued U.S. patents and over 115 unexpired issued foreign patents (which include granted European patent rights that have been validated in various EU member states). In addition, we have over 20 pending U.S. patent applications and over 175 foreign applications pending in Europe, Australia, Japan, Canada and other countries.

There can be no assurance that the pending patent applications will be granted. Further, there can be no assurance that VCU will not attempt to terminate their license to us, which termination could result in the loss of our rights to certain of these patent families.

The patent positions of pharmaceutical companies, including ours, are uncertain and involve complex legal and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued. Consequently, our patent applications or those that are licensed to us may not issue into patents, and any issued patents may not provide protection against competitive technologies or may be held invalid if challenged. Our competitors may also independently develop products similar to ours or design around or otherwise circumvent patents issued to us or licensed by us. In addition, the laws of some foreign countries may not protect our proprietary rights to the same extent as U.S. law, if at all.

We also rely upon trade secrets, technical know-how and continuing technological innovation to develop and maintain our competitive position. We require our employees, consultants, advisors and collaborators to execute confidentiality and

assignment-of-inventions agreements with us. These agreements typically provide that all materials and confidential information developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances, and that all inventions arising out of the individual's relationship with us will be our exclusive property. These agreements may be breached, and in some instances, we may not have an appropriate remedy available for breach of the agreements. Furthermore, our competitors may independently develop substantially equivalent proprietary information and techniques, reverse engineer our information and techniques, or otherwise gain access to our proprietary technology.

We may be unable to meaningfully protect our rights in trade secrets, technical know-how and other non-patented technology. We may have to resort to litigation or arbitration to protect our intellectual property rights, or to determine their scope, validity or enforceability. In addition, interference, derivation, post-grant oppositions, and similar proceedings may be necessary to determine rights to inventions in our patents and patent applications. Enforcing or defending our proprietary rights is expensive, could cause diversion of our resources and may be unsuccessful. Any failure to enforce or protect our rights could cause us to lose the ability to exclude others from using our technology to develop or sell competing products. In addition, in some circumstances our collaborators have the first right to enforce our patents against third party infringers, and such collaborators may not enforce such claims adequately or successfully or in the manner that we would do ourselves.

Our collaboration agreements may depend on our intellectual property

We are party to collaborative agreements with Innocoll and Orient Pharma, among others. Our third-party collaborators have entered into these agreements based on the exclusivity that our intellectual property rights confer on the products being developed. The loss or diminution of our intellectual property rights could result in a decision by our third-party collaborators to terminate their agreements with us. In addition, these agreements are generally complex and contain provisions that could give rise to legal disputes, including potential disputes concerning ownership of intellectual property and data under collaborations. Such disputes can lead to lengthy, expensive litigation or arbitration requiring us to devote management time and resources to such disputes which we would otherwise spend on our business.

We may be sued by third parties claiming that our products or product candidates infringe on their intellectual property rights, particularly because there is substantial uncertainty about the validity and breadth of biopharmaceutical patents

We or our collaborators may be exposed to future litigation by third parties based on claims that our products, product candidates or activities infringe the intellectual property rights of others or that we or our collaborators have misappropriated the trade secrets of others. This risk is exacerbated by the fact that the validity and breadth of claims covered in medical technology, pharmaceutical and biotechnology patents and the breadth and scope of trade secret protection involve complex legal and factual questions for which important legal principles are unresolved. Any litigation or claims against us or our collaborators, whether or not valid, could result in substantial costs, could place a significant strain on our financial resources and could harm our reputation and business prospects. We also may not have sufficient funds to litigate, particularly against parties with substantially greater resources. In addition, pursuant to our collaborative agreements, we have provided our collaborators with the right, under specified circumstances, to defend against any claims of infringement of the third-party intellectual property rights, and such collaborators may not defend against such claims adequately or successfully or in the manner that we would do ourselves. Intellectual property litigation or claims could force us or our collaborators to do one or more of the following, any of which could harm our business or financial results:

- cease selling, incorporating or using any of our products or product candidates that incorporate the challenged intellectual property;
- obtain a license from the holder of the infringed intellectual property right, which license may be costly or may not be available on reasonable terms, if at all; or
- redesign our products or product candidates, which would be costly and time-consuming and may not be successful.

Risks Related To Our Industry

The markets for our pharmaceutical products, product candidates and for our ALZET product line are rapidly changing and competitive, and new products or technologies developed by others could impair our ability to establish, maintain or grow our business and remain competitive

The pharmaceutical industry is subject to rapid and substantial technological change. Developments by others may render our products, product candidates under development or technologies noncompetitive or obsolete, or we may be unable to keep pace with technological developments or other market factors. Technological competition in the industry from pharmaceutical and biotechnology companies, universities, governmental entities and others diversifying into the field is intense and is expected to increase.

We may face competition from other companies in numerous industries including pharmaceuticals, biotechnology, medical devices and drug delivery. Competition for larsucosterol, if approved, will depend on the specific indication(s) for which larsucosterol is approved. 89Bio, AbbVie, Afimmune, Akaza Bioscience, Akero Therapeutics, Ascletis, AstraZeneca, Axcella Health, Bristol Myers Squibb, Cirius Therapeutics, CytoDyn, Dr. Falk Pharma, Eli Lilly, Enanta, ENYO Pharma, Evive Biotech, Galectin, Galmed,

Genentech, Genfit, Gilead, Hanmi, HighTide Biopharma, Intercept, Inventiva Pharma, Ionis Pharmaceuticals, Isotechnika, Kowa, LifeMax, Lipidio, Lipocine, Madrigal, MediciNova, MedImmune, Mitsubishi Tanabe, NGM Biopharmaceuticals, Nimbus, NorthSea Therapeutics, Novartis, Novo Nordisk, Pfizer, PharmaKing, Poxel, Promethera Biosciences, Seal Rock Therapeutics, Surrozen, Terns Pharmaceutical, Thera Technologies, Viking Therapeutics, and others have development plans for products to treat NAFLD/NASH, AH or other liver diseases.

Competition for our ALZET product line primarily consists of customers choosing to utilize delivery methods for their research projects other than an osmotic pump. We also face competition for our ALZET product line from other companies including low cost foreign competitors.

We are engaged in the development of novel therapeutic technologies. Our resources are limited and we may experience technical challenges inherent in such novel technologies. Competitors have developed or are in the process of developing technologies that are, or in the future may be, the basis for competitive products. Some of these products may have an entirely different approach or means of accomplishing similar therapeutic effects than our products and product candidates. Our competitors may develop products that are safer, more effective or less costly than our products and product candidates and, therefore, present a serious competitive threat to our product candidates and product offerings.

The widespread acceptance of therapies that are alternatives to ours may limit market acceptance of our products and product candidates if commercialized. Post-operative pain is currently being treated by oral medication, transdermal drug delivery systems, such as drug patches, long-acting and short-acting injectable products and implantable drug delivery devices which will be competitive with our products and product candidates. Many of these treatments are widely accepted in the medical community and have a long history of use. The established use of these competitive products may limit the potential for our products and product candidates to receive widespread acceptance if and when commercialized.

Our relationships with physicians, patients and third-party payers are subject to anti-kickback, fraud and abuse, privacy and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings

Healthcare providers, physicians and third-party payers will play a primary role in the recommendation and prescription of POSIMIR and any additional product candidates for which we obtain marketing approval. Our future arrangements with third-party payers and customers may expose us and our partners to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we and our partners may market, sell and distribute our products. As a pharmaceutical company, even though we do not and may not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payers, federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. These regulations include:

- the Federal Healthcare Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid, and which will constrain our marketing practices and the marketing practices of our licensees, educational programs, pricing policies, and relationships with healthcare providers or other entities;

- the federal physician self-referral prohibition, commonly known as the Stark Law, which prohibits physicians from referring Medicare or Medicaid patients to providers of "designated health services" with whom the physician or a member of the physician's immediate family has an ownership interest or compensation arrangement, unless a statutory or regulatory exception applies;

- federal false claims laws that prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other government reimbursement programs that are false or fraudulent, and which may expose entities that provide coding and billing advice to customers to potential criminal and civil penalties, including through civil whistleblower or qui tam actions, and including as a result of claims presented in violation of the Federal Healthcare Anti-Kickback Statute, the Stark Law or other healthcare-related laws, including laws enforced by the FDA;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also created federal criminal laws that prohibit knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services, and which as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- federal physician sunshine requirements under the Affordable Care Act, which requires manufacturers of drugs, devices, biologics and medical supplies to report annually to HHS information related to payments and other transfers of value to

physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members and applicable group purchasing organizations;

•the Federal Food, Drug, and Cosmetic Act, which, among other things, strictly regulates drug product marketing, prohibits manufacturers from marketing drug products for off-label use and regulates the distribution of drug samples;

•state and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non- governmental third-party payers, including private insurers, state laws requiring pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and which may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures, many of which differ from each other in significant ways and often are not preempted by federal laws such as HIPAA, thus complicating compliance efforts; and

•HIPPA and other state and foreign laws governing the privacy and security of health information or other personal information, such as the European Union General Data Protection Regulation, or GDPR, (EU 2016/679), which require limitations regarding access and use of certain personal and health information.

Efforts to ensure that our business arrangements with third parties comply with applicable healthcare and privacy laws and regulations do and will in the future involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare or privacy laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any physicians or other healthcare providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

**Healthcare reform measures could hinder or prevent our product candidates' commercial success*

In the United States and some non-U.S. jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities, affect our ability to profitably sell any product or product candidates for which we obtain marketing and otherwise affect our future revenue and profitability and the future revenue and profitability of our collaborators or potential collaborators.

For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care Education and Reconciliation Act(collectively, the Affordable Care Act), was enacted in the United States to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. The law appears likely to continue the downward pressure on the pricing of medical items and services, especially under the Medicare program, and increased the industry's regulatory burdens and operating costs.

The previous U.S. presidential administration signed several Executive Orders designed to delay or eliminate the implementation of certain provisions of the Affordable Care Act. Concurrently, Congress considered legislation that would repeal or repeal and replace all or part of the Affordable Care Act. While Congress has not passed comprehensive repeal legislation, several bills affecting the implementation of certain taxes under the Affordable Care Act have been signed into law. For example, the Tax Cuts and Jobs Act of 2017 included a provision that repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the Affordable Care Act is unconstitutional in its entirety because the individual mandate was repealed by Congress. Thus, the Affordable Care Act will remain in effect in its current form. It is possible that the Affordable Care Act will be subject to judicial or Congressional challenges in the future. It is unclear how any such challenges and other litigation, and the healthcare reform measures of the current U.S. presidential administration will impact the Affordable Care Act and our business.

Further, prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the Affordable Care Act marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the Affordable Care Act. In addition, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022 (the "IRA") into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in Affordable Care Act marketplaces through plan year 2025 and includes several measures intended to lower the cost of prescription drugs and related healthcare reforms. Specifically, the IRA authorizes and directs the Department of Health and Human Services to set drug price caps

for certain high-cost Medicare Part B and Part D qualified drugs, with the initial list of drugs to be selected by September 1, 2023, and the first year of maximum price applicability to begin in 2026. The IRA further authorizes the Department of Health and Human Services to penalize pharmaceutical manufacturers that increase the price of certain Medicare Part B and Part D drugs faster than the rate of inflation. Finally, the IRA creates significant changes to the Medicare Part D benefit design by capping Part D beneficiaries' annual out-of-pocket spending at $2,000 and eliminates the "donut hole" under the Medicare Part D program, both beginning in 2025, by significantly lowering the beneficiary maximum out-of-pocket cost through a newly established manufacturer discount program. The implementation of government imposed cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates if approved.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. These changes include reductions to Medicare payments to providers of up to 2% per fiscal year that will remain in effect through 2031, except for a temporary suspension from May 1, 2020 through March 31, 2022 and limited reductions to 1% from April 1, 2022 through June 30, 2022 due to the COVID-19 pandemic with the 2% payment reduction having resumed on July 1, 2022. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 3% in the final fiscal year of this sequester. Further, the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. More recently, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several presidential executive orders, Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical products. For example, the marketing, pricing and sale of the Company's products are subject to regulation, investigations and legal actions including under the Medicaid Drug Rebate Program under the Affordable Care Act, which has increased the statutory minimum rebates a manufacturer must pay under the program as well as a new methodology by which rebates are owed for drugs that are inhaled, infused, instilled, implanted or injected. We are also subject to federal and state false claims acts, as well as federal and state antitrust and consumer protection laws. Increased scrutiny of health care industry business practices in recent years by government agencies and state attorneys general in the U.S., and any resulting investigations and prosecutions, carry risk of significant civil and criminal penalties including, but not limited to, debarment from participation in such government healthcare programs.

Individual states in the United States have also become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical product and medical device pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. For example, in October 2017, California passed a law, effective in January 2019, which requires transparency from biopharmaceutical companies regarding price increases for prescription drugs. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and medical devices to purchase and which suppliers will be included in their prescription drug and other healthcare programs.

We expect that the Affordable Care Act, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria, new payment methodologies and in additional downward pressure on the price that we receive for any approved or cleared product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we or our partners are slow or unable to adapt to new requirements or policies, or if we or our partners are not able to maintain regulatory compliance, our products and product candidates may lose any regulatory approval that may have been obtained, which would reduce the likelihood that we may achieve or sustain profitability, or be able to enter attractive collaboration agreements, which would adversely affect our business.

We could be exposed to significant product liability claims which could be time consuming and costly to defend, divert management attention and adversely impact our ability to obtain and maintain insurance coverage

The testing, clinical development, manufacture, marketing and sale of our products and product candidates involve an inherent risk that product liability claims will be asserted against us. Although we are insured against such risks up to an annual aggregate limit in connection with clinical trials and commercial sales of our products and product candidates, our present product liability insurance may be inadequate and may not fully cover the costs of any claim(s) or any ultimate damages we might be required to pay. Product liability claims or other claims related to our products and product candidates, regardless of their outcome, could require us to spend significant time and money in litigation or to pay significant damages. Any successful product liability claim may prevent us from obtaining adequate product liability insurance in the future on commercially desirable or reasonable terms. In addition, product liability coverage may cease to be available in sufficient amounts or at an acceptable cost. An inability to obtain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or inhibit the commercialization of our products or product candidates if and when approved. A product liability claim could also significantly harm our reputation and delay or prevent market acceptance of our products and product candidates.

Market acceptance of our products or product candidates is uncertain, and failure to achieve market acceptance will delay our ability to generate or grow revenues

Our future financial performance will depend upon the successful introduction and customer acceptance of our products or products we have licensed to others, including larsucosterol, if approved, and Innocoll's POSIMIR, Indivior's PERSERIS and Orient Pharma's Methydur. Even if approved for marketing, these products and product candidates may not achieve market acceptance. The degree of market acceptance will depend upon a number of factors, including:

- the degree of unmet need in the market for the approved indication(s);
- the receipt of regulatory clearance of marketing claims for the uses that we are developing;
- the approved product labeling;
- pricing, reimbursement and formulary access;
- the degree of resources applied to promotion and other commercial activities;
- the establishment and demonstration in the medical community of the safety and clinical efficacy of our products and their potential advantages over existing therapies; and
- pricing, access and reimbursement policies of government and third-party payors such as insurance companies, health maintenance organizations, hospital formularies and other health plan administrators.

Physicians, patients, payers or the medical community in general may be unwilling to accept, utilize or recommend any of the products we have developed. If these products do not achieve widespread market acceptance, we will not achieve meaningful revenues.

If users of our products are unable to obtain adequate reimbursement from third-party payers, obtain access to our product(s), or if new restrictive legislation is adopted, market acceptance of our products may be limited and we may not achieve meaningful revenues or profitability

The continuing efforts of government and insurance companies, health maintenance organizations and other payers of healthcare costs to contain or reduce costs of health care may affect our future revenues and profitability, and the future revenues and profitability of our potential customers, suppliers and third-party collaborators and the availability of capital. For example, in certain foreign markets, pricing, access and/or profitability of prescription pharmaceuticals is subject to government control. In the United States, recent federal and state government initiatives have been directed at lowering the total cost of health care, and the U.S. Congress and state legislatures will likely continue to focus on health care reform, the cost of prescription pharmaceuticals and on the reform of the Medicare and Medicaid systems. While we cannot predict whether any such legislative or regulatory proposals will be adopted, the announcement or adoption of such proposals could materially harm our business, financial condition and results of operations.

The successful commercialization of our current and future products will depend in part on the extent to which appropriate reimbursement levels for the cost of our products and related treatment are obtained from governmental authorities, private health insurers and other organizations, such as HMOs. Third-party payers often limit access, payments and/or reimbursement for medical products and services. Also, the trend toward managed health care in the United States and the concurrent growth of organizations such as HMOs, which could control or significantly influence the purchase of health care services and products, as well as legislative proposals to reform health care or reduce government insurance programs, may limit access, reimbursement or payment for our products. The cost containment measures that health care payers and providers are instituting and the effect of any health care reform could materially harm our ability to operate profitably and access capital.

If we or our third-party collaborators are unable to train physicians to use our products and product candidates to treat patients' diseases or medical conditions, we may not achieve market acceptance of our products

Broad use of certain of our products or out-licensed products, such as POSIMIR, will require extensive training of numerous physicians on their proper and safe use. The time required to train physicians could delay introduction of our products and adversely affect market acceptance of our products. We or third parties selling our products may be unable to rapidly train physicians in numbers sufficient to generate adequate demand for our products. Any delay in training would materially delay the demand for our products and harm our business and financial results. In addition, we or our partners may expend significant funds towards such training before any orders are placed for our products, which would increase our expenses and harm our financial results.

Potential new accounting pronouncements and legislative actions are likely to impact our future financial position or results of operations

Future changes in financial accounting standards may cause adverse, unexpected fluctuations in the timing of the recognition of revenues or expenses and may affect our financial position or results of operations. New pronouncements and varying interpretations of pronouncements have occurred with frequency and may occur in the future and we may make changes in our accounting policies in the future. Compliance with changing regulation of corporate governance and public disclosure may result in additional expenses. Changing laws, regulations and standards relating to corporate governance and public disclosure, including the Sarbanes-Oxley Act of 2002, new SEC regulations, state and local laws and regulations, PCAOB pronouncements and Nasdaq rules, are creating uncertainty

for companies such as ours and insurance, accounting and auditing costs are high as a result of this uncertainty and other factors. Compliance with evolving corporate governance and public disclosure standards may result in increased general and administrative expenses and a diversion of management time and attention from value-creating activities to compliance activities.

**We may be adversely affected by the effects of inflation*

Inflation has the potential to adversely affect our liquidity, business, financial condition and results of operations by increasing our overall cost structure. The existence of inflation in the economy has resulted in, and may continue to result in, higher interest rates and capital costs, supply shortages, increased costs of labor, increased manufacturing costs and clinical trial costs, weakening exchange rates and other similar effects. As a result of inflation, we have experienced and may continue to experience cost increases. Although we may take measures to mitigate the impact of this inflation, if these measures are not effective our business, financial condition, results of operations and liquidity could be materially adversely affected. Even if such measures are effective, there could be a difference between the timing of when these mitigating actions impact our results of operations and when the cost inflation is incurred.

Risks related to actions on trade by the U.S. and foreign governments could adversely affect the Company's results of operations and financial condition

The U.S. government under the previous administration indicated its intent to adopt a new approach to trade policy and in some cases to renegotiate, or potentially terminate, certain existing bilateral or multilateral trade agreements. It also initiated the imposition of tariffs on certain foreign products. Changes in U.S. trade policy have resulted in, and could continue to result in, one or more U.S. trading partners adopting responsive trade policy making it more difficult or costly for us to export our products to those countries. These measures could also result in increased costs for goods imported into the United States. This in turn could require us to increase prices to our customers which may reduce demand, or, if we are unable to increase prices, result in lowering our margin on products sold.

There is also a concern that the imposition of additional tariffs by the United States could result in the adoption of additional tariffs by other countries. A potential resulting trade war could have a significant adverse effect on world trade and the world economy. We cannot predict future trade policy or the terms of any renegotiated trade agreements and their impact on our business. The adoption and expansion of trade restrictions, the occurrence of a trade war, or other governmental action related to tariffs or trade agreements or policies has the potential to adversely impact demand for our products, our costs, our customers, our suppliers, and the U.S. economy, which in turn could adversely impact our business, financial condition, access to capital and results of operations.

Risks Related To Our Common Stock

**Our stock price has in the past and currently does not meet the minimum bid price for continued listing on Nasdaq. Our ability to continue operations or to publicly or privately sell equity securities and the liquidity of our common stock could be adversely affected if we are delisted from Nasdaq*

In several instances in the past and on February 9, 2022, we received written notifications from Nasdaq informing us that because the closing bid price of our common stock was below $1.00 for 30 consecutive trading days (the "Minimum Closing Bid Price Requirement"), our shares no longer complied with the Minimum Closing Bid Price Requirement for continued listing on Nasdaq under Nasdaq Marketplace Rules. While we have regained compliance within the applicable time periods in the past, we can provide no assurance that we will be able to once again regain the Minimum Closing Bid Price requirement for continued listing on the Nasdaq Capital Market under Nasdaq Marketplace Rule 5550(a)(2). If we do not regain compliance by January 23, 2023, Nasdaq will notify us that our securities will be subject to delisting. One strategy to regain compliance in such circumstances would be to implement a reverse stock split. We could appeal Nasdaq's determination to delist its securities to a Hearings Panel. During any appeal process, shares of our common stock would continue to trade on the Nasdaq Capital Market.

On August 9, 2022, we received approval from the Listing Qualifications Department of Nasdaq for an additional 180-day grace period, or until February 6, 2023, to regain compliance with the Minimum Bid Price Requirement. To regain compliance with the Minimum Bid Price Requirement and to qualify for continued listing on the Nasdaq Capital Market, the minimum bid price per share of our common stock must be at least $1.00 for at least ten consecutive business days during the additional 180-day grace period. If we do not regain compliance during this additional grace period, our common stock will be subject to delisting by Nasdaq. As part of our request for an additional 180-day grace period, we notified Nasdaq that (i) we met the continued listing standard for market value of publicly-held shares and all other continued listing standards for the Nasdaq Capital Market, other than the Minimum Bid Price Requirement, and (ii) if the price of our common stock does not recover sufficiently during the additional grace period, we anticipated implementing and completing a reverse stock split by no later than January 23, 2023, if necessary.

Delisting from Nasdaq would constitute an event of default under our loan facility with Oxford, entitling Oxford to accelerate our obligations under such facility, among other actions. Under such circumstances, we could be required to renegotiate the repayment terms of our loan facility, on terms which would not be as favorable to the Company as our current terms, or we could be required to take other actions, such as discontinuing some or all of our operations, selling assets, or other action. Delisting could also adversely affect our ability to raise additional capital through the public or private sale of equity securities, would significantly affect the ability of investors to trade our securities and would negatively affect the value and liquidity of our common stock. Delisting could also have

other negative results, including the potential loss of confidence by employees, the loss of institutional investor interest and fewer business development opportunities. Further, delisting from the Nasdaq Capital Market or any Nasdaq market could make trading our common stock more difficult for investors, potentially leading to declines in our share price and liquidity. In addition, without a Nasdaq market listing, stockholders may have a difficult time getting a quote for the sale or purchase of our common stock, the sale or purchase of our common stock would likely be made more difficult and the trading volume and liquidity of our common stock could decline. Delisting from Nasdaq could also result in negative publicity and could also make it more difficult for us to raise additional capital. The absence of such a listing may adversely affect the acceptance of our common stock as currency or the value accorded by other parties. Further, if we are delisted, we would also incur additional costs under state blue sky laws in connection with any sales of our securities. These requirements could severely limit the market liquidity of our common stock and the ability of our stockholders to sell our common stock in the secondary market. If our common stock is delisted by Nasdaq, our common stock may be eligible to trade on an over-the-counter quotation system, such as the OTCQB market, where an investor may find it more difficult to sell our common stock or obtain accurate quotations as to the market value of our common stock. We cannot assure you that our common stock, if delisted from Nasdaq, will be listed on another national securities exchange or quoted on an over-the counter quotation system. If our common stock is delisted, it may come within the definition of "penny stock" as defined in the Exchange Act, and would be covered by Rule 15g-9 of the Exchange Act. Rule 15g-9 imposes additional sales practice requirements on broker-dealers who sell securities to persons other than established customers and accredited investors. For transactions covered by Rule 15g-9, the broker-dealer must make a special suitability determination for the purchaser and receive the purchaser's written agreement to the transaction prior to the sale. Consequently, Rule 15g-9, if it were to become applicable, would affect the ability or willingness of broker-dealers to sell our securities, and accordingly would affect the ability of stockholders to sell their securities in the public market. These additional procedures could also limit our ability to raise additional capital in the future.

**Effecting a reverse stock split, if determined necessary by our board of directors in its discretion, may not achieve one or more of our objectives.*

There can be no assurance that the market price per share of our common stock after a reverse stock split will remain unchanged or increase in proportion to the reduction in the number of shares of our common stock outstanding before the reverse stock split. The market price of our shares may fluctuate and potentially decline after a reverse stock split. Accordingly, the total market capitalization of our common stock after a reverse stock split may be lower than the total market capitalization before the reverse stock split. Moreover, the market price of our common stock following a reverse stock split may not exceed or remain higher than the market price prior to the reverse stock split.

Additionally, there can be no assurance that a reverse stock split will result in a per-share market price that will attract institutional investors or investment funds or that such share price will satisfy investing guidelines of institutional investors or investment funds. As a result, the trading liquidity of our common stock may not necessarily improve. Further, if a reverse stock split is effected and the market price of our common stock declines, the percentage decline may be greater than would occur in the absence of a reverse stock split.

We have scheduled a special meeting of our stockholders on November 22, 2022, for stockholders to approve a reverse stock split of our common stock of a ratio of not less than 1-for-10 and not greater than 1-for-20. The approval of a reverse stock split will provide us with another means to regain compliance with the Minimum Closing Bid Price Requirement. There are no certainties that we will receive stockholder approval for the reverse stock split. If approved by our stockholders, our board of directors may determine in its discretion to effect a reverse stock split.

Our operating history makes evaluating our stock difficult

Our quarterly and annual results of operations have historically fluctuated and we expect will continue to fluctuate for the foreseeable future. We believe that period-to-period comparisons of our operating results should not be relied upon as predictive of future performance. Our prospects must be considered in light of the risks, expenses and difficulties encountered by companies with a limited number of approved pharmaceutical products, particularly companies in new and rapidly evolving markets such as pharmaceuticals and biotechnology. To address these risks, we must, among other things, obtain regulatory approval for and commercialize our product candidates, which may not occur. We may not be successful in addressing these risks and difficulties. We expect to require additional funds to complete the development of larsucosterol or our other product candidates, and to fund operating losses to be incurred in the next several years.

Investors may experience substantial dilution of their investment

In order to raise capital and for other purposes, we may in the future offer and issue additional shares of our common stock or other securities convertible into or exchangeable for our common stock, and the price per share at which we sell additional shares of our common stock or other securities convertible into or exchangeable for our common stock in future transactions may be higher or lower than the price per share at which investors in our common stock bought their shares. In July 2021, we filed the 2021 Registration Statement to sell up to $250 million of securities from time to time in one or more public offerings, including up to $75.0 million of shares of common stock through the 2021 Sales Agreement. When the 2021 Registration Statement was declared effective in August 2021, the 2021 Sales Agreement replaced the 2015 Sales Agreement with Cantor Fitzgerald. Any sales in the public market of our common stock, under our 2021 Sales Agreement, in offerings under our shelf registration statement or otherwise, could adversely affect prevailing market prices for our common stock. Through several financings between 2019 and November 1, 2022, and through our 2015 Sales Agreement, 2018 Sales Agreement and 2021 Sales Agreement with Cantor Fitzgerald during this period, we have raised an aggregate of $79.5 million. As of November 1, 2022, we had up to $250.0 million of our securities available for sale under the 2021 Registration Statement, of which $75.0 million of our common stock are available pursuant to the 2021 Sales Agreement.

In addition, as of September 30, 2022, 28,494,974 shares of our common stock were issuable upon exercise of stock options outstanding under our stock option plans at a weighted average exercise price of $1.30 per share, 21,646,463 additional shares of common stock were reserved for potential future issuance under our stock option plan, and an aggregate of 313,408 shares of common stock were reserved for potential future issuance under our 2000 Employee Stock Purchase Plan. Further, our stockholders at our 2022 Annual Meeting of Stockholders held on June 15, 2022 approved an amendment to our Certificate of Incorporation to increase the number of authorized shares of common stock from 350,000,000 to 600,000,000 shares and approved an amendment to our 2000 Stock Plan to increase the number of shares of our common stock authorized for issuance thereunder by 18,000,000 shares. Although the number of authorized shares of the Company's common stock could be reduced from 600,000,000 to 150,000,000 in connection with our reverse stock split if it is approved by our stockholders and implemented by our board of directors, we will still have the ability to issue significantly more shares and options in the future, which would result in substantial dilution to our stockholders, including investors in this offering.

Our ability to use net operating losses and certain other tax attributes is uncertain and may be limited

Our ability to use our federal and state net operating losses to offset potential future taxable income and related income taxes that would otherwise be due is dependent upon our generation of future taxable income before the expiration dates of the net operating losses, and we cannot predict with certainty when, or whether, we will generate sufficient taxable income to use any or all of our net operating losses. In addition, utilization of net operating losses to offset potential future taxable income and related income taxes that would otherwise be due is subject to annual limitations under the "ownership change" provisions of Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the "Internal Revenue Code") and similar state provisions, which may result in the expiration of net operating losses before future utilization. In general, under the Code, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating losses and other pre-change tax attributes (such as research and development credit carryforwards) to offset its post-change taxable income or taxes may be limited. Our equity offerings and other changes in our stock ownership, some of which are outside of our control, may have resulted or could in the future result in an ownership change. If an ownership change limitation were to apply, utilization of our net operating losses and tax credit carryforwards could be limited in future periods and a portion of the carryforwards could expire before being available to reduce future income tax liabilities.

**Because the Company is a "smaller reporting company," we may take advantage of certain scaled disclosures available to us, resulting in holders of our securities receiving less Company information than they would receive from a public company that is not a smaller reporting company*

We are a "smaller reporting company" as defined in the Exchange Act. As a smaller reporting company, we may take advantage of certain of the scaled disclosures available to smaller reporting companies and will be able to take advantage of these scaled disclosures for so long as (i) our voting and non-voting common stock held by non-affiliates is less than $250 million measured on the last business day of our second fiscal quarter, or (ii) our annual revenue is less than $100 million during the most recently completed fiscal year and our voting and non-voting common stock held by non-affiliates is less than $700 million measured on the last business day of our second fiscal quarter. To the extent we take advantage of any reduced disclosure obligations, it may make it harder for investors to analyze the Company's results of operations and financial prospectus in comparison with other public companies.

The price of our common stock may be volatile

The stock markets in general, and the markets for pharmaceutical stocks in particular, have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. These broad market fluctuations may adversely affect the trading price of our common stock.

Price declines in our common stock could result from general market and economic conditions and a variety of other factors, including:

•adverse results (including adverse events or failure to demonstrate safety or efficacy) or delays in our clinical and non-clinical trials of larsucosterol or other product candidates;

•announcements of FDA non-approval of our product candidates, approvals with narrow indications, commercially limiting labels, clinical holds or delays in the FDA or other foreign regulatory agency review process;

•adverse actions taken by regulatory agencies or law enforcement agencies with respect to our products and product candidates, clinical trials, manufacturing processes, accounting practices or sales and marketing activities, or those of our third-party collaborators;

•announcements of technological innovations, patents, product approvals, sales performance or new products by our competitors;

•failure of third-party collaborators to continue development or successful commercialization of the respective products and product candidates they are developing or commercializing;

•failure by our commercial licensee (Innocoll) to successfully manufacture and store adequate supplies, and/or to achieve sales expectations and successfully commercialize POSIMIR;

•regulatory, judicial and patent developments in the United States and foreign countries;

•any lawsuit or arbitration involving us or our products and product candidates including intellectual property infringement or product liability suits;

•announcements concerning our competitors, or the biotechnology or pharmaceutical industries in general;

•developments concerning our strategic alliances or acquisitions or termination of such alliances;

•actual or anticipated variations in our operating results;

•changes in recommendations by securities analysts, misstatements or mischaracterizations in analyst reports or dropping or lack of analyst coverage;

•negative press coverage or online or social media misinformation about the Company or its partners or their respective products or personnel;

•deviations in our operating results from the estimates of analysts;

•sales of our common stock by our executive officers or directors or sales of substantial amounts of common stock by us or others;

•potential failure to meet continuing listing standards from The Nasdaq Capital Market;

•loss or disruption of facilities due to natural disasters;

•acceleration of our debt obligations due to a determination by our lender that a material adverse change has occurred;

•changes in accounting principles; or

•loss of any of our key scientific or management personnel.

The market price of our common stock may fluctuate significantly in response to factors which are beyond our control. The stock market in general has periodically experienced extreme price and volume fluctuations. For example, the outbreak of the COVID-19 coronavirus and the impact of new variants of the virus, pronouncements by the Federal Reserve, inflation, outbreaks of war such as between Russia and Ukraine, oil price volatility and other factors have caused broad stock market and industry fluctuations. In addition, the market prices of securities of technology and pharmaceutical companies have also been extremely volatile, and have experienced fluctuations that often have been unrelated or disproportionate to the operating performance of these companies. These broad market fluctuations could result in extreme fluctuations in the price of our common stock, which could cause a decline in the value of our common stock.

In the past, following periods of volatility in the market price of a particular company's securities, litigation has often been brought against that company. If litigation of this type is brought against us, it could be extremely expensive, particularly if we were to lose the lawsuit and have to pay damages, and divert management's attention and our company's resources.

We have broad discretion over the use of our cash and investments, and their investment may not always yield a favorable return

Our management has broad discretion over how our cash and investments are made and used. We may from time to time invest in ways with which our stockholders may not agree and that do not yield favorable returns.

Our certificate of incorporation, our bylaws and Delaware law contain provisions that could discourage another company from acquiring us

Provisions of Delaware law, our certificate of incorporation and bylaws may discourage, delay or prevent a merger or acquisition that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions include:

- authorizing the issuance of "blank check" preferred stock without any need for action by stockholders;
- providing for a classified board of directors with staggered terms;
- requiring supermajority stockholder voting to effect certain amendments to our certificate of incorporation and bylaws;
- eliminating the ability of stockholders to call special meetings of stockholders;
- prohibiting stockholder action by written consent; and
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted on by stockholders at stockholder meetings.

Our bylaws provide that the Court of Chancery of the State of Delaware is the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees

Our bylaws provide that the Court of Chancery of the State of Delaware is the exclusive forum for any derivative action or proceeding brought on behalf of the Company, any action asserting a claim of breach of a fiduciary duty owed by any director, officer or other employee of the Company, any action asserting a claim arising pursuant to any provision of the General Corporation Law of Delaware or our Certificate of Incorporation or bylaws or any action asserting a claim governed by the internal affairs doctrine. The choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees.

Alternatively, if a court were to find the choice of forum provision contained in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition.

Item 6. Exhibits

Exhibit Number	Exhibit Name
10.1*	First Amendment to License Agreement by and between the Company and Innocoll Pharmaceuticals Limited dated September 19, 2022.
31.1*	Certification of Chief Executive Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Exchange Act as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Chief Financial Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Exchange Act as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1**	Certification of Chief Executive Officer pursuant to Rule 13a-14(b) of the Exchange Act and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2**	Certification of Chief Financial Officer pursuant to Rule 13a-14(b) of the Exchange Act and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101	The following financial statements from the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2022, formatted in Inline XBRL: (i) Condensed Balance Sheets, (ii) Condensed Statements of Operations, (iii) Condensed Statements of Comprehensive Income, (iv) Condensed Statements of Changes in Stockholders' Equity, (v) Condensed Statements of Cash Flows and (vi) Notes to Condensed Financial Statements, tagged as blocks of text and including detailed tags.
104	The cover page from the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2022, formatted in Inline XBRL (included as Exhibit 101).

* Filed herewith.
** Furnished, not filed.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

DURECT CORPORATION

By: /S/ JAMES E. BROWN
James E. Brown
Chief Executive Officer

Date: November 3, 2022

By: /S/ TIMOTHY M. PAPP
Timothy M. Papp
Chief Financial Officer
(Principal Accounting Officer)

Date: November 3, 2022